

ETHIOPIAN MEDICINES FORMULARY 2nd ed



ETHIOPIAN MEDICINES FORMULARY

Second Edition

Food, Medicine and Healthcare
Administration and Control Authority of Ethiopia

2013

ETHIOPIAN MEDICINES FORMULARY

**Second Edition
2013**

Addis Ababa, Ethiopia

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PREFACE

An independent and up-to-date medicines information is essential for the safe and effective use of medicines. In the absence of such information resource, promotion of rational use of medicines is at stake, which eventually harm the health of individuals and affect the overall healthcare delivery system.

Recognising this unmet need on medicines information, the Ethiopian Food, Medicine and Healthcare Administration and Control Authority (EFMHACA) has been striving to develop and make accessible medicines information materials including, medicines formularies and standard treatment guidelines, good prescribing and dispensing manuals, leaflets/posters in various issues, bulletins, and others both in print copies and also availing them in its website www.fmhaca.gov.et.

The EMF aims to provide unbiased and up-to-date information on medicines. And it targets all health professionals involved in patient care, training, research and others. Therefore the over all goal of the EMF is to help health professionals base their practice on solid information and knowledge to promote rational use of medicines.

The second edition of the Ethiopian Medicines Formaulary (EMF) is hereby revised based on the latest developments in the fields of medicine and pharmacy. The second edition of the EMF contains all the medicines included in the 6th edition and its supplements of the Ethiopian Medicines List (EML). The EMF contains key information on medicines which are essential for medicines good prescribing, dispensing, administration and use. It tries to address demands of all medicines prescribers, dispensers and others who are involved in handling and use of medicines.

We hope that, this EMF will be of great help in providing useful information to you in promoting the rational use of medicines and provision of quality health services for improved health outcomes. It is of particular importance to those healthcare providers working at health facilities who have little access to adequate and up to date information on medicines.

Although the EMF has expanded in its current volume; it still will be used as digest for rapid reference and it may not always include all the information needed for prescribing and dispensing of medicines and also does not substitute standard treatment guidelines.

Finally, I would like to express my gratitude to all those who have directly or indirectly extended their helping hands in the revision and printing of the EMF. I call upon all health professionals and interested parties to continue their feedback for the regular updating of the formulary by forwarding comments and suggestions to:

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This second edition of Ethiopian Medicines Formulary (EMF) has passed intensive works starting from preparation of the draft document by arranging monographs for each medicine to preparing detailed document. It was commented by a national workshop, by professional associations and by finalizing technical working group emanated from different specialities and finally edited and formatted.

The Ethiopian Medicines Healthcare Administration and Control Authority (EFMHACA) would like to present heart felt thanks all professional associations, national workshop participants and members of finalizing technical working group, and individuals mentioned below for sacrificing their time and use their expertise for providing inputs to the enrichment of this formulary.

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ACRONYMS and ABBREVIATIONS

AAU	Addis Ababa Univeristy
ACE	Angiotensin-converting enzyme
ADR	Adverse drug reaction
AIDS	Acquired immuno deficiency syndrome
APD	Action potential duration
ATP	Adenosine triphosphate
AV	Atrioventricular
BMI	Body mass index
BMT	Bone marrow transplantation
BPH	Benign prostatic hyperplasia
BSA	Body surface area
CAD	Coronary artery disease
CCR5	Chemokine receptor 5
CFC	Chlorofluorocarbon
cGMP	Cyclic guanosine monophosphate
CHD	Coronary heart disease
CHF	Congestive heart failure
CHOP	Cyclophosphamide,Hydroxydaunorubicin (doxorubicin or Adriamycin), Oncovin (Vincristine), Prednisone (Prednisolone).
CIU	Chronic idiopathic urticarial
CKD	Chronic kidney disease
Clcr	Creatinine clearance
CMV	Cytomegalovirus
CML	Chronic myeloid leukemia
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CSF	Cerebrospinal fluid
CTC	Common toxicity criteria
CTCL	Cutaneous T-cell lymphoma
CVD	Cardiovascular disease

CYP	cytochrome P450
D ₂	dopaminergic
D5W	Dextrose 5% in water
DIC	disseminated intravascular coagulation
DME	diabetic macular oedema
DNS	Dextrose in normal saline
DOT	Direct observation of therapy
DVT	deep vein thrombosis
DW	Dextrose in water
EEG	Electro-encephalogram
eGFR	estimated Glomerular Filtration Rate
EMF	Ethiopian medicines formulary
EPTB	Extrapulmonary tuberculosis
FDA	Food and Drug Administration
FDCs	Fixed dose combinations
FH	Familial hypercholesterolemia
FIs	Fusion inhibitors
G6PD	Glucose 6-phosphate dehydrogenase
G6PD	G6PD glucose-6-phosphate dehydrogenase
GABA	Gamma –aminobutyric acid
GAD	Generalized anxiety disorder
GERD	Gastro-oesophageal reflux disease
GFR	Glomerular filtration rate
GI	Gastrointestinal
GIT	Gastrointestinal
GPP	Good dispensing practice
GPP	Good prescribing practice
GU	Gastric ulcer
<i>H.p.</i>	<i>Helicobacter pylori</i>
H ₂	Histamine receptor
HAART	Highly active antiretroviral treatment
HDL	High density lipoproteins

HeFH	Heterozygous familial hypercholesterolemia
HF	Heart failure
HFA	Hydrofluoroalkane
HIV	Human immunodeficiency virus
HMG-CoA	Hydroxy-3-methyl glutaryl co enzyme A
HRT	Hormone replacement therapy
hs-CRP	High-sensitivity C-reactive protein
HTN	Hypertension
5 HT ₃	5-hydroxytryptamine
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
ICD	International classification of diseases
IgE	Immunoglobulin E
IIs	Integrase inhibitors
IM	Intramuscular
IO	Intraosseous
IU	International Units
IUD	Intrauterine device
IV	Intravenous
Kg	Kilogram
LDL	Very low density lipoproteins
LR	
LVH	left ventricular hypertrophy
MAC	<i>M. avium-intracellulare</i> complex
MAOI	Monoamine oxidase inhibitor
MB	Multibacillary leprosy
Mcg, mcg	Microgram
MDI	Metered dose inhaler
MDR TB	Multi-drug resistant tuberculosis
MEOS	Microsomal enzyme oxidizing system
Mg, mg	Milligram
mm Hg	millimeter mercury

MOPP	Mustargen (Chlormethine), Oncovin (Vincristine), Procarbazine, Prednisolone
MRSA	Methicillin-resistant Staphylococcus aureus
MTCT	Mother to child transmission
MU	Million Units
NDRI	Norepinephrine-dopamine reuptake inhibitor
NIDDM	Noninsulin dependent diabetes mellitus (type 2 diabetes mellitus)
NNRTI	Non nucleoside reverse transcriptase inhibitor
NRTIs	Nucleoside reverse transcriptase inhibitors
NS	Normal saline (0.9% NaCl)
NSAID	Non steroidal anti inflammatory drug
OCD	Obsessive-compulsive disorder
ORS	Oral Rehydration Salts
OTC	Over the counter
PAR	Perennial allergic rhinitis
PAS	Para-Amino Salicylic Acid
PB	Paucibacillary leprosy
PBPC	Peripheral blood progenitor cell
PCP	Pneumocystis carinii
PDE5	Phosphodiesterase type 5 inhibitor
PEP	Post Exposure prophylaxis
pH	Concentration of hydrogen ion
PI	Protease inhibitor
PMTCT	Prevention of mother to child transmission
PONV	Postoperative nausea and vomiting
PSVT	Paroxysmal supraventricular tachycardia
PTB	Pulmonary tuberculosis
RBC	Red blood cells
RDA	Recommended dietary allowance
RVO	Retinal vein occlusion
SA	Sinatrial node

SAR	Seasonal allergic rhinitis
SBP	Spontaneous bacterial peritonitis
SC	Subcutaneous
SCN	Severe chronic neutropenia
SLE	Systemic lupus erythematosus
SNRIs	Serotonin noradrenaline re-uptake inhibitors
SSRIs	Selective Serotonin Re-uptake Inhibitors
STD	Sexually transmitted disease
SVT	Supraventricular tachycardia
TC	Total cholesterol
TCAs	Tricyclic Antidepressants
TG	Triglycerides
TIA	Transient ischaemic attack
TURP	transurethral resection of the prostate
ULN	Upper Limit of Normal
URTI	Upper respiratory tract infection
UTI	Urinary tract infections
VEGF	Vascular endothelial growth factor
VF	Ventricular fibrillation
VT	Ventricular tachycardia
VTE	Venous thromboembolism
WPW	Wolff-Parkinson-White

STRUCTURE and HOW to USE THE EMF

Changes from the First Edition

This second edition of Ethiopia Medicines Formulary (EMF) is revised based on the sixth edition of the Ethiopian Medicines List, which incorporated more than 1140 medicines. It incorporated monographs of more than 250 new medicines that have been added to the edition of the List and that do not exist in the first edition of the formulary. The formulary also links with ongoing changes to the program medicines regimens and treatment guidelines such as TB, HIV and malaria. It also incorporated the new combination therapy regimens monographs in addition to the single medicines monographs. There are also deletions of some medicines. The users have to bear in mind that there may also be changes to any of the components of the monographs of the medicines (indications, cautions, contraindications, side effects, dose and administration, etc) incorporated in this formulary in contrast to the first edition based on the product updates. Furthermore, this edition of the EMF contains some additional useful topics at the beginning and appendices that are useful to the readers and for promotion of rational use of medicines.

How the EMF is developed

The EMF is based on the Ethiopian medicine list 6th edition 2010. EMF has tried to bring together essential information; it has brought together current and independent information on medicines and also added additional information and guidance in the appendices. All these are aimed at enabling healthcare professionals to select safe and effective medicines for promoting the rational use medicines and improved health outcomes for individual patients and the community.

Sources of EMF information

In the revision of the second edition of EMF; a number of current and independent information on medicines and diseases have been consulted. It may not be possible to list all which are used

by the different contributors of the formulary; nevertheless we have mentioned only some of those used in this EMF.

Literature and systematic reviews: Research papers and reviews in some medical and pharmaceutical journals relating to drug therapy are consulted.

Consensus guidelines: The information compiled in the EMF is checked against consensus guidelines. Reference

sources: Textbooks and reference sources have provided valuable information for the review of the EMF. These include but not limited to the latest editions of Martindale: The Complete Drug Reference, British National Formulary for adults and children, Goodman & Gilman's The Pharmacological Basis of Therapeutics, Harrison's Principles of Internal Medicine, AHFS drug information, expert guidelines, and others.

How to Use and Search Information in EMF

The EMF has listed all the contributors in the development process in the acknowledgment part. As much as possible abbreviations and acronyms are minimized but when used will be written in full the first time it is entered and abbreviated afterwards in the abbreviations and acronyms part of the EMF. These facilitate reading and understanding in the text of the EMF. It is a useful reference to cross-check.

There are useful guides before the main text of EMF such as medicines prescription, prescribing, dispensing, labeling, counseling, adherence to medicines, monitoring treatment, and antimicrobial prescribing in general practice and for prophylaxis use. The main contents of the EMF presented by body systems or systemic disease categories and divided into 21 chapters. Each chapter is then subdivided into subtopics. Each subsection begins with some notes and then followed by description of the individual medicines. In all medicines entries generic names/International Non-proprietary names of medicines are used throughout the EMF. In this EMF the following information about each medicine are included: Indications: Cautions: Drug interactions: Contraindications: Side effects: Dose and

Administration (adult and child by age or by body weight); and sometimes notes on the dosage and administration are added which are useful to the health care providers and for patients; and finally Storage of the dosage form.

The EMF has essential glossary and Appendices information which have high relevance to the formulary and importance to the readers.

The EMF is also indexed by medicines but left by disease for now which will help to easily pinpoint the page in which the medicine is cited.

Readers are kindly requested to provide their suggestions for the improvement of the future editions of EMF at:

FMHACA, P.o.Box 5681; Fax. 251-115-521392; Addis Ababa;

Free call line: 8482

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Website: <http://www.fmhaca.gov.et>

MEDICINES PRESCRIPTION, PRESCRIBING, DISPENSING, and COUNSELING

Prescription Form

The most important requirement is that the prescription be clear. It should be legible and indicate precisely what should be given. The local language is preferred. It should be legible and not ambiguous. A prescription should contain the following details should be filled on the form:

- Name, address, age body weight of the medicine consumer and Date of the prescription; Diagnosis; Generic name, dosage form and strength and directions for use of the medicines. The pharmaceutical form (for example ‘tablet’, ‘oral solution’, ‘eye ointment’) should also be stated. The strength of the drug should be stated in standard units using abbreviations that are consistent with the Systéme Internationale (SI). ‘Microgram’ and ‘nanogram’ should not, however, be abbreviated. Also, ‘units’ should not be abbreviated. Avoid decimals whenever possible. If unavoidable, a zero should be written in front of the decimal point.
- Fill the diagnosis or ICD code for proper communication with the dispenser and choice of the drug among the available generic options. Readers are kindly requested to read “Medicines Good Prescribing Practices (GPP)” manual 2012 edition.

PRESCRIPTION PAPER

Patient's full Name: _____
 Sex: _____ Age: _____ Weight: _____ Card No. _____
 Region: _____ Town _____ Woreda _____ Kebele _____
 House No. _____ Tel. No: _____ Inpatient Outpatient
 Diagnosis, if not ICD _____

Drug Name, Strength, Dosage Form, Dose, Frequency, Duration, Quantity, How to use & other information	Price (dispensers use only)
Rx	
Total Price	

Prescriber's	Dispenser's
Full name _____	_____
Qualification _____	_____
Registration # _____	_____
Signature _____	_____
Date: _____	_____

See overleaf

Prescription Writing

A prescription is an instruction from a prescriber to a dispenser. The prescriber is not always a doctor but can also be a paramedical worker, such as a medical assistant, a midwife or a nurse. The dispenser is not always a pharmacist, but can be a pharmacy technician, an assistant or a nurse. The following guidelines will help to ensure that prescriptions are correctly interpreted and leave no doubt about the intention of the prescriber. The guidelines are relevant for primary care prescribing; they may, however, be adapted for use in hospitals or other specialist units.

A prescription is a written therapeutic transaction between the prescriber and dispenser. It is a written order by the prescriber to the dispenser on how the drug should be dispensed. It serves as a means of communication among the prescriber, dispenser and medicines consumer pertaining to treatment or prophylaxis. A prescription should be written on a standard prescription blank, in ink and in generics.

Directions for use: Directions specifying the route, dose and frequency should be clear and explicit; use of phrases such as 'take as directed' or 'take as before' should be avoided. For preparations which are to be taken on an 'as required' basis, the minimum dose interval should be stated together with, where relevant, the maximum daily dose. It is good practice to qualify such prescriptions with the purpose of the medication (for example 'every 6 hours as required for pain', 'at night as required to sleep'). It is good practice to explain the directions to the patient; these directions will then be reinforced by the label on the medicinal product and possibly by appropriate counseling by the dispenser. It may be worthwhile giving a written note for complicated regimens although it must be borne in mind that the patient may lose the separate note.

Factors affecting Dose and Response

Success in drug treatment depends not only on the correct choice of drug but on the correct dose regimen. Unfortunately

drug treatment frequently fails because the dose is too small or produces adverse effects because it is too large. However, the use of standard doses in the marketing literature suggest that standard responses are the rule, but in reality there is considerable variation in drug response. As a result many prescribed doses are far too low or too high, leading to treatment failure or toxicity. There are many reasons for this variation which include adherence (see below), drug formulation, body weight and age, variation in absorption, distribution, metabolism and excretion, variation in pharmacodynamics, disease variables, genetic and environmental variables.

Drug Formulation: Poorly formulated drugs may fail to disintegrate or to dissolve. Enteric-coated drugs are particularly problematic, and have been known to pass through the gastrointestinal tract intact. Some drugs like digoxin or phenytoin have a track record of formulation problems, and dissolution profiles and can vary not only from manufacturer to manufacturer but from batch to batch of the same company. The problem is worse if there is a narrow therapeutic to toxic ratio, as changes in absorption can produce sudden changes in drug concentration. For such drugs quality control surveillance should be carried out.

Body Weight and Age: Although the concept of varying the dose with the body weight or age of children has a long tradition, adult doses have been assumed to be the same irrespective of size or shape. Yet adult weights vary two to threefold, while a large fat mass can store large excesses of highly lipid soluble drugs compared to lean patients of the same weight. Age changes can also be important. Adolescents may oxidize some drugs relatively more rapidly than adults, while the elderly may have reduced renal function and eliminate some drugs more slowly.

Physiological and Pharmacokinetic Variables: Drug absorption rates may vary widely between individuals and

within the same individual at different times and in different physiological states. Drugs taken after a meal are delivered to the small intestine much more slowly than in the fasting state, leading to much lower drug concentrations. In the case of drugs like paracetamol with a high rate of metabolism on 'first pass' through the liver, this may render a standard dose completely ineffective. In pregnancy gastric emptying is also delayed, while some drugs may increase or decrease gastric emptying and affect absorption of other drugs.

Drug Distribution: Drug distribution varies widely: fat soluble drugs are stored in adipose tissue, water soluble drugs are distributed chiefly in the extracellular space, acidic drugs bind strongly to plasma albumin and basic drugs to muscle cells. Hence variation in plasma albumin levels, fat content or muscle mass may all contribute to dose variation. With very highly albumin bound drugs like warfarin, a small change of albumin concentration can produce a big change in free drug and a dramatic change in drug effect.

Drug Metabolism and Excretion: Drug metabolic rates are determined both by genetic and environmental factors. Drug acetylation shows genetic polymorphism, whereby individuals fall clearly into either fast or slow acetylator types. Drug oxidation, however, is polygenic, and although a small proportion of the population can be classified as very slow oxidizers of some drugs, for most drugs and most subjects there is a normal distribution of drug metabolizing capacity, and much of the variation is under environmental control. Many drugs are eliminated by the kidneys without being metabolized. Renal disease or toxicity of other drugs on the kidney can therefore slow excretion of some drugs.

Pharmacodynamic Variables: There is significant variation in receptor response to some drugs, especially central nervous system responses, for example pain and sedation. Some of this is genetic, some due to tolerance, some due to interaction with

other drugs and some due to addiction, for example, morphine and alcohol.

Disease Variables: Both liver disease and kidney disease can have major effects on drug response, chiefly by the effect on metabolism and elimination respectively (increasing toxicity), but also by their effect on plasma albumin (increased free drug also increasing toxicity). Heart failure can also affect metabolism of drugs with rapid hepatic clearance (for example lidocaine, propranolol). Respiratory disease and hypothyroidism can both impair drug oxidation.

Environmental Variables: Many drugs and environmental toxins can induce the hepatic microsomal enzyme oxidizing system (MEOS) or cytochrome P450 oxygenases, leading to more rapid metabolism and elimination and ineffective treatment. Environmental pollutants, anaesthetic drugs and other compounds such as pesticides can also induce metabolism. Diet and nutritional status also impact on pharmacokinetics. For example in infantile malnutrition and in malnourished elderly populations drug oxidation rates are decreased, while high protein diets, charcoal cooked foods and certain other foods act as metabolizing enzyme inducers. Chronic alcohol use induces oxidation of other drugs, but in the presence of high circulating alcohol concentrations drug metabolism may be inhibited.

The Effect of Food on Drug Absorption: Food delays gastric emptying and reduces the rate of absorption of many drugs; the total amount of drug absorbed may or may not be reduced. However, some drugs are preferably taken with food, either to increase absorption or to decrease the irritant effect on the stomach.

Drug Interactions: Though some drug interactions could be beneficial most are harmful. Hence it is always important to note the possible drug interactions prior to concomitant drug/food or drink administration. Drug interactions could occur at different levels including: Pharmaceuticals, which are

physicochemical interactions in an infusion or in the same solution; Pharmacokinetics, which may take place at the level of absorption, distribution, biotransformation or excretion; Pharmacodynamics, which could occur directly at receptor level or indirectly where a drug induced disease alters the response to another drug. Drug interactions could be summation (the effect is simple algebraic sum), synergism (the total effect is more than the algebraic sum) potentiation (the effect of one drug increases by the presence of another drug), or antagonism (the effect of the agonist is blocked by the antagonist when given together). Drug interactions are some of the most common causes of adverse reactions. As drug reactions could also occur between a drug and food or a drug and drink. We should always inform our patients the type of food or drink which they have to avoid while taking the drug.

Drug incompatibilities: Drugs should not be added to blood, amino acid solutions or fat emulsions. Some drugs, when added to IV fluids, may be inactivated due to change in pH, precipitate formation or chemical reaction. For example, benzylepenicillin and ampicillin lose potency after 6-8 hours if added to dextrose solutions, due to the acidity of the solutions. Some drugs, such as diazepam and insulin, bind to plastic containers and tubing. Aminoglycosides are incompatible with penicillins and heparin. Hydrocortisone is incompatible with heparin, tetracycline and chloramphenicol.

Medicines use for elderly patients: There is no major alteration in drug absorption in elderly patients. Conditions associated with age may alter the rate of absorption of some drugs. Such conditions include altered nutritional habits, alteration in gastric emptying, which is often slower and the concurrent administration of other drugs. Aged people have reduced lean body mass, reduced body water and an increase in fat as a percentage of body mass. There is a decrease in serum albumin, and the ratio of bound to free drug is significantly changed. There is a decline with age of the liver's ability to

recover from injury. Diseases that affect hepatic function like congestive cardiac failure are more common in the elderly. Severe nutritional deficiencies in the elderly may impair hepatic function. Creatinine clearance declines in the elderly leading to marked prolongation of the half life of drugs. The increased incidence of active pulmonary disease in the elderly could compromise drug elimination through exhalation. There is also a change in the sensitivities of receptors to drugs in aged people. The quality and quantity of life in elderly patients can be improved by intelligent use of drugs. Compliance to the doses is absolutely required in these patients. Unfortunately patient noncompliance in the elderly is common because of forgetfulness, confusion, deliberate skipping of doses and physical disabilities as in the case of tremors which cause errors in measurement by spoon.

Medicines use in renal failure: Many drugs are excreted through the kidneys and impairment of renal function alters the excretion of these drugs and may result in renal as well as nonrenal toxicity unless doses are adjusted on the basis of the degree of renal impairment. For dose adjustment in renal failure it may occasionally be necessary to measure drug levels and adjust doses accordingly. Factors that potentiate renal dysfunction and contribute to the nephrotoxic potential of renally excreted drugs include: intravascular volume depletion either due to external losses or fluid sequestration (as in ascites or edema); concomitant use of two or more nephrotoxic agents e.g. Nonsteroidal anti-inflammatory agents, aminoglycosides, radio contrast agents. In general in the presence of renal impairment to avoid worsening of renal dysfunction: Avoid potentially nephrotoxic drugs and use alternative drugs that are excreted through other routes. If there are no alternative drugs to use, adjust the dose. Dose adjustment may be accomplished in three different ways: Decreasing each individual dose and maintaining the same dose frequency; Maintaining the same individual dose but administering each dose less frequently; and

Modifying both individual doses and the frequency of administration, which is a combination method; Insure that the patient is adequately hydrated; If the patient is on dialysis check if the drug is eliminated by the specific dialysis modality and consider administering a supplemental dose at the end of the dialysis session; and Serially monitor kidney function.

Medicines use in liver disease: The liver is a site for the metabolism and elimination of many drugs but it is only in severe liver disease that changes in drug metabolism occur. Unfortunately, routine determination of liver enzymes and other tests of liver function cannot predict the extent to which the metabolism of a certain drug may be impaired in an individual patient. In general, drug prescription should be kept to a minimum in all patients with severe liver disease. Major problems occur in patients with advanced liver disease who have ascites, jaundice or hepatic encephalopathy. The hypoproteinemia in patients with severe liver disease is associated with reduced protein binding and with increased toxicity when highly protein bound drugs are used. One must exercise caution in the use of some drugs like sedatives, opioids and diuretics which may precipitate hepatic encephalopathy in patients with advanced liver disease. It is always advisable to consult tables in standard textbooks or drug formularies before prescribing drugs for patients with severe liver disease.

Medicines use for pregnant women: The kinetics of drug is altered during pregnancy. The rate of absorption decreases, while volume of distribution, metabolism and glomerular filtration rate increase during pregnancy. The embryonic period, where, organogenesis takes place, is the most susceptible period of pregnancy to drug effects. Administration of drugs, except those proved safe, in the first trimester, is therefore not generally recommended. It is advisable not to prescribe any drug during at any stage of pregnancy, if possible. This, however, should not preclude the importance of prescribing in life threatening conditions of the mother. Prior to prescribing

any drug for pregnant women, the benefit risk ratio of prescribing should be considered.

Medicines use for breast feeding mothers: Most drugs administered are detectable in breast milk. The concentration, however, is low. If the woman has to take the drug and the drug is relatively safe, she should optimally take it 30-60 minutes after nursing, and 3-4 hours before next feeding in order to allow time for many drugs to be cleared from the mother's blood, and the concentration in breast milk to be relatively low. Drugs for which no data are available on safety during lactation should be avoided or breast feeding discontinued while they are being given. Most antibiotics taken by nursing mothers can be detected in breast milk e.g., tetracycline and chloramphenicol. Most sedative hypnotics achieve concentrations in breast milk. Opioids also achieve concentrations in breast milk. Antineoplastic drugs are contraindicated in breast feeding. So it is worth noting not to prescribe drugs secreted in milk to the nursing mother.

Prescribing for infants/children: Physiologic processes that influence drug kinetics in the infant change significantly in the first year of life, specially the first few months, while there is no much difference in the dynamics but all the four parameters of kinetics are, therefore, affected in children. So drugs, which are partially or totally inactivated by the low pH of gastric content, should not be administered orally. GI enzymes are lower in the neonates than in adults. Neonates have less bile acid so that absorption of lipid soluble drugs is less. Gastric emptying time is prolonged in the first day. So drugs, which are absorbed primarily in the stomach, may be absorbed more completely. For drugs absorbed in the small intestine, therapeutic effects may be delayed. Peristalsis in neonates is slow. More drugs, therefore, will get absorbed from the small intestine. The volume of distribution is low in children, and drug metabolizing enzymes are not well developed. The glomerular filtration rate is slower than adults (30-40%). So the clearance of drugs is

slower in children than in adults. This definitely demands for dose adjustment in this age group. Doses for children are generally based on body-weight, age or body surface area (Annex 3). The following age ranges are often used: first month (neonate); up to 1 year (infant); 1–6 years; and 6–12 years. For most drugs the adult maximum dose should not be exceeded. For example if the dose is stated as 8 mg/kg (max. 300 mg), a child weighing 10 kg should receive 80 mg but a child weighing 40 kg should receive 300 mg (rather than 320 mg). Body surface area (BSA) estimates are sometimes preferable to body-weight for calculation of paediatric doses since many physiological phenomena correlate better with body surface area.

Narcotic Drugs and Psychotropic Substances use: The prescribing of a medicinal product that is liable to abuse requires special attention and may be subject to specific statutory requirements. Practitioners may need to be authorized to prescribe controlled substances; in such cases it might be necessary to indicate details of the authority on the prescription. In particular, the strength, directions and the quantity of the controlled substance to be dispensed should be stated clearly, with all quantities written in words as well as in figures to prevent alteration. Other details such as patient particulars and date should also be filled in carefully to avoid alteration.

Use of topical steroids: Absorption from the skin depends on the sites (high at axilla, face and scalp; medium at limbs and trunk; and low at palm, elbow and knee) and nature of lesion (high in exfoliative dermatitis and low in hyperkeratinised skin). Strong preparations should be avoided at highly absorption sites and on acute lesions, they may, however, be used for chronic lesions. Lotions/creams are better for exudative lesions for they allow evaporation, have a cooling, drying and antipruritic effect. Sprays and gels are good for hairy regions. Ointments form occlusive film and are good for chronic scaly conditions. Occlusive dressing enhances steroid absorption,

retains moisture and results in maceration of horny layer. Absorption is more in pediatric patients, hence milder preparations should be used. Strong preparations should be restricted for short term use only. Sudden withdrawal should be avoided. Twice a day application is enough; do not exceed three times application a day.

Good Dispensing Practices: Good dispensing practices ensure that the correct drug is delivered to the right patient, in the required dosage and quantities, with clear information, and in package that maintains an acceptable potency and quality of the drug. Dispensing includes all the activities that occur between the times the prescription or oral request of the patient or care provider is presented and the medicine is issued. This process may take place in health institutions and community drug retail outlets. It is often carried out by pharmacy professionals. No matter where dispensing takes place or who does it, any error or failure in the dispensing process can seriously affect the care of the patient mainly with health and economic consequences. Therefore, the dispenser plays a crucial role in the therapeutic process. The quality of dispensing may be determined by the training and supervision the dispenser has received. During medicines dispensing and counseling the information mentioned under prescribing above, the “Medicines Good Dispensing Practices” manual 2012 edition and also medicines dispensing and counseling guides are good resources to use. Finally, an application of the professional code of ethics by pharmacy professionals is an important issue that needs due consideration particularly with respect to confidentiality of patient data, withholding therapeutic interventions and varying cost of drug.

Labeling of Medicines: There is a legal requirement to be added on the label of any prescribed or over the counter medicine: Generic name, total quantity, directions for use, route of administration, precautions relating to the use, and storage of

the medicine. If a product is dispensed in more than one container, reference should be made to the amount in each container; other common labeling words include: 'Keep out of the reach of children' when necessary 'For external use only'; expiry or end of use dates; Shake the bottle, Store in a cool place, Discard . . . Days after opening and Do not use after . . . , which apply particularly to antibiotic mixtures, diluted liquid and topical preparations, and to eye-drops and name and address of the person dispensing the medicine. A pharmacist can add or modify to use more appropriate labeling and words that corresponds with the individual medicine, patient, or disease conditions. Avoid use of compound names or unofficial abbreviations which may create confusion for the purposes of generic prescribing and can be misinterpreted. Care should also be exercised when writing sustained or extended release preparations which may lead confusion between formulations with different lengths of action.

Counseling of Patients: The prescriber and the patient should agree on the health outcomes that the patient desires and on the strategy for achieving them. Taking the time to explain to the patient (and careers) the rationale and the potential adverse effects of treatment may improve adherence. For some medicines there is a special need for counseling (e.g. appropriate posture during administration of doxycycline); this is shown in counseling statements of the individual medicines. Counseling should be tailored to the age, experience, background, and understanding of the individual patient. The pharmacist should ensure that the patient understands how to take or use the medicine and how to follow the correct dosage schedule, refer medicines dispesing and counsling guides. For some preparations there is a special need for counselling, such as an unusual method or time of administration or a potential interaction with a common food or domestic remedy, and this is indicated where necessary. Patients must be warned to keep all

medicines out of the reach of children. All solid dose and all oral and external liquid preparations must be dispensed in a reclosable *child-resistant container* unless: the medicine is in an original pack or patient pack.

Adherence with Medicines Treatment: The health care provider and the patient should agree on the health outcomes that the patient desires and on the strategy for achieving them ('concordance'). It is often assumed that once the appropriate drug is chosen, the prescription correctly written and the medication correctly dispensed, that it will be taken correctly and treatment will be successful. Unfortunately, this is very often not the case, and health care providers overlook one of the most important reasons for treatment failure—poor adherence (compliance) with the treatment plan. Patient compliance is the extent to which the patient follows a prescribed drug regime, while adherence is participation of patients in their care plan resulting in understanding, consent and partnership with the provider. The health care provider should be sensitive to religious, cultural, and personal beliefs that can affect a patient's acceptance of medicines. There are different factors which contribute to patients' non-adherence. These factors include: purpose and instructions for administration not clear; perceived lack of efficacy; real or perceived adverse effects; nature of treatment, which in turn depends on the complexity of the regime (more frequency of administration and more number of drugs prescribed); characteristics of the patient such as forgetfulness about taking the medication, unable to finish because of feeling better, lack of understanding of the prescription, fear of dependence, social or physical problems to go to drug shops, unable to pay prescription charges, inconvenience of taking drugs everyday; type of illness like schizophrenia; health care system (long waiting times, uncaring staff, uncomfortable environment, exhausted drug supply, inaccessibility of the health institution); behavior of prescribers;

not winning confidence of medicines consumers irrational prescribing, giving inadequate information on the treatment, poor attitude to patients, negligence, poor perception to team work; physical difficulty in taking medicines (e.g. swallowing the medicine, handling small tablets, or opening medicine containers); and unattractive formulation (e.g. unpleasant taste). Patient adherence can be improved by supervising drug administration; simplifying therapeutic regime; educating patients on the importance of adhering to the prescribed medication; improving behavior of prescribers. Group of people who adhere less to their medication include: Men, Youngsters, Elderly patients, people living alone, etc.

Monitoring drug treatment: Patients should be monitored to ensure they are achieving the expected benefits from drug treatment without any unwanted side-effects.

ANTIMICROBIAL PRESCRIBING

General antimicrobials prescribing practice

Rates of Antimicrobial resistance are increasing in health facilities and the communit. The prevalence of Antimicrobial resistance in any population is related to the proportion of the population that receives Antimicrobial, and the total Antimicrobial exposure. Increased Antimicrobial use leads to more resistance.

Prescribing of antimicrobials requires knowledge of the common causative pathogens and the local antimicrobials resistance pattern/ level to choose the most appropriate antimicrobial. Factors related to the patient which must be considered include history of allergy, renal and hepatic function, susceptibility to infection (i.e. whether immuno-compromised), ability to tolerate drugs by mouth, severity of illness, age, whether taking other medications and, if female, whether pregnant, breast-feeding or taking oral contraceptive. The known or likely organism and its antibacterial sensitivity,

in association with the above factors, will suggest one or more antibacterials; the final choice depends on the microbiological, pharmacological, and toxicological properties.

Initially, when the infecting organism or the source of infection is unknown, 'broad-spectrum' antimicrobial may be appropriate. When a bacterial pathogen is isolated from a clinical specimen and sensitivities are known, treatment will be easy and should be adjusted to use the narrowest-spectrum antimicrobial. This will reduce the likelihood of selection and emerging bacterial resistance and other adverse effects. Other factors that need to be considered in the selection of an antibacterial are changing renal and hepatic function, and information on side-effects. Duration of therapy, dosage, and route of administration depend on site, type and severity of infection and response. An example of a rational approach to the selection of an antibacterial is treatment of a urinary-tract infection in a patient complaining of nausea and symptoms of a urinary tract infection in early pregnancy. The organism is reported as being resistant to ampicillin but sensitive to nitrofurantoin (can cause nausea), gentamicin (can be given only by injection and best avoided in pregnancy), tetracycline (causes dental discoloration) and trimethoprim (folate antagonist, theoretical teratogenic risk). The safest antibiotics in pregnancy are the penicillins and cephalosporins. The following precepts should be considered before prescribing antimicrobials. Viral infections should not be treated with antibacterials. However, antibacterials may be used to treat secondary bacterial infection (e.g. bacterial pneumonia secondary to influenza). Samples should be taken for culture and sensitivity testing; 'blind' antibacterial prescribing for unexplained pyrexia usually leads to further difficulty in establishing the diagnosis. Knowledge of prevalent organisms and their current sensitivity is of great help in choosing an antibacterial before bacteriological confirmation is available.

The dose of an antibacterial: varies according to a number of factors including age, weight, hepatic function, renal function, and severity of infection. The prescribing of the so-called 'standard' dose in serious infections may result in failure of treatment or even death of the patient; therefore it is important to prescribe a dose appropriate to the condition. An inadequate dose may also increase the likelihood of antibacterial resistance. On the other hand, for an antibacterial with a narrow therapeutic index (toxic and therapeutic dose) (e.g. an aminoglycoside) it is also important to avoid an excessive dose and the concentration of the drug in the plasma may need to be monitored.

Duration of therapy: depends on the nature of the infection and the response to treatment. Duration of treatment should not be unduly prolonged because they encourage resistance, they may lead to side-effects and they are costly. The prescription for an antibacterial should specify the duration of treatment or the date when treatment is to be stopped.

Route of Administration: The route of administration of an antibacterial often depends on the severity of the infection. Life-threatening infections require intravenous therapy. Antibacterials that are well absorbed may be given by mouth even for some serious infections. For a significant proportion of patients, the oral route of administration will be appropriate either on initiation or after 2 to 3 days of intravenous therapy. Certain infections e.g. serious sepsis, bacterial meningitis and neutropenic sepsis require intravenous antimicrobial for the full period of treatment. Parenteral administration is also appropriate when the oral route cannot be used (e.g. because of vomiting) or if absorption is inadequate. Whenever possible, painful intramuscular injections should be avoided in children. All intravenous therapy should be reviewed ideally daily or at least at 48 hours. A switch from intravenous to oral therapy should be considered as soon as it is clinically appropriate with the exception of patients with osteomyelitis, necrotising fasciitis, septic arthritis and infections mentioned above. When

considering a switch from the intravenous to oral route: Confirm that the oral route is suitable for the condition being treated. Ensure that the oral dose is at the upper end of the oral dose range to help maximize tissue antimicrobial concentrations. Ensure that the patient is able to swallow. Ensure the oral antibiotic is compatible with the feed and administration route.

Recommendations for better outcomes

1. **Documentation:** The use of antimicrobial carries significant risks to the patient and the community. The decision to prescribe an antimicrobial should always be justified following a risk-benefit assessment. All subsequent decisions (the reasons) relating to antimicrobial therapy should be documented clearly in the patient's medical record. All prescribers have a duty to comply with current antimicrobial prescribing guidance available. Empirical antimicrobial prescribing should be the last resort in prescribing antimicrobials.
2. **Microbiology Support for Antimicrobial Prescribing:** Appropriate microbiological samples will be taken prior to the commencement of antimicrobial therapy. The results of these cultures will be used to rationalise the empirical prescription in the individual, to guide future empirical therapy advice and for surveillance purposes. Appropriate antimicrobial sensitivity testing will be carried out by the laboratory on clinical specimens received.
3. **Correct Dosing and Administration:** Antimicrobials will be administered at the most appropriate dose for treatment of infection taking into account modifications required for current clinical condition renal and/or liver dysfunction and current medications and adjustments which may be required for drug allergy or interactions. All aminoglycoside and glycopeptide antimicrobials will be administered and monitored according to guidelines. Oral administration is

preferable to intravenous wherever possible to avoiding the risks.

4. **Preferential Use of Narrow Spectrum or Minimising the use of broad-spectrum Antimicrobials:** Antimicrobial therapy should be targeted to treat the specific infection using as narrow-spectrum an antimicrobial agent as possible.

Prescribers should therefore avoid/minimize indiscriminate/widespread use of cephalosporins, quinolones, broad-spectrum penicillins (including amoxicillin) and clindamycin unless there are clear clinical indications for their use. In addition there is evidence to show an association between total antimicrobial use and MRSA prevalence. Broad-spectrum antibiotics should be restricted to the treatment of serious infections when the pathogen is not known or when other effective agents are unavailable.

5. **Use of Oral Preparations and IV to Oral Switch Where Appropriate:** Intravenous therapy should only be used for patients with severe infections, patients who have a focus of infection requiring high doses of antimicrobials, patients who are unable to take or absorb oral antimicrobials, and when there are no alternative suitable agents. IV antimicrobials should be reviewed on a daily basis and, if appropriate, the patient switched to an oral equivalent. Oral therapy should be considered once patients are afebrile for 24hrs and improving, exceptions to this include some serious infections or following microbiological advice.

6. **Appropriate Duration of Therapy:** Antimicrobials will be prescribed for as short a time period as possible. The duration of antimicrobial therapy depends on the infecting organism(s), the site of the infection, the patient's own immune response and other additional features such as surgical and medical interventions. Each antimicrobial prescription needs to be assessed on a daily basis and the review documented in the clinical notes.

7. **Available Guidance for Antimicrobial Prescribing:** Antimicrobials will be prescribed following the standard treatment guidelines which are available to the prescriber at the point of care.
8. **Support and Education for Management of Infection Prevention and Control:** All staff has a duty of care to the patients and themselves to ensure they deliver high standards of infection control practices including antimicrobial prescribing practice at all times. Wherever there is deficiency in their knowledge or experience this must be highlighted to the department/ward head that is responsible for ensuring the staff to receive the appropriate training, education or advice.
9. **Antimicrobials allergy:** Patients with a reported antimicrobial allergy should have this clearly documented in the appropriate section of the Patients Medication Record and medical notes. The nature of the allergy should also be recorded. Patients with such note should not the medicines.
10. **Antimicrobials resistance:** If a patient has been in hospital for more than five days, has been previously colonized with MRSA or is at risk of MRSA colonization, consider using Vancomycin or Teicoplanin. If a patient has been previously colonized or infected with Extended Spectrum Beta-Lactamase (ESBL) infection or is at risk of ESBL infection (i.e. recurrent urinary tract infections, consider using an alternative antibiotic regime.
11. **Review of antibiotic treatment:** It is important to develop practice which includes daily review, appropriate de-escalation from intravenous to oral therapy and setting a maximum duration for treatment without repeat prescription, unless there is a clear indication in the medical record that antibiotics should be continued. Antibiotics should generally be prescribed for a maximum of seven days or a shorter period if this is clinically appropriate; however, some specific conditions require a longer course (e.g. infective endocarditis). Antibiotics prescribed empirically in life-

threatening situations should be reviewed early in the light of microbiological results and clinical progress, and where necessary changed or discontinued as soon as is reasonable. Individual patient and drug-specific factors to consider in all cases include. Clinical Pharmacists will review all prescription charts on a regular, mostly daily, basis.

Antimicrobials Use for Surgical Prophylaxis

The purpose of antibiotic prophylaxis in surgical procedures is not to sterilize tissues but to reduce the colonization pressure of microorganisms introduced at the time of operation to a level that the patient's immune system is able to overcome. Prophylaxis does not prevent infection caused by postoperative contamination. Prophylactic antimicrobial use differs from treatment with antimicrobial in that the former is intended to prevent infection, whereas the latter is intended to resolve an established infection, typically requiring a longer course of therapy. Prophylaxis is intended for elective procedures in which the incision will be closed in the operating room. It must be safe and inexpensive, and it must be effective against organisms likely to be encountered in the surgical procedure. The agent must be administered in a way that ensures that serum and tissue levels are adequate before an incision is made and that therapeutic levels of the agent can be maintained in serum and tissue. Prophylactic antimicrobial has an important part to play in the prevention of post-operative wound and deep site infections. The key principle is to have a high concentration of the antimicrobial in the relevant tissues at the time of operation, when bacteria may contaminate the tissues.

Whether antimicrobials are required and the antimicrobial course length depends on the classification of the surgical procedure and if any prosthetic material is being implanted. Most clean-contaminated procedures require only a single dose of the antimicrobial at induction of anaesthesia. Timing of

administration of prophylaxis is important to ensure that there are maximum tissue levels at the time of first incision. Oral and intramuscular antimicrobial should be given one hour and IV antimicrobial given 30-40 minutes pre-operatively so that the infusion or dose has just been completed at the time of incision.

Use of single dose for surgical prophylaxis: Prophylactic antimicrobial use has an important part to play in the prevention of post-operative wound and deep site infections. The key principle in this use is to have a high concentration of the antimicrobial agent in the relevant tissues at the time of the operation, when bacteria may contaminate the tissues. For most operations, this requires only a single dose of the antimicrobial at induction of anaesthesia. If surgery is prolonged (over 4 hours) or there is excessive blood loss, a further dose of intra-operative antibiotics may be needed depending on the half-life of the antimicrobial.

Dosage selection: It is generally accepted as good practice that the dosage of an antimicrobial required for prophylaxis is the same as that for the therapy of infection. A single standard therapeutic dose of antibiotic is sufficient for prophylaxis under most circumstances.

Duration of prophylaxis: For many types of commonly performed surgery there is consistent evidence that a single dose of antimicrobial with a long enough half-life to achieve activity throughout the operation is adequate. There is evidence for prophylaxis during surgery that longer dosage duration has no increased benefit over a short course.

Route of Administration: Systemic antimicrobial prophylaxis, typically given by the parenteral intravenous route, has historically proven to be reliable and effective prophylaxis.

Oral Administration: Serum and tissue concentrations after oral administration are determined in part by the rate of absorption, which varies between individuals. There is relatively little evidence about the effectiveness of orally administered

antibiotic prophylaxis. A further problem is that often the correct time of administration is difficult to guarantee.

The use of antimicrobial prophylaxis has become an essential component of the standard of care in virtually all surgical procedures and has resulted in a reduced risk of postoperative infection when sound and appropriate principles of prophylaxis are applied which include: There is probable risk of infection in the absence of a prophylactic agent. There must be knowledge of the probable contaminating flora associated with the operative wound or organ site. The activity of the chosen prophylactic agent should encompass the majority of pathogens likely to contaminate the wound or operative site. Single antimicrobial agent is preferable. The prophylactic agent must be administered in a dose which provides an effective tissue concentration prior to intra-operative bacterial contamination. Administration must occur 30-45 minutes prior to incision (usually with the induction of anesthesia). The effective dose should be governed by the patient's weight. In procedures lasting 3 hour or less, a single prophylactic dose is usually sufficient. Procedures lasting greater than three hours require an additional effective dose. Procedures in which there is rapid blood loss and/or fluid administration will dictate more frequent prophylactic dosing. Under no circumstance should any prophylactic agent be given on-call because it often results in less than effective tissue levels at the time of incision. Postoperative prophylaxis is strongly discouraged except in the scenario of a bioprosthetic insertion in which case 2 or 3 additional prophylactic doses may be deemed. An effective and thoughtful prophylactic regimen is no substitute for exquisite surgical technique and competent postsurgical management.

Antimicrobial Prophylaxis in Selected Surgeries

Type of procedure	Medicine	Route	Dosage	Time of administration	Rationale (likely infective agent)
I. Clean surgery a. Insertion of synthetic biomaterial device/prosthesis b. Patients with impaired immunity	Cefazolin Or Cefuroxime	IV	750mg	30-45min before skin incision, 2 nd dose if procedure lasts > 3hrs	Gm positive cocci (<i>S. aureus</i> and epidermidis), aerobic coliforms (<i>E. coli</i>)
II. Upper GIT and elective bowel surgeries (stomach, small bowel, pancreas, hepatobiliary etc)	Ciprofloxacin Or Cefazolin Plus Metronidazole	IV IV IV	400mg 750mg 500mg	30-45min before skin incision,	Coliforms > Enterococcus > Streptococci > Aerobic > Clostridia > Pepto-Streptococci Bacteriodes > Prevotella
III. Large bowel resection	Bisacodyl Neomycin Plus Erythromycin Cefazolin Or Ceftetan	PO PO PO IV IV	2tablets 500mg 500mg 1-2gm 1-2gm	2 days before surgery 1pm, 2pm and 10pm before surgery 30-45min before skin incision, 2 nd dose if procedure lasts > 3hrs	Coliforms, enterococci, Bacteriodes, peptostreptococci, Clostridia
IV. Acute appendicitis (Non-perforated) In perforated or gangrenous cases treatment should continue as clinically indicated	Cefazolin Plus Metronidazole	IV IV	1gm 500mg	30-45min before skin incision	Coliforms, anaerobes
V. Trauma surgery (penetrating abdominal trauma)	Ampicillin Or Cefazolin Plus metronidazole	IV IV IV	3gm 1-2gm 500mg	30-45min before skin incision, 2 nd dose if surgery lasts > 3hrs	Coliforms and anaerobes (gm positive and negative)

Type of procedure	Medicine	Route	Dosage	Time of administration	Rationale (likely infective agent)
VI. Gynecology and Obstetrics a. Vaginal and abdominal hysterectomy including radical hysterectomy b. Ceasarean section/ hysterectomy	Ceftizoxime Or Cefazolin Ceftizoxime Or Cefazolin	IV	1gm 1gm 1gm	30-45min before skin incision In high risk patients 2gm may be used after clamping the umbilical cord	Coliforms, enterococci, streptococci, clostridia, bacteroides
VII. Urology Prostatectomy VIII. Head and neck surgery a. Clean procedure (skin incision and dissection) b. Mandibular fracture IX. Orthopedics (Traumatic open fractures)	Cefazolin Or Ciprofloxacin Cefazolin Or Pencillin G Pencillin G Cefazolin Or Ceftizoxime	IV IV IV IV	1gm 400mg 1gm 2-4MU 2-4MU 2gms	30-45min before skin incision 30-45min before skin incision	Coliforms, staphylococci, Pseudomonads Staphylococci Staphylococci Staphylococci
X. Neurosurgery	Cefazolin	IV	1gm	30-45min before skin incision	Staphylococci

Antimicrobials Prophylaxis in Gynaecologic Procedures Recommendations

1. All women undergoing an abdominal or vaginal hysterectomy should receive antibiotic prophylaxis.
2. All women undergoing laparoscopic hysterectomy or laparoscopically assisted vaginal hysterectomy should receive prophylactic antibiotics.
3. The choice of antibiotic for hysterectomy should be a single dose of a first-generation cephalosporin. If patients are allergic to cephalosporin, then clindamycin, erythromycin, or metronidazole should be used.
4. Prophylactic antibiotics should be administered 15 to 60 minutes prior to skin incision. No additional doses are recommended.
5. If an open abdominal procedure is lengthy (e.g. > 3 hours), or if the estimated blood loss is > 1500 mL, an additional dose of the prophylactic antibiotic may be given 3 to 4 hours after the initial dose.
6. Antibiotic prophylaxis is not recommended for laparoscopic procedures that involve no direct access from the abdominal cavity to the uterine cavity or vagina.
7. All women undergoing surgery for pelvic organ prolapse and/or stress urinary incontinence should receive a single dose of first-generation cephalosporin.
8. Antibiotic prophylaxis is not recommended for hysteroscopic surgery.
9. All women undergoing an induced (therapeutic) surgical abortion should receive prophylactic antibiotics to reduce the risk of post-abortion infection.
10. Prophylactic antibiotics are not suggested to reduce infectious morbidity following surgery for a missed or incomplete abortion.
11. Antibiotic prophylaxis is not recommended for insertion of an intrauterine device. However, health care professionals

could consider screening for sexually transmitted infections in high-risk populations.

12. There is insufficient evidence to support the use of antibiotic prophylaxis for an endometrial biopsy.
13. The best method to prevent infection after hysterosalpingography is unknown. Women with dilated tubes found at the time of hysterosalpingography are at highest risk, and prophylactic antibiotics (e.g.,doxycycline) should be given.
14. Antibiotic prophylaxis is not recommended for urodynamic studies in women at low risk, unless the incidence of urinary tract infection post-urodynamics is > 10%.
15. In patients with morbid obesity (BMI > 35 kg/m²), doubling the antibiotic dose may be considered.
16. Administration of antibiotics solely to prevent endocarditis is not recommended for patients who undergo a genitourinary procedure.

1. GASTROINTESTINAL SYSTEM MEDICINES

1.1. Antacids

Antacids are inorganic salts that dissolve in acid gastric secretions releasing anions that partially neutralized gastric hydrochloric acid.

Antacids (usually containing aluminium or magnesium compounds) can often relieve symptoms in ulcer dyspepsia and in non-erosive gastro-oesophageal reflux; they are also sometimes used in non-ulcer dyspepsia but the evidence of benefit is uncertain. Antacids also are used for the relief of, acid indigestion, heart burn and sour stomach; for the prevention of stress ulceration and gastrointestinal bleeding; and to reduce the risk associated with gastric aspiration and for the management of hyperphosphatemia.

Antacids are best given when symptoms occur or are expected, usually between meals and at bedtime, 4 or more times daily; additional doses may be required up to once an hour.

Conventional doses, for example, 10 ml 3 or 4 times daily of liquid magnesium–aluminium antacids promote ulcer healing, but less well than antisecretory drugs (such as an H₂-receptor antagonist); proof of a relationship between healing and neutralizing capacity is lacking. Liquid preparations are more effective than solids. Aluminium- and magnesium-containing antacids (for example aluminium hydroxide and magnesium hydroxide), being relatively insoluble in water, are long-acting if retained in the stomach. They are suitable antacids for most purposes.

Aluminium and/or magnesium containing antacids are the most commonly used and are often administered concurrently or in commercially available combinations to control the frequency and consistency of bowel movements.

Aluminium salts tend to produce constipation and to delay gastric emptying because of its astringent property, while magnesium salts have the reverse effect; a combination of the two may reduce adverse gastro-intestinal effects. Another advantage of combined antacid formulations is that a slow-acting antacid such as aluminium hydroxide may be combined with a more rapidly acting agent such as magnesium hydroxide to improve the onset and duration of effect.

Some of the antacid combinations contain other ingredients that have no antacid properties. Simethicone, antiflatulent, has been added as an aid in those conditions in which the retention of gas may be a problem; however, in the treatment of peptic ulcer disease, the advantage of using antacid and simethicone combinations rather than antacids alone has not been clearly established.

Alginate taken in combination with an antacid increases the viscosity of stomach contents and can protect the oesophageal mucosa from acid reflux. Some alginate-containing preparations form a viscous gel ('raft') that floats on the surface of the stomach contents, thereby reducing symptoms of reflux.

The role of calcium carbonate in the management of peptic ulcer is controversial because this antacid may cause acid rebound, which is especially important when the medicine is administered at bedtime. However, it is useful because it has a rapid onset of action, high acid effect and is relatively inexpensive.

Antacids should not be given to young children (up to 6 years of age) unless prescribed by a physician. Use of magnesium-containing antacids is contraindicated in very young children because there is a risk of hypermagnesemia, especially in dehydrated children or children with renal failure. Use of aluminum-containing antacids is contraindicated in very young children because there is a risk of aluminum toxicity, especially

in dehydrated infants and children or infants and children with renal failure.

Antacids interfere with the gastro-intestinal absorption of a number of medicines taken orally by forming insoluble complexes, altering the gastric PH, or by effects on gastric emptying rates (fluoroquinolones, isoniazid, ketoconazole, tetracyclines, oral phosphates); changes in the urinary PH also affect tubular reabsorption (mecamylamine, methenamine; concurrent use is not recommended). Antacids may also damage enteric coatings designed to prevent dissolution in the stomach. The interaction between an antacid and another orally administered medicine may be minimized by giving the drug 2 to 3 hours before or after antacid administration.

Osteomalacia, encephalopathy, dementia, and microcytic anaemia have been associated with aluminium accumulation in patients with chronic renal failure. Patients with renal failure taking aluminium compounds should avoid citrate - containing preparations.

Use of magnesium-containing antacids is contraindicated in patients with renal failure because of increased risk of hypermagnesemia. Chronic administration of magnesium trisilicate infrequently produces silica renal stones.

Aluminium Hydroxide

Mixture or Gel, 320 mg/5ml.

Suspension, 360mg/5ml.

Chewable tablet, 500mg

Indications: ulcer and non ulcer dyspepsia; gastro-oesophageal reflux disease (GERD), hyperphosphatemia.

Cautions: See notes above, uremia, congestive heart failure, renal failure and renal dialysis, edema, cirrhosis, low sodium diets, gastrointestinal hemorrhage, and elderly.

Drug interactions: allupurinol, antibiotics (tetracycline, quinolones, some cephalosporins), biphosphonate derivatives, corticosteroids, cyclosporine, iron salts, imidazole antifungals, isoniazide, phenytoin, phenothiazines- absorption will be decreased; citric acid derivatives may decrease absorption of aluminum hydroxide. See also notes above

Contraindications: see notes above, hypophosphatemia, undiagnosed gastro intestinal or rectal bleeding; appendicitis; porphyria.

Side effects: see notes above, constipation, stomach cramps, fecal impaction, nausea, vomiting, and discoloration of feces, hypophosphatemia, and hypomagnesemia.

Dose and Administration: Dyspepsia, gastro-oesophageal reflux disease (GERD): Oral: **Adult:** 5–10 ml suspension 4 times daily between meals and at bedtime. **Child:** 6–12 years 5 ml up to three times daily

Hyperphosphatemia: Oral: **Adult:** 2–10 g daily in divided doses with meals

Note: Do not take other medicines within 2–4 hours of aluminium hydroxide preparations.

Storage: at room temperature, avoid freezing.

Aluminium Hydroxide and Magnesium Hydroxide*

Suspension, 220mg+220mg/ 5 ml

Tablet (chewable), 400mg + 400mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see under individual preparations and notes above.

Note: a combination of Aluminium Hydroxide and Magnesium Hydroxide may reduce adverse gastro-intestinal effects. Another advantage of combined antacid formulations is that a

* And any other combination ratio proven to be therapeutically effective can be used

slow-acting antacid aluminium hydroxide may be combined with a more rapidly acting agent such as magnesium hydroxide to improve the onset and duration of effect.

Dose and Administrations: Oral: shake the bottle well before use. 5-10 ml (2 teaspoonfuls) or 1-2 tablets every 6 hours usually between meals and at bedtime, or as required.

Storage: at room temperature.

Aluminium Hydroxide + Magnesium Hydroxide + Simethicone*

Suspension, 225mg+200 mg+25 mg/ 5 ml

Indications: temporary relief of hyperacidity associated with gas; may also be used for indications associated with other antacids.

Indications, cautions, drug interactions, contraindications and side effects; see under individual preparations and notes above.

Note: Simethicone, antiflatulent, has been added as an aid in those conditions in which the retention of gas may be a problem.

Dose and Administration: Oral: **Adult:** 10-20ml 4-6 times / day between meals and at bedtime; may be used every hour for severe symptoms.

Storage: at room temperature.

Aluminium Hydroxide and Magnesium Trisilicate*

Suspension, 310mg+620mg in 5ml

Tablet (chewable), 120 mg+250 mg; 250mg+500mg

Indications, cautions, drug interactions, contraindications, and side effects; see under individual preparations and notes above.

* And any other combination ratio proven to be therapeutically effective can be used

Dose and Administrations:*Oral: Adult:* shake the bottle well before use. 5-10 ml (2 teaspoonfuls) every 6 hours usually between meals and at bedtime, or as required. *Note: Chew 1 - 2 tablets when required.*

Storage: at room temperature.

Note: Magnesim trisilicate is often given in conjunction with other antacids in order to reduce adverse gastro-intestinal effects

Calcium Carbonate

Tablet, 350mg, 500mg, 700mg

Indications: used as an antacid, and treatment or prevention of calcium deficiency or hyperphosphatemia.

Cautions: renal impairment; renal calculi; hypercalcemia; hypophosphatemia.

Drug interactions: thiazide diuretics, levothyroxine, digoxin, tetracycline, atenolol, iron, quinolones, sodium fluoride, and verapamil.

Side effects: headache, hypophosphatemia, hypercalcaemia, constipation, laxative effect, acid rebound, nausea, vomiting, anorexia, abdominal pain, xerostomia, and flatulence.

Dose and Administration: Oral: **Adult:** Antacid: 1-2 tablets every 2 hours; maximum 7000 mg per 24 hours.

Famotidine+calciumcarbonate+Magnesium hydroxide

Tablet, 10mg+800mg+165mg

Indications: to relieve heartburn associated with acid indigestion and sour stomach

Caution: allergic to famotidine or other acid reducers, not swallow tablet whole

Contraindications: trouble or pain swallowing food, vomiting with blood, or bloody or black stools

Dose and administration: adults and children 12 years and over: to relieve symptoms, 1 tablet to be chewed before swallowing; Maximum 2 chewable tablets in 24 hours.

Storage: store at 20-25°C; protect from moisture

Magnesium Hydroxide

Suspension, 375 mg/5ml, 7.75 %

Tablet (chewable), 300 mg, 311 mg

Indications: ulcer and non-ulcer dyspepsia; GERD.

Cautions: renal impairment, hypermagnesemia, hepatic impairment, notes above.

Drug interactions: as for Aluminum hydroxide, also see notes above.

Contraindications: see notes above, hypersensitivity to any component of the formulation, severe renal impairment.

Side effects: diarrhoea, abdominal cramps, muscle weakness, respiratory depression, hypermagnesemia and hypotension.

Dose and Administration: Tablet, **Adult:** Chew 2 - 4 tablets repeated according to patients needs with maximum daily dose of 16 tablets. **Child** (7-14 years): one tablet with maximum of 4 tablets per day. Mixture, **Adult:** 5 -15 ml repeated according to patient's needs with maximum daily dose of 60 ml. **Child:** 2.5-5ml as needed up to 4 times /day.

Storage: at room temperature, avoid freezing.

Magnesium Trisilicate

Tablet (Chewable), 500 mg

Indications, Cautions, Drug interactions, Contraindications, Storage, see notes above.

Side effects: see notes above, silica renal stones; diarrhea.

Dose and Administration: Oral, Chew 2 tablets as required. *Note: the antacid action is exerted slowly, so it does not give such rapid symptomatic relief as magnesium hydroxide.*

Sodium Alginate+Magnesium Hydroxide+Aluminum Hydroxide+Siiimethicone

Oral suspension, 100mg+250mg+125mg+50mg in 5ml

Sodium bicarbonate+ Sodium Alginate+ Calcium carbonate

Tablet, 276mg+500mg+160mg

Alginate taken in combination with an antacid increases the viscosity of stomach contents and can protect the oesophageal mucosa from acid reflux. Some alginate-containing preparations form a viscous gel ('raft') that floats on the surface of the stomach contents, thereby reducing symptoms of reflux. Antacids may damage enteric coatings designed to prevent dissolution in the stomach.

1.2. Anti-ulcer Agents

Anti-ulcer agents, used in the treatment and prophylaxis of peptic ulcer disease, may be broadly divided into the antisecretory agents which suppress the production of gastric acid (e.g. cimetidine), and agents with cytoprotective or mucosal protectant properties (e.g. sucralfate). Antacids (see above) also play an adjuvant role in the symptomatic treatment of peptic ulcer and therapy to treat *Helicobacter pylori* is becoming more important.

H2-receptor antagonists

The H₂-receptor antagonists, which include cimetidine, ranitidine, nizatidine and famotidine, reduce acid secretion by blocking the action of histamine at the H₂-receptors in the parietal cells of the stomach. Gastric acid secretion in response to other secretagogues (e.g. acetylcholine, gastrin) is also reduced. They are used in the management of peptic ulcer disease, reflux oesophagitis and hypersecretory states such as Zollinger-Ellison syndrome. High doses of H₂-receptor

antagonists have been used in Zollinger–Ellison syndrome, but a proton-pump inhibitor is now preferred. H₂-receptor antagonists should be used with caution in renal impairment, pregnancy and breast feeding.

Maintenance treatment with low doses of H₂-receptor antagonists has largely been replaced in *Helicobacter pylori*-positive patients by eradication regimens. Maintenance treatment may occasionally be used for those with frequent severe recurrences and for the elderly who suffer ulcer complications. Treatment of undiagnosed dyspepsia with H₂-receptor antagonists may be acceptable in younger patients but care is required in older people because their symptoms may be caused by gastric cancer.

H₂-receptor antagonist therapy can promote healing of NSAIDs-associated ulcers (particularly duodenal). Treatment also reduces the risk of acid aspiration in obstetric patients at delivery (Mendelson syndrome).

Side-effects of the H₂-receptor antagonists include diarrhoea, headache, and dizziness. Rash (including erythema multiforme and toxic epidermal necrolysis) occurs less frequently. Other side-effects reported rarely or very rarely include hepatitis, cholestatic jaundice, bradycardia, psychiatric reactions (including confusion, depression, and hallucinations) particularly in the elderly or the very ill, blood disorders (including leucopenia, thrombocytopenia, and pancytopenia), arthralgia, and myalgia. Gynaecomastia and impotence occur occasionally with cimetidine and there are isolated reports with the other H₂-receptor antagonists.

Cimetidine is used in conditions where inhibition of gastric acid secretion may be beneficial, such as duodenal and gastric ulcers. Cimetidine binds to cytochrome P450 and inhibits the breakdown of medicines metabolized by this system; many interactions have been reported but only a few are of clinical

significance. Ranitidine differs structurally from cimetidine; it has been shown to be at least as effective as cimetidine as an ulcer-healing medicine, and is less inclined to cross the blood-brain barrier. Ranitidine and nizatidine do not appear to bind microsomal cytochrome P450 and thus the potential for drug interactions is lower. Unlike cimetidine, they have little or no antiandrogenic effect. Famotidine has been shown to be 20-150 or 3-20 times as potent on a molar basis as cimetidine or ranitidine, respectively, in inhibiting stimulated gastric acid secretion.

Cimetidine

Injection, 200mg/ml in 2ml ampoule

Syrup, 200mg/5ml

Tablet, 200mg, 400mg, 800mg

Tablet, (chewable), 200mg

Indications: benign gastric and duodenal ulceration, stomach ulceration, GERD, Zollinger-Ellison syndrome, and other conditions where gastric acid reduction is beneficial.

Cautions: hepatic impairment; renal impairment; pregnancy; breastfeeding; middle aged or older patients and in those whose symptom change may mask gastric cancer; preferably avoid intravenous injection (use intravenous infusion) particularly in high dosage and in cardiovascular impairment (risk of arrhythmias).

Drug interactions: tricyclic antidepressants, benzodiazepines, metoprolol, propranolol, carbamazepine, phenytoin, procainamide, quinidine, theophylline, valproic acid,azole antifungals and warfarin.

Contraindications: hypersensitivity to the drug.

Side effects: gastrointestinal disturbances, headache, dizziness, somnolence, diarrhea, rash and tiredness; reversible confusional states, gynaecomastia and impotence, hypersensitivity reactions

(rare), *less* commonly tachycardia; rarely interstitial nephritis; very rarely pancreatitis, galactorrhoea, vasculitis, alopecia.

Dose and Administration: Adult: Short-term treatment of active ulcers: Oral: 300mg 4 times/day or 400mg twice daily or 800mg at bedtime for up to 8 weeks.

Note: Higher doses of 1600 mg at bedtime for 4 weeks may be beneficial for a subpopulation of patients with larger duodenal ulcers (>1 cm defined endoscopically) who are also heavy smokers (≥1 pack/day).

I.M, I.V: 200mg 4-6 hourly (for IV, dilute in 20ml 0.9% sodium chloride solution and give slowly, over at least 2 minutes).

In cardiovascular disease or if a higher dose is required, IV infusion is recommended: 400mg, diluted in 100ml 0.9% sodium chloride and given over 0.5-1 hour, may be repeated 4-6 hourly; or continuous infusion at a rate of 50-100mg/hour; maximum 2.4g/24 hours.

Duodenal ulcer prophylaxis: oral: 400mg-800mg at bed time.

Gastric hypersecretory conditions: Oral, I.M., I.V.; 300mg – 600mg every 6 hours; dosage not to exceed 2.4g/day.

Child ≥ 12 years and Adult: Oral: heart burn, acid indigestion, sour stomach: 200mg up to twice daily; may take 30 minutes prior to eating foods or beverages expected to cause heart burn or indigestion.

Child: Oral, I.M., I.V.: 20-40mg/kg/day in divided doses every 6 hours.

Note: Oral: Administer with meals so that the medicine's peak effect occurs at the proper time. Peak inhibition of gastric acid secretion occurs at 1 and 3 hours after dosing in fasting subjects and approximately 2 hours in non fasting subjects; this correlates well with the time food is no longer in the stomach offering a buffering effect.

Renal Impairment: when Clcr 10-50 mL/minute: Administer 50% of normal dose. When Clcr <10 mL/minute: Administer 25% of normal dose

Slightly dialyzable (5% to 20%); administer after dialysis.

Hepatic Impairment: Usual dose is safe in mild liver disease but use with caution and in reduced dosage in severe liver disease. Increased risk of CNS toxicity in cirrhosis suggested by enhanced penetration of CNS.

Storage: store in airtight containers at a temperature of 15 to 30°C. Protect from light.

Famotidine

Tablet, 20 mg, 40 mg

Indications: maintenance therapy and treatment of duodenal ulcer, gastric ulcer, to control gastric pH in critically-ill patients, symptomatic relief in gastritis, GERD, active benign gastric ulcer, and pathological hypersecretory conditions.

Caution: see under cimetidine.

Drug interactions: ketoconazole, itraconazole and ethanol; the potential for drug interaction is much less than with cimetidine.

Contraindication: hypersensitivity to the medicine and other H₂ antagonists, or any component of the formulation.

Side effects: see under cimetidine; it has little if any anti-androgenic effect.

Dose and Administration: Oral: **Adult:** Duodenal ulcer: Acute therapy: 40mg/day at bed time (or 20 mg twice daily) for 4-8 weeks. Maintenance therapy: 20mg/day at bedtime. Gastric ulcer: Acute therapy: 40mg/day at bedtime. Hypersecretory conditions: initial: 20mg every 6 hours; may increase in increments up to 160mg every 6 hours. Gastro-oesophageal reflux disease (GERD): 20mg twice daily for 6 weeks. **Child:** Peptic ulcer: 1-16 years: 0.5mg/kg/day at bedtime or divided twice daily (maximum dose: 40mg/day). GERD: <3 months: 0.5mg/kg once daily; 3 to 12 months: 0.5mg/kg twice daily; 1 to 16 years: 1mg/kg/day divided twice daily (maximum dose: 40mg twice daily); Adult and Child ≥ 12 years: Heart burn,

indigestion, sour stomach: 10-20mg every 12 hours; dose may be taken 15-60 minutes before eating foods known to cause heartburn.

Storage: store at room temperature; protect from moisture.

Nizatidine

Capsule, 150mg, 300mg

Injection, 25mg/ml

Indications: see under dose.

Cautions, Drug interactions, see under cimetidine above.

Side effects: sweating, rarely vasculitis, hyperuricaemia, exfoliative dermatitis

Dose and Administration: Adult: Oral: Benign gastric, duodenal or NSAID associated ulceration, treatment, 300mg in the evening or 150 mg twice daily for 4-8 weeks; maintenance, 150mg at night;

Gastro-oesophageal reflux disease: 150-300mg twice daily for up to 12 weeks. IV infusion: for short term use in peptic ulcer hospital inpatients as alternative to oral route, by intermittent IV infusion over 15 minutes, 100mg 3 times daily, or by continuous IV infusion, 10mg/hour; max 480mg daily. **Child not recommended.**

Ranitidine

Injection, 10 mg/ml in 5ml ampoule; 25mg/ml in 10ml ampoule

Tablet, 150 mg, 300mg

Indications: benign gastric and duodenal ulceration, GERD, Zollinger–Ellison syndrome, other conditions where gastric acid reduction is beneficial

Cautions, Side effects, see under cimetidine above.

Drug interactions: ranitidine does not appear to bind to microsomal cytochrome P450 thus the potential for interactions

is less than with cimetidine; sacralfate reduces absorption of ranitidine.

Dose and Administration: Benign gastric and duodenal ulceration: oral:**Adult:** 150 mg twice daily *or* 300 mg at night for 4–8 weeks, up to 6 weeks in chronic episodic dyspepsia, and up to 8 weeks in NSAID-associated ulceration (in duodenal ulcer 300 mg can be given twice daily for 4 weeks to achieve a higher healing rate); maintenance, 150 mg at night; **Child:**(*peptic ulcer*) 2–4 mg/kg twice daily, maximum 300 mg daily. Benign gastric and duodenal ulceration, reflux oesophagitis, Zollinger–Ellison syndrome: IM: **Adult:** 50 mg every 6–8 hours or by slow intravenous injection, 50 mg diluted to 20 ml and given over at least 2 minutes, may be repeated every 6–8 hours or by intravenous infusion, 25 mg/hour for 2 hours, may be repeated every 6–8 hours. Prophylaxis of NSAID-induced duodenal ulcer: oral: **Adult:** 150 mg twice daily. Reflux oesophagitis: oral:**Adult:** 150 mg twice daily or 300 mg at night for up to 8 weeks, or if necessary 12 weeks (moderate to severe, 150 mg 4 times daily for up to 12 weeks); long-term treatment of healed oesophagitis, 150 mg twice daily. Zollinger–Ellison syndrome: oral:**Adult:** 150 mg 3 times daily; up to 6 g daily in divided doses has been used. Gastric acid reduction (prophylaxis of acid aspiration) in obstetrics: oral:**Adult:** 150 mg at onset of labour, then every 6 hours; surgical procedures, IM or slow IV injection: **Adult:** 50 mg 45–60 minutes before induction of anaesthesia (intravenous injection diluted to 20 ml and given over at least 2 minutes), or orally, 150 mg 2 hours before induction of anaesthesia, and also, when possible on the preceding evening. Prophylaxis of stress ulceration: **Adult:** initial slow IV injection of 50 mg diluted to 20 ml and given over at least 2 minutes then by continuous IV infusion, 125–250 micrograms/kg per hour (may

be followed by 150 mg twice daily by mouth when oral feeding commences).

Use half normal dose if eGFR less than 50 mL/minute/1.73 m².

Storage: store injections between 4-30°C; and tablet between 15-30°C.

Misoprostol

Tablet, 20mcg, 40mcg

Indications: protection against NSAID associated gastric and duodenal ulceration. *Misoprostol is a synthetic prostaglandin E₁ analogue used to inhibit gastric acid secretion by a direct action on the parietal cells and also have mucosal protectant property.*

Cautions: renal impairment and elderly, inflammatory bowel disease (may exacerbate intestinal inflammation and produce severe diarrhea); patients prone to dehydration or in whom its consequence would be dangerous. Patients should understand misoprostol's abortifacient properties and attendant risks, and that the medicine is intended only for their use for the specific condition for which it was prescribed.

Drug interactions: oxytocin, diclofenac, phenylbutazone

Contraindications: pregnancy and allergy to prostaglandins.

Side effects: diarrhoea is the most common side effects (may occasionally be severe and require withdrawal, reduced by giving single doses not exceeding 200 micrograms and by avoiding magnesium-containing antacids); abdominal pain, dyspepsia, flatulence, and nausea and vomiting, increased uterine contractility, abnormal vaginal bleeding (including intermenstrual bleeding, menorrhagia, and postmenopausal bleeding), skin rashes, headache, dizziness, and constipation.

Dose and Administration: Adult: Oral: Prevention against NSAID associated duodenal ulcer: 800 mcg/day in four divided doses, with meals and at bedtime. Where appropriate, NSAIDs should be taken simultaneously.

Prevention against NSAID associated gastric ulcer: 200mcg twice daily with food and the prescribed NSAID; increased to 200mcg three times daily (maximum 200 mcg 4 times daily) to correspond with the NSAID administration schedule or if clinically indicated. Misoprostol therapy should be started at the onset of treatment with NSAIDs, and continue for the duration of NSAIDs therapy. If required, antacids may be administered before or after misoprostol for the relief of pain. However, magnesium-containing antacids are not recommended since they may aggravate misoprostol-induced diarrhea.

Storage: store at or below 25°C.

Note: Taking with food or milk will lessen adverse effects such as loose stools, diarrhea, and abdominal cramping.

Proton pump inhibitors

The proton pump inhibitors, which include omeprazole, esomeprazole and lansoprazole are the most potent suppressors of gastric acid secretion. They inhibit gastric acid secretion by blocking the hydrogen-potassium adenosine triphosphatase enzyme system (the H⁺/K⁺ ATPase enzyme, the 'proton pump') of the gastric parietal cell. They are indicated for short-term management of peptic ulcer disease and gastro-oesophageal reflux disease (GERD), long-term prevention of relapse of GERD, and as part of H. pylori eradication regimens. Following endoscopic treatment of severe peptic ulcer bleeding, an intravenous, high-dose proton pump inhibitor reduces the risk of rebleeding and the need for surgery. In addition, omeprazole is registered for the treatment of Zollinger-Ellison syndrome, and the treatment and prevention of NSAID-associated erosions. In patients who need to continue NSAID treatment after an ulcer has healed, the dose of proton pump inhibitor should normally not be reduced because asymptomatic ulcer deterioration may occur. A proton pump inhibitor can be

used to reduce the degradation of pancreatic enzyme supplements in patients with cystic fibrosis.

Proton pump inhibitors may mask the symptoms of gastric cancer; particular care is required in those presenting with 'alarm features', in such cases gastric malignancy should be ruled out before treatment. Patients at risk of osteoporosis should maintain an adequate intake of calcium and vitamin D, and, if necessary, receive other preventative therapy (see section 6.6). Measurement of serum-magnesium concentrations should be considered before and during prolonged treatment with a proton pump inhibitor, especially when used with other drugs that cause hypomagnesaemia or with digoxin. A proton pump inhibitor should be prescribed for appropriate indications at the lowest effective dose for the shortest period; the need for long-term treatment should be reviewed periodically.

Side-effects of the proton pump inhibitors include gastrointestinal disturbances (including nausea, vomiting, abdominal pain, flatulence, diarrhoea, constipation), and headache. Less frequent side-effects include dry mouth, peripheral oedema, dizziness, sleep disturbances, fatigue, paraesthesia, arthralgia, myalgia, rash, and pruritus. Other side-effects reported rarely or very rarely include taste disturbance, stomatitis, hepatitis, jaundice, hypersensitivity reactions (including anaphylaxis, bronchospasm), fever, depression, hallucinations, confusion, gynaecomastia, interstitial nephritis, hyponatraemia, hypomagnesaemia (usually after 1 year of treatment, but sometimes after 3 months of treatment), blood disorders (including leucopenia, leucocytosis, pancytopenia, thrombocytopenia), visual disturbances, sweating, photosensitivity, alopecia, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

By decreasing gastric acidity, proton pump inhibitors may increase the risk of gastro-intestinal infections (including *Clostridium difficile* infection).

Proton pump inhibitors can increase the risk of fractures, particularly when used at high doses for over a year in the elderly. Rebound acid hypersecretion and protracted dyspepsia may occur after stopping prolonged treatment with a proton pump inhibitor.

Esomeprazole

Capsule, 20mg

Tablet (e/c), 20mg, 40mg

Oral suspension (pediatric), 20mg, 40mg/sachet

Powder for injection, 20mg, 40mg/5ml vial

Indications: see under dose and administration.

Cautions, Drug interactions, Contraindications, Side effects and **Storage** see under omeprazole.

Dose and Administration: **Adult:** *Oral:* Erosive reflux oesophagitis: 40mg once daily for 4-8 weeks. Maintenance to prevent relapse, 20mg once daily. GERD (without oesophagitis): 20mg once daily for 4 weeks. NSAID-associated gastric ulcer: adult over 18 years, 20 mg once daily for 4-8 weeks; prophylaxis in patients with an increased risk of gastroduodenal complications who require continued NSAID treatment, 20 mg daily. Zollinger-Ellison syndrome: adult over 18 years, initially 40 mg twice daily, adjusted according to response; usual range 80-160 mg daily (above 80 mg in 2 divided doses). Eradication of *H. pylori*: esomeprazole 20mg plus amoxicillin 1g and clarithromycin 500mg, all twice daily for 7 days.

IV over at least 3 minutes or by intravenous infusion, adult over 18 years, gastro-oesophageal reflux disease, 40 mg once daily;

symptomatic reflux disease without oesophagitis, treatment of NSAID-associated gastric ulcer, prevention of NSAID-associated gastric or duodenal ulcer, 20 mg daily; continue until oral administration possible. Severe peptic ulcer bleeding (following endoscopic treatment), adult over 18 years, initial intravenous infusion of 80 mg over 30 minutes, then by continuous intravenous infusion 8 mg/hour for 72 hours, then by mouth 40 mg once daily for 4 weeks

Lansoprazole

Capsule, 15mg, 30mg

Tablet, 15mg, 30mg (enteric coated)

Oral suspension (granule), 30mg/sachet

Indications: see under dose and administration.

Cautions, Drug interactions, Contraindications, Side effects and Storage see under omeprazole. Contraindicated in liver impairment.

Dose and Administration: Adult: *Oral:* 30mg daily for 2-8 weeks depending on the condition. Prevention of GERD: 15mg daily for upto 1 year. No efficacy or safety data available for therapy longer than 1 year. Functional dyspepsia: 15mg daily for 2-4 weeks. Eradication of *H. pylori*: see under omeprazole. Heartburn and hyperacidity: 15mg daily for up to 14 days

Omeprazole

Capsule (enclosing e/c granules), 20 mg

Tablet, 20mg (enteric coated)

Indications: management of gastric and duodenal ulcers, reflux oesophagitis and Zollinger Ellison syndrome; also eradication of *H. Pylori* in combination with appropriate antibiotics.

Cautions: pregnancy, lactating women, liver disease; porphyria.

Drug interactions: diazepam, warfarin, phenytoin, fluoxetine, propranolol, indinavir, ketoconazole, and carbamazepine.

Contraindications: known hypersensitivity to the drug, exclude malignancy.

Side effects: diarrhoea, headache, skin rashes, nausea, vomiting, constipation, flatulence and abdominal pain, pruritus, urticaria, dizziness.

Dose and Administration: *Oral: Adult:* Active duodenal ulcer: 20mg/day for 4-8 weeks. Gastric ulcers: 40mg/day for 4-8 weeks. NSAID-associated erosions: 20mg daily for 4-8 weeks. Prevention, 20mg daily. Eradication of *H.pylori*: 20mg twice daily or 40 mg once daily for 7-14 days in combination with appropriate antibiotics (clarithromycin 500 mg twice daily, amoxicillin 1 g twice daily, or as an alternative amoxicillin 1 g twice daily, metronidazole 500 mg (or tinidazole 500mg) twice daily). Zollinger-Ellison syndrome: initially 60mg once daily; dosages range 20- 120mg/day, with doses over 80mg given in 2 divided doses. Gastric acid reduction during general anaesthesia (prophylaxis of acid aspiration), 40 mg on the preceding evening then 40 mg 2–6 hours before surgery. **Child:** Severe ulcerative reflux oesophagitis: 10-20kg, 10mg once daily, increased to 20mg daily if necessary; over 20kg, 20mg once daily, increased to 40mg daily if necessary.

Storage: store at room temperature.

Note:-Taking the medication at least 1 hour before a meal will have maximum benefit.

Pantoprazole

Tablet, 20mg, 40mg (enteric coated)

Indications: benign gastric ulcer, Gastro-oesophageal reflux disease (GERD), duodenal ulcer, duodenal ulcer associated with *Helicobacter pylori*, Prophylaxis of NSAID-associated gastric or duodenal ulcer in patients with an increased risk of

gastroduodenal complications who require continued NSAID treatment, Zollinger–Ellison syndrome (and other hypersecretory conditions).

Cautions: should be used with caution in patients with liver disease, in pregnancy and in breast-feeding. May mask the symptoms of gastric cancer; particular care is required in those presenting with ‘alarm features in such cases gastric malignancy should be ruled out before treatment, renal impairment

Contraindications: sensitivity to pantoprazole, hepatic disease

Side effects: gastro-intestinal disturbances (including nausea, vomiting, abdominal pain, flatulence, diarrhoea, constipation), and headache. Less frequent side-effects include dry mouth, peripheral oedema, dizziness, sleep disturbances, fatigue, paraesthesia, arthralgia, myalgia, rash, and pruritus. And also see the above note.

Dose and administration: benign gastric ulcer: oral: adult over 18 years, 40 mg daily in the morning for 4 weeks, continued for further 4 weeks if not fully healed.

Gastro-oesophageal reflux disease (GERD): adult and child over 12 years: 20–40 mg daily in the morning for 4 weeks, continued for further 4 weeks if not fully healed; maintenance 20 mg daily, increased to 40 mg daily if symptoms return. Duodenal ulcer: adult over 18 years: 40 mg daily in the morning for 2 weeks, continued for further 2 weeks if not fully healed. Duodenal ulcer associated with *Helicobacter pylori* (eradication): pantoprazole 40mg twice daily + clarithromycin 250mg twice daily + metronidazole 400mg twice daily. If a patient has been treated with metronidazole for other infections pantoprazole 40mg twice daily + amoxicillin 1g twice daily + clarithromycin 500mg three times daily. Prophylaxis of NSAID-associated gastric or duodenal ulcer in patients with an increased risk of gastroduodenal complications who require continued NSAID treatment: adult over 18 years: 20 mg daily.

Zollinger–Ellison syndrome (and other hypersecretory conditions): adult over 18 years: initially 80 mg once daily adjusted according to response (elderly max. 40 mg daily); daily doses above 80 mg given in 2 divided doses

Bismuth compounds

Bismuth compounds have been used for their antacid action and for their mildly astringent action in various gastro-intestinal disorders, including diarrhoea and dyspepsia. Tripotassium dicitratobismuthate and the subsalicylate formulations are active against *H. Pylori* and commonly used as part of a multi drug regimen for *H. Pylori* eradication to reduce the risk of duodenal ulcer recurrence. Excessive or prolonged use may lead to bismuth accumulation and toxicity, including renal failure, liver damage, and encephalopathy.

Bismuth subsalicylate

Liquid, 262 mg/15ml

Tablet, 300 mg

Indications: as part of a multidrug regimen for *H.pylori* eradication to reduce the risk of duodenal ulcer recurrence.

Cautions: patients taking aspirin, children < 3 years of age and those with viral illness.

Drug interactions: warfarin, aspirin, hypoglycemics, tetracyclines and uricosurics.

Contraindications: hypersensitivity to the medicine, severe GI bleeding, history of coagulopathy, pregnancy (3rd trimester), renal impairment.

Side effects: anxiety, confusion, headache, discoloration of the tongue, grayish black stools, hearing loss, tinnitus, nausea and vomiting.

Dose and Administration:Adult: *Oral:* 524mg four times/day with meals and at bedtime; requires combination therapy.

Storage: store in airtight containers and protect from light.

Tripotassium Dicitratobismuthate

Liquid, 120 mg/5ml

Tablet, 120 mg

Indications: used as a mucosal protectant for the treatment of peptic ulcer disease; active against *Helicobacter pylori* and has been used as triple therapy (with metronidazole and either tetracycline or amoxicillin) to eradicate this organism and thereby prevent relapse of duodenal ulcer.

Cautions, Drug interactions, Contraindications, Side effects and Storage see under bismuth subsalicylate.

Dose and Administration: Adult: *Oral:* Gastric and Duodenal ulceration: 240mg twice daily or 120mg four times daily before meals for 4 weeks, extended to 8 weeks if necessary. When used as part of triple therapy 120mg 4 times daily for 2 weeks.

Storage: store in airtight containers and protect from light.

Sucralfate

Sucralfate, a sucrose hydrogen sulphate aluminium complex, is a mucosal protective agent. It has a local protective action on the ulcer base, without the side-effects that may occur with other systemic agents. In the stomach a paste-like gel is formed from a reaction with HCl, which adheres to the base of ulcer craters (both in the stomach and duodenum), protecting ulcer epithelium from ulcerogenic substances such as gastric acid, pepsin and bile. It also directly adsorbs bile and pepsin. Sucralfate requires a strict, frequent administration dosage regimen which may produce problems with compliance, but if used correctly, its efficacy compares favourably with that of other ulcer-healing agents.

Sucralfate

Tablet, 1 g (Scored)

Indications: for treatment of gastric and duodenal ulcers, chronic gastritis and reflux oesophagitis.

Caution: renal impairment.

Drug interactions: other antacids, tetracyclines, phenytoin, oral anticoagulants, digoxin, cimetidine.

Contraindications: hypersensitivity of the medicine.

Side effects: constipation, diarrhoea, nausea, abdominal discomfort and indigestion.

Dose and Administration: **Adult:***Oral:* 1g 4 times daily, 1 hour before meals and at bedtime. In *duodenal ulcer*, 2g twice daily has also been shown to be effective. Maintenance 1g twice daily, half an hour before morning and evening meals.

Storage: store at room temperature.

1.3. Antispasmodics and other medicines altering gut motility.

Antispasmodic medicines are used to treat symptoms such as pain and spasm in irritable bowel syndrome (IBS). There are two main types: Antimuscarinics such as hyoscine, atropine, propantheline; and Smooth muscle relaxants (medicines believed to be direct relaxants of intestinal smooth muscles). Intestinal antispasmodics have the major functions of muscle relaxation and convulsion control, thus alleviating spasmodic pain. The smooth muscle relaxant properties of antimuscarinics and other antispasmodic medicines may be useful in IBS and diverticular diseases. The Smooth muscle relaxant properties of antimuscarinic (formerly termed 'anticholinergics') and other antispasmodic medicines (e.g. Camylofin Hydrochloride) may be useful in some forms of dyspepsia, in IBD and in diverticular disease. Other indications of antimuscarinic medicines include arrhythmias, asthma and airways disease, motion sickness, parkinsonism, urinary incontinence, mydriasis and cycloplegia, premedication and as an antidote to organophosphorous poisoning.

Antimuscarinics that are used for gastro-intestinal smooth muscle spasm include the tertiary amines atropine sulphate and scopolamine (Hyoscine) hydrobromide and the quaternary ammonium compounds scopolamine (Hyoscine) butylbromide and propantheline bromide.

Antimuscarinics are commercially available in combination with phenothiazines, or benzodiazepines or other anxiolytics (e.g. chlordiazepoxide + clidinium bromide) for the benefit of its supportive role in patients with IBD who respond to sedatives or in some patients with peptic ulcer disease.

The side effects frequently associated with the use of antimuscarinics include xerostoma (dry mouth), blurred vision, cycloplegia, mydriasis, photophobia, anhidrosis, urinary hesitancy and retention, tachycardia, palpitation, and constipation. Side effects that occur occasionally include confusion (particularly in elderly), nausea, vomiting and giddiness.

Antimuscarinics should be used with caution in geriatric patients, and children, and also in patients with hyperthyroidism, hepatic or renal disease, or hypertension, tachyarrhythmias, congestive heart failure, or coronary artery disease; autonomic neuropathy, gastro-esophageal reflux, known or suspected GI infections, diarrhea and mild to moderate ulcerative colitis, and in patients who may be exposed to elevated environmental temperatures or in patients who are febrile.

The medicines are contraindicated in patients with severe ulcerative colitis, obstructive disease of the GI tract, paralytic ileus, or intestinal atony, prostatic enlargement, known hypersensitivity to the medicines, angle-closure glaucoma, obstructive uropathy (caution for patients with partial obstructive uropathy) and myasthenia gravis (unless the

antimuscarinic is used to reduce adverse muscarinic effects of an anticholinesterase agent).

The effect of antimuscarinic agents may be enhanced by the concomitant administration of other medicines with antimuscarinic properties, such as amantadine, some antimuscarinic, butyrophenones and phenothiazine, and tricyclic antidepressants. The reduction in gastric motility caused by antimuscarinic agents may affect the absorption of other medicines.

Atropine Sulphate

Injection, 1 mg/ml in 1ml ampoule

Indications: dyspepsia, irritable bowel syndrome, diverticular disease; preoperative medication to inhibit salivation and secretions; mydriasis and cycloplegia; organophosphate or carbamate insecticide poisoning (section 17); see also notes above.

Cautions, Drug interactions, Contraindications, Side effects;
See notes above

Dose and Administration: Adult: *IM, S.C., I.V:* 0.4 - 0.6 mg every four to six hours. **Child:** *SC:* 0.01 mg/kg of body weight, not to exceed 0.4 mg, every four to six hours.

Storage: at room temperature, protect from freezing.

Chlordiazepoxide + Clidinium Bromide

Tablet, 5 mg + 2.5 mg

Indications: used in the treatment of functional disturbances of GI motility such as irritable bowel syndrome, see also notes above.

Cautions, Drug interactions, Contraindications, Side effects -
see notes above

The precautions and contraindications associated with chlordiazepoxide must be considered (see section 4.2).

Dose and Administrations: Adult: *Oral:* one or two tablets 3 or 4 times daily (i.e. 2.5 or 5 mg of Clidinium bromide 3 or 4 times a day)

Storage: store at room temperature in a tight, light resistant container.

Drotaverine

Tablet, 40 mg

Injection, 40mg/2ml ampoule

Indications: smooth muscle spasm in connection with biliary tract diseases: cholecystolithiasis, cholangiolithiasis, cholecystitis, pericholecystitis, cholangitis, and papillitis. Smooth muscle spasm in connection with urinary tract diseases: nephrolithiasis, ureterolithiasis, pyelitis, cystitis, and cramp of urinary bladder.

Cautions: hypotension, people with lactase insufficiency, galactosaemia.

Drug interactions: phosphodiesterase inhibitors like papverine decrease the antiparkinsonian effect of levodopa.

Contraindications: hypersensitivity reactions; severe hepatic, renal and cardiac insufficiency; children < 1 year of age.

Side effects: gastrointestinal disorders (nausea, constipation); nervous system disorders (headache, dizziness, insomnia); cardiovascular disorders (palpitation, hypotension).

Dose and Administration: Adult: the usual average daily dose is 120-240 mg/day (in 2-3 divided doses).

Child > 1 year old: 40-120 mg/day divided in 2 to 3 doses between 1 and 6 years. 80-200 mg/day divided in 2 to 5 doses over 6 years.

Storage: store at a temperature not exceeding 25 °C.

Scopolamine (Hyoscine) Butylbromide

Drops, 5mg/5ml

Injection, 20mg/ml

Tablet, 10mg

Suppository, 7.5mg, 10mg

Indications: symptomatic relief of visceral spasms of the gastro-intestinal tract, painful spasm of the biliary and genitourinary system, bowel colic and excessive respiratory secretions.

Cautions, Contraindications, Side effect; see notes above

Drug interactions: CNS depressants see also notes above.

Dose and Administrations: **Adult:***Oral:* Smooth muscle spasm: 20mg four times daily; IM or IV (acute spasm and spasm in diagnostic procedures), 20 mg repeated after 30 minutes if necessary. (May be repeated more frequently in endoscopy), maximum 100 mg daily.

Irritable bowel syndrome: 10 mg 3 times daily, increased if required up to 20 mg 4 times daily.**Child:***Oral:* 6-12 years, 10mg 3 times daily; parenteral use not recommended.

Storage: at room temperature, in a well-closed container.

Note: Scopolamine (hyoscine) hydrobromide should not be interchanged with scopolamine butylbromide formulations. Dosages are not equivalent.

Scopolamine (hyoscine) Hydrobromide

Injection, 0.4 mg/ml, 0.6 mg/ml in 1ml ampoule

Tablet, 0.6 mg

Indications: prevention and control of motion sickness, and also used as an adjunct to anesthesia to inhibit salivation and excessive respiratory secretions and to produce sedative and amnesia; see also notes above. Not indicated for peptic ulcer.

Note: Hyoscine butylbromide is preferable to hyoscine hydrobromide in the relief of visceral spasms of the gastro-intestinal tract and pain associated with other smooth muscle spasm.

Cautions, Contraindications, Side effects; see notes above

Drug interactions: CNS depression - producing medications; see notes above.

Dose and Administration: **Adult:** *Oral:* 0.3 mg 30 minutes before a journey to prevent motion sickness then 0.3 mg every 6 hours if required up to a maximum of 3 doses in 24 hours; *IM, IV, or SC,* 0.3 to 0.6 mg; if necessary, the dose may be repeated 3 or 4 times daily.

Child: *Oral:* aged 4 to 10 years, 75 to 150 microgram and those over 10 years, 150 to 300 microgram; *IM, IV, or SC,* 0.006 mg/Kg

Storage: store in a light - resistant container at room temperature. Protect from freezing.

Propantheline Bromide

Tablet, 15 mg, 30 mg

Indications: adjunctive treatment of peptic ulcer, irritable bowel syndrome, pancreatitis, ureteral and urinary bladder spasm (urinary frequency); reduce duodenal motility during diagnostic radiologic procedure, gustatory sweating.

Cautions, Drug interactions, Contraindications, Side effects; see notes above.

Dose and Administration: *Oral:* Antisecretory: **Adult:** 15 mg 3 times/day before meals or food and 30mg at bedtime, maximum 120 mg daily. **Child:** 1-2 mg/kg/day in 3-4 divided doses. **Elderly:** 7.5 mg 3 times/day before meals and at bedtime. Antispasmodic: **Adult:** 15mg 3 times/day before meals or food and 30mg at bedtime max. 120 mg daily. **Child:** 2-3mg/kg/day in divided doses every 4-6 hours and at bedtime
Storage: at room temperature in a well closed container.

1.4. Antiemetics

Antiemetics are a diverse group of medicines used to treat or prevent nausea and vomiting, including that associated with

cancer therapy, anaesthesia and surgery, and motion sickness. Antiemetics described here include: the dopamine antagonists such as metoclopramide and chlorpromazine hydrochloride; antihistamines such as dimenhydrinate, meclizine hydrochloride and promethazine hydrochloride; and the phenothiazine thiethylperazine maleate.

The choice of medicine depends partly on the cause of nausea and vomiting. For example, hyoscine (see section 1.3.) or antihistamines are used in motion sickness whereas dopamine antagonists, which act selectively on the chemoreceptor trigger zone, are ineffective for the treatment of motion sickness. Conversely, nausea and vomiting associated with cancer chemotherapy is often hard to control and special regimens have been devised including the use of metoclopramide in high doses and more recently 5 HT₃ antagonists such as ondansetron.

The antihistamines may be slightly less effective than hyoscine against motion sickness but are often tolerated. There is no evidence that any one antihistamine is superior to another but their duration of action and incidence of adverse effects (drowsiness, and antimuscarinic effects) differ. For example dimenhydrinate causes drowsiness more frequently; meclizine has a longer duration of action than scopolamine and most other antihistamines. If a sedative effect is desired promethazine is useful. Promethazine is a phenothiazine that in addition to D₂ dopaminergic blockade, it has pronounced histamine H₁ and muscarinic receptor blocking properties. It is effective in the prevention and treatment of vertigo and motion sickness. Promethazine may be useful in the prevention and treatment of postoperative and drug-induced nausea and vomiting. It has limited effect on chemotherapy induced mild to moderate emesis.

A popular choice of antiemetic is metoclopramide which is effective against nausea and vomiting following surgery and

chemotherapy. It is also effective against radiation-induced nausea and vomiting. Metoclopramide is effective against nausea and vomiting associated with gastrointestinal disorders or migraine. Combining metoclopramide with corticosteroids (such as dexamethasone) can improve its antiemetic effect in chemotherapy-induced nausea and vomiting. Metoclopramide may be useful in the management of gastro-oesophageal reflux disease and gastroparesis, as well as preoperatively in the prevention of aspiration syndromes. It is also used to facilitate intubation of the small bowel during radiographic examinations. Metoclopramide may cause acute dystonic reactions with facial and skeletal muscle spasms and oculogyric crises. These reactions are most common in the young (especially girls and young women) and the elderly; they occur shortly after the start of treatment and subside within 24 hours of medication withdrawal.

Granisetron, ondansetron, and palonosetron are specific 5HT₃-receptor antagonists which block 5HT₃ receptors in the gastro-intestinal tract and in the CNS. Granisetron and ondansetron are of value in the management of nausea and vomiting in patients receiving cytotoxics and in postoperative nausea and vomiting. Palonosetron is licensed for prevention of nausea and vomiting associated with moderately or highly emetogenic cytotoxic chemotherapy.

Antiemetics are unnecessarily and sometimes harmful when the cause can be treated, e.g. as in diabetic ketoacidosis, or in excessive digoxin or antiepileptic dosage. Pregnancy induced nausea and vomiting or “morning sickness” is common in the first trimester, but generally does not require medicine therapy. Dietary modification such as taking of small frequent carbohydrate meals often helps. A few pregnant women may require a short-term promethazine treatment.

Chlorpromazine Hydrochloride

Drop, 25 mg/ml

Injection, 25mg/1ml, 25mg/2ml, 50mg/2ml in 1ml and 2ml ampoule

Syrup, 25 mg/5 ml

Tablet, 25 mg, 100 mg (film/sugar coated)

Indications: For the prevention and control of severe nausea and vomiting, other indications (see section 4.2)

Note: It should not be used for motion sickness

Cautions, Drug interactions, Contraindications, and Side effects; see section 4.2 under chlorpromazine

Dose and Administration: Adult: Oral: 12.5 – 25mg every 4 – 6 hours, as necessary. Slow, deep I.M: 25 mg as a single dose, the dosage being increased to 25 – 50mg every 3 – 4 hours until vomiting stops; it is then given orally if necessary. **Child** (6 month and over): *Oral or slow, deep I.M:* 0.55mg/kg every 6 – 8 hour as necessary.

Storage: at room temperature. Protect from light and freezing. Do not use if solution is markedly discolored or if a precipitate is present.

Note: Patients should remain lying down for at least 30 minutes after injection.

Dimenhydrinate

Tablet, 50 mg

Indications: prevention and treatment of nausea, vomiting and/or vertigo associated with motion sickness; see also notes above.

Cautions: as for meclizine hydrochloride; also pregnant and nursing mothers.

Drug interactions: as for meclizine hydrochloride; ototoxic drugs such as aminoglycoside antibiotics (dimenhydrinate may mask the early symptoms of ototoxicity)

Side effects: as for meclizine hydrochloride; also, tinnitus.

Dose and Administration: Adult: *Oral*, 50 to 100 mg every four to six hours. **Child:** *Oral*, 6-12 Years of age, 25 to 50 mg every six to eight hours as needed, not to exceed 150 mg per day; 2-6 years of age, 12.5 to 25 mg every six to eight hours as needed, not to exceed 75 mg per day.

Storage: at room temperature, in a well-closed container.

Note: Oral dosage forms used for motion sickness should be taken 30 minutes before motion

Domperidone

Tablets, 10 mg

Indications: nausea and vomiting, dyspepsia, gastro-oesophageal reflux

Cautions: children, renal impairment, pregnancy, breast feeding

Drug Interactions: antimuscarinics, bromocriptine, cabergoline, erythromycin, ketoconazole, opioid analgesics, telaprevir.

Contra-indications: prolactinoma; if increased gastro-intestinal motility harmful, hepatic impairment

Side effects: gastro-intestinal disturbances (including cramps) and hyperprolactinaemia; ventricular arrhythmias, agitation, drowsiness, nervousness, seizures, extrapyramidal effects, headache, and rashes; also reported QT-interval prolongation.

Dose and Administration: *oral Adult and child body-weight over 35 kg*, 10–20 mg 3–4 times daily; max. 80 mg daily; **child body-weight up to 35kg** (nausea and vomiting only), 250–500 micrograms/kg 3–4 times daily; max. 2.4 mg/kg daily.

Granisetron Hydrochloride

Tablet, 2mg

Indications: prevention and treatment of nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy and postoperative nausea and vomiting

Drug Interactions: granisetron may enhance the hypotensive effect of apomorphine.

Contraindications: hypersensitivity to medicine, other 5-HT₃ receptor antagonists or any component of the formulation.

Sideeffects: constipation, nausea, diarrhoea, vomiting, abdominal pain; headache, drowsiness, asthenia; fever; rarely hepatic dysfunction, chest pain, arrhythmia; very rarely anorexia, dizziness, insomnia, agitation, movement disorders, and rash.

Dose and Administration: Nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy: Oral, 1–2 mg within 1 hour before start of treatment, then 2 mg daily in 1–2 divided doses during treatment; when intravenous infusion also used, maximum combined total 9 mg in 24 hours; **CHILD:** 20 micrograms/kg (maximum 1 mg) within 1 hour before start of treatment, then 20 micrograms/kg (maximum 1 mg) twice daily for up to 5 days during treatment. By intravenous injection (diluted in 15 mL sodium chloride 0.9% and given over not less than 30 seconds) *or* by intravenous infusion (over 5 minutes), prevention, 3 mg before start of cytotoxic therapy (up to 2 additional 3-mg doses may be given within 24 hours); treatment, as for prevention (the two additional doses must not be given less than 10 minutes apart); max. 9 mg in 24 hours; child, by intravenous infusion, (over 5 minutes), prevention, 40 micrograms/kg (max. 3 mg) before start of cytotoxic therapy; treatment, as for prevention—one additional dose of 40 micrograms/kg (max. 3 mg) may be given within 24 hours (not less than 10 minutes after initial dose). Postoperative nausea and vomiting: by intravenous injection (diluted to 5 mL and given over 30 seconds), prevention, 1 mg before induction of anaesthesia; treatment, 1 mg, given as for prevention; maximum 2 mg in one day; **child:** not recommended

Storage: Store between 20-25⁰C; Keep container closed tightly. Protect from light

Meclizine Hydrochloride

Tablet, 12.5 mg, 25 mg

Indications: prevention and treatment of nausea, vomiting and/or vertigo associated with motion sickness; see also notes above.

Cautions: warn the patients not to perform hazardous activities requiring mental alertness or physical condition; patients with angle closure glaucoma or prostatic hypertrophy bladder neck obstruction, coma, Jaundice; use with caution in hot weather, and during exercise. Elderly may be at risk for anticholinergic side effects

Drug interactions: alcohol, CNS depressants including barbiturates, tranquilizers, medicines with anti cholinergic effects including tricyclic antidepressants.

Contraindications: hypersensitive to the medicine, pregnant women, children younger than 12 years of age.

Side effects: drowsiness, fatigue and rarely blurred vision, dryness of mouth, nose and throat, palpitations, thickening of bronchial secretions, increase appetite, weight gain, arthralgia, and pharyngitis.

Dose and Administration: Adult and Child (>12 years of age): Motion sickness (prophylaxis and treatment): Oral: 25 to 50 mg one hour before travel. Dose may be repeated every twenty-four hours as needed. Vertigo (prophylaxis and treatment): Oral: 25 to 100 mg a day as needed; in divided doses.

Storage: at room temperature, in a well - closed container.

Metoclopramide Hydrochloride

Drop, 0.2 mg/drop

Injection, 5 mg/ml, 5ml/2ml in 2 ml ampoule

Syrup, 5mg/5ml

Tablet, 10 mg

Indications: nausea and vomiting in gastrointestinal disorders and treatment with cytotoxics or radiotherapy; gastro-oesophageal reflux; gastroparesis; premedication and postoperatively; aid to gastrointestinal intubation; nausea and vomiting in migraine.

Cautions: elderly, children and young patients are at increased risk of extrapyramidal reactions; hepatic and renal impairment; may mask underlying disorders such as cerebral irritation, avoid for 3 - 4 days after gastrointestinal surgery; pregnancy; breast feeding; parkinson disease; depression; porphyria; patients should be warned that the drug may impair their ability to perform activities requiring mental alertness or physical coordination.

Drug interactions: alcohol, barbiturates, CNS depressants; phenothiazines and butyrophenones, lithium, antidepressants, antiepileptics, and sympathomimetics; antimuscarinic agents and opioid analgesics; digoxin, aspirin or paracetamol, suxamethonium, bromocriptine.

Contraindications: convulsive disorders, gastrointestinal hemorrhage, mechanical obstruction or perforation; pheochromocytoma; 3-4 days after gastrointestinal surgery; hypersensitivity to the medicine.

Side effects: extrapyramidal symptoms (especially in children and young adults), tardive dyskinesia on prolonged use; hyperprolactinaemia; drowsiness, restlessness, dizziness, headache, diarrhoea, depression, hypotension and hypertension; rarely, neuroleptic malignant syndrome; cardiac conduction abnormalities following IV administration.

Dose and Administration: Nausea and vomiting, gastro-oesophageal reflux, gastroparesis:

Adult: Oral or IM, or slow IV injection: 10 mg 3 times daily; young adult: 15 - 19 years (under 60 Kg) 5 mg 3 times daily; **Child:** Oral, or IM, or slow IV injection: up to 1 year (up to 10 Kg) 1 mg twice daily, 1 - 3 years (10-14 Kg) 1 mg 2 - 3 times daily, 3 - 5 years (15 - 19 Kg) 2 mg 2 - 3 times daily, 5 - 9 years (20-28 Kg.) 2.5 mg 3 times daily, 9 - 14 years (30 Kg and over) 5 mg 3 times daily. (Usual maximum 500 micrograms/Kg daily, particularly for children and young adults); **Pre-medication: Adult,** by slow I.V., 10 mg as a single dose.

Aid to gastrointestinal intubation, Orally, or IM or by Slow intravenous injection: **Adult:** 10 - 20 mg as a single dose 5 - 10 minutes before examination; **Young Adult** (15 - 19 years) 10mg; **Child** under 3 years 1 mg, 3 - 5 years 2 mg, 5 - 9 years 2.5 mg, 9 - 14 years 5 mg.

Storage: at room temperature, protect from light.

Ondansetron

Solution for injection and Infusion, 4mg/2ml

Indications: For the prevention of nausea and vomiting associated with moderately-to highly emetogenic cancer chemotherapy, radiotherapy in patients receiving total body irradiation or fractions to the abdomen and postoperation. Also used for the treatment of postoperative nausea and vomiting.

Cautions: Avoid concomitant use of medicines that prolong QT interval; sub acute intestinal obstruction; adenotonsillar surgery, In patients with cardiac rhythm or conduction disturbances, in patients treated with anti-arrhythmic agents or beta-adrenergic blocking agents and in patients with significant electrolyte disturbance, in patients with hepatic impairment, pregnancy, breast feeding.

Drug interactions: Apomorphine, CYP3A4-inducers (such as aminoglutethimide, carbamazepine, nafcillin, nevirapine, Phenobarbital, phenytoin and rifampicin), tramadol

Contraindications: Hypersensitivity to medicine, other selective 5-HT₃ antagonists, or any component of the formulation.

Side effects: Constipation; headache; flushing; injection site-reactions; less commonly hiccups, hypotension, bradycardia, chest pain, arrhythmias, movement disorders, seizures; on intravenous administration, rarely dizziness, transient visual disturbances (very rarely transient blindness).

Dose and Administration: Moderately emetogenic chemotherapy or radiotherapy, **Adults over 18 years**, by mouth, 8 mg 1–2 hours before treatment or by intramuscular injection or slow intravenous injection, 8 mg immediately before treatment then by mouth, 8 mg every 12 hours for up to 5 days or by rectum, 16 mg daily for up to 5 days. Severely emetogenic chemotherapy: **ADULT over 18 years**, by intramuscular injection or slow intravenous injection, 8 mg immediately before treatment, where necessary followed by 2 further doses of 8 mg at intervals of 2–4 hours (or followed by 1 mg/hour by continuous intravenous infusion for up to 24 hours) then by mouth, 8 mg every 12 hours for up to 5 days or by rectum, 16 mg daily for up to 5 days; Alternatively, by intravenous infusion over at least 15 minutes, 32 mg immediately before treatment or by rectum, 16 mg 1–2 hours before treatment then by mouth, 8 mg every 12 hours for up to 5 days or by rectum, 16 mg daily for up to 5 days. Chemotherapy-induced nausea and vomiting: **CHILD 6 months–18 years**: by intravenous infusion over 15 minutes, 5 mg/m² (max. 8 mg) immediately before chemotherapy, then for body-surface area less than 0.6 m² 2 mg by mouth every 12 hours for up to 5 days; for body-surface area 0.6 m² or greater 4 mg by mouth every 12 hours for up to 5 days; max. total daily dose 32 mg; alternatively, by intravenous infusion over 15 minutes, 150 micrograms/kg (max. 8 mg) immediately before

chemotherapy repeated at intervals of 4 hours for 2 further doses, then for body-weight 10 kg or less 2 mg by mouth every 12 hours for up to 5 days; for body-weight over 10 kg 4 mg by mouth every 12 hours for up to 5 days; maximum total daily dose 32 mg. Prevention of postoperative nausea and vomiting: by mouth, 16 mg 1 hour before anaesthesia or 8 mg 1 hour before anaesthesia followed by 8 mg at intervals of 8 hours for 2 further doses; alternatively, by intramuscular or slow intravenous injection, 4 mg at induction of anaesthesia; **Child 1 month–18 years:** by slow intravenous injection over at least 30 seconds, 100 micrograms/kg (max. 4 mg) before, during, or after induction of anaesthesia. Treatment of postoperative nausea and vomiting: by intramuscular or slow intravenous injection, 4 mg; **Child 1 month–18 years,** by slow IV injection over at least 30 seconds, 100 micrograms/kg (max. 4 mg)
Storage: store between 2 and 30 °C

Promethazine Hydrochloride

Elixir, 5 mg/5 ml.

Injection, 25 mg/ml, 25/2ml in 1 ml and 2 ml ampoules

Suppository, 25 mg, 50 mg

Tablets, 10 mg, 25 mg (film/sugar coated)

Indications: control of nausea, vomiting, and vertigo of various causes, as a sedative and hypnotic, and as a common ingredient of cough and cold preparations; also see notes above.

Cautions: As for under Meclizine Hydrochloride, intravenous injection of promethazine hydrochloride must be given slowly and extreme care must be taken; should not be given by subcutaneous injection, avoid in porphyria.

Drug interactions: As for meclizine hydrochloride; epinephrine, extrapyramidal reaction causing medications, levodopa, metrizamide and monoamine oxidase (MAO) inhibitors including furazolidone, procarbazine, and selegiline.

Contraindications: patients who have exhibited hypersensitivity to the medicine; also in those who have received large doses of CNS depressants and/or in those who are comatose, in epileptic seizures.

Side effects: see under Meclizine Hydrochloride, and blood dyscrasias, sedative effect is more pronounced.

Dose and Administration: Antiemetic: Oral: **Adult:** 25 mg initially, then 10 to 25 mg every 4 - 6 hours as needed. **Child** (>2 years of age): 0.25 to 0.5 mg per Kg of body weight every 4 to 6 hours or 10 to 25 mg every four to six hours as needed. **IM** or **IV:** **Adult:** 12.5 to 25 mg every 4 hours as needed. **Child** (> 2 years of age): 0.25 to 0.5 mg per Kg of body weight every 4 to 6 hours as needed. **Rectal:** **Adult:** 25mg initially, then 12.5 to 25mg every 4 to 6 hours as needed. **Child** (> 2 years of age): 0.25 to 0.5mg per kg of body weight, or 12.5 to 25mg every 4 to 6 hours as needed.

Note: For motion sickness, the initial 25 mg dose should be taken one half to one hour before travel, and the dose repeated 8 - 12 hours later, if necessary.

Antivertigo agent: Oral: **Adult:** 25mg 2 times a day as needed. **Child** (> 2 years of age): 0.5mg to 1mg per kg of body weight or 10 to 25mg 2 times a day as needed.

Rectal: **Adult:** 25mg 2 times a day as needed. **Child** (> 2 years of age): 0.5mg per kg of body weight, or 12.5 to 25mg 2 times a day as needed.

Storage: Suppositories: store between 2 and 8°c, in a tight, light-resistant container. Tablet & Injection - at room temperature protect from light and from freezing.

Thiethylperazine Maleate

Injection, 6.5 mg/ ml

Suppository, 6.5 mg

Tablet, 6.5 mg (film/ sugar coated)

Indications: for the control of nausea and vomiting associated with surgical procedures and cancer therapy.

Cautions, Drug interactions, Contraindications, and Side effects; as for Meclizine Hydrochloride

Dose and Administration: Adult: Oral, Rectal, IM, 10mg 1-3 times a day. **Child:** Safety and efficacy has not been established.

Storage: protect from light. It should be stored in tight, light-resistant container at room temperature.

1.5. Cathartics and Laxative

Laxatives (purgatives or cathartics) promote defaecation and are used in the treatment of constipation and for bowel evacuation before investigational procedures, such as endoscopy or radiological examination, or before surgery. Before prescribing laxatives, it is important to be sure that the patient is constipated and that the constipation is not secondary to an underlying undiagnosed complaint. It is also important that the patient understands that bowel habit can vary considerably in frequency without doing harm. For example, some people consider themselves constipated if they do not have a bowel movement each day. A useful definition of constipation is the passage of hard stools less frequently than the patient's own normal pattern; this should be explained to the patient since misconceptions about bowel habits have led to excessive laxative use, which in turn has led to hypokalaemia.

Laxatives should generally be avoided except where straining will exacerbate a condition such as angina or increase the risk of rectal bleeding, as in haemorrhoids.

Laxatives are of value in medicine-induced constipation, for the expulsion of parasites after anthelmintic treatment (section 6.1) and to clear the alimentary tract before surgery and radiological procedures. Prolonged treatment of constipation is

sometimes necessary. Laxatives are usually subdivided into several categories including the bulk forming laxatives such as cellulose derivatives, psyllium preparations; stimulant laxatives (contact laxatives) that include anthraquinone-containing agents such as senna and cascara, diphenylmethane derivatives such as bisacodyl and also other miscellaneous agent such as castor oil, osmotic laxatives such as glycerin, lactulose and the saline laxative such as magnesium sulphate are also included in this group; faecal softeners (emollient laxatives) include sodium salt of docusate and the lubricant laxative liquid paraffin. Bulk forming laxatives relieve constipation by causing retention of fluid and an increase in faecal mass resulting in stimulation of peristalsis; the full effect may take some days to develop and patients should be told this. They are of particular value in those with small hard stools, but should not be required unless fiber cannot be increased in the diet. They are useful in the management of patients with colostomy, ileostomy, haemorrhoids and fissure, chronic diarrhoea associated with diverticular disease, irritable bowel syndrome and as adjuncts in ulcerative colitis. Owing to their hydrophilic nature, bulk laxatives may also be used to control acute diarrhoea and to regulate the consistency of effluent in colostomy patients. Adequate fluid intake must be maintained to avoid intestinal obstruction. Unprocessed wheat bran taken with food or fruit juice, is a most effective bulk forming preparation. Methylcellulose is useful in patients who cannot tolerate bran. Methylcellulose also acts as a faecal softener.

Stimulant laxatives which increase intestinal motility and often cause abdominal cramp; they should be avoided in intestinal obstruction. Prolonged use of stimulant laxatives can precipitate the onset of an atonic non-functioning colon and hypokalaemia; however, prolonged use may be justifiable in some circumstances. Glycerin suppositories act as a rectal

stimulant by virtue of the mildly irritant action of glycerin. Powerful stimulants such as cascara and castor oil are obsolete. Docusate sodium probably acts both as a stimulant and as a softening agent. This group of laxatives is most commonly associated with abuse. In general, use of stimulant laxatives should be avoided in children younger than 6-10 years of age unless prescribed by physician.

Faecal softeners such as liquid paraffin, which is the classical lubricant, lubricate and soften impacted faeces. Bulk laxatives and non-ionic surfactant 'wetting' agents e.g. docusate sodium also have softening properties. Such medicines are useful for oral administration in the management of haemorrhoids and anal fissures.

Osmotic laxatives act by retaining fluid in the bowel by osmosis or by changing the pattern of water distribution in the faeces. Saline purgatives such as magnesium salts are useful where rapid bowel evacuation is required. Lactulose is a semi-synthetic disaccharide, which is not absorbed from the gastrointestinal tract. It produces osmotic diarrhoea of low faecal PH, and discourages the proliferation of ammonia producing organisms. It is therefore useful in the treatment of hepatic encephalopathy.

Bulk-forming laxatives, stool softeners, or mineral oil are preferred to other laxatives in patients with conditions in which straining at defecation should be avoided (e.g. myocardial infarction, vascular diseases, diseases of the anus or rectum, hernias, recent rectal surgery). Oral stool softeners or mineral oil are preferred to bulk-forming laxatives to ease evacuation of feces in patients with constipation associated with hard, dry stools. Many clinicians consider the stool softeners to be the treatment of choice in childhood constipation associated with hard, dry stools and to be safer and more efficacious than

mineral oil for conditions in which straining at defecation is to be avoided.

Bulk-forming and stimulant laxatives have been used to treat constipation that occurs following prolonged bed rest or hospitalization.

Saline laxatives have been used to eliminate parasites and toxic anthelmintics prior to and/or after therapy with some anthelmintics. However, most clinicians agree that with the newer anthelmintics use of laxatives to eliminate parasites or the anthelmintic is not necessary, may complicate identification of the parasite, and may be harmful to the patient.

Bisacodyl

Tablet, 5 mg

Suppository, 5 mg, 10 mg

Indications: constipation and for bowel evacuation.

Cautions: inflammatory bowel disease, the suppositories should be used with caution in patients with rectal fissures or ulcerated haemorrhoids; it should be preferably avoided in children. See also notes above.

Contraindications: appendicitis, rectal bleeding, congestive heart failure, hypertension, diabetes mellitus, intestinal obstruction or undiagnosed abdominal symptoms. See also notes above.

Side effects: abdominal discomfort (such as colic or cramp); gripping (tablets); local irritation (suppositories). Diarrhoea with excessive loss of water and electrolytes may occur on prolonged use. See also notes above.

Dose and Administration: Oral:**Adult** and **Child (>12 years):** 5-15mg daily as a single dose and up to 30mg when complete evacuation of bowel is required. **Child (> 6 years):** 5-10mg or 0.3 mg/kg daily as a single dose at bedtime or before breakfast. Rectal: **Adult** and **Child (>12 years):** 10mg daily as a single

dose. **Child** 2-11 years: 5-10mg daily given as a single dose.
Child (< 2 years of age): 5mg daily as a single dose.

Note: It is usually effective within 6 to 12 hours following oral administration and within 15 to 60 minutes following rectal administration. Oral bisacodyl should be administered the evening before a morning bowel-movement is desired. Swallow the enteric-coated bisacodyl whole and not crushed to avoid gastric irritation. Take each dose with a full glass of water. Rectal bisacodyl suppositories and enemas may be administered at the time a bowel movement is desired.

Storage: at room temperature in a well-closed container.

Cascara Sagrada

Tablet, 125 mg

Indications: constipation

Cautions: care should be taken in patients with inflammatory bowel disease prolonged use should be avoided, it should be preferably avoided in children; avoid habitual use; See also notes above.

Contraindications: see notes under bisacodyl

Side effects: mild abdominal discomfort, diarrhoea (prolonged use), reversible melanosis coli, the urine may be coloured yellowish brown or red and also see notes above.

Dose and Administrations: **Adult** and **Child** (10 years and over): 0.3 - 1g, usually at bedtime. A laxative effect usually occurs 6 to 8 hours after administration. As discussed above such laxatives have a limited role in the management of constipation.

Storage: at room temperature, in airtight container. Protect from light.

Castor oil

Liquid, 30ml

Indications: to facilitate defecation in geriatric patients with diminished colonic motor response; constipation occurring secondary to idiopathic slowing of transit time, to constipating drugs or to irritable bowel or spastic colon syndrome; neurologic constipation and to empty the bowel prior to surgery or radiologic proctoscopic or sigmoidoscopic procedure.

Cautions: avoid prolonged use, and use in children up to six years of age; elderly patient.

Drug interactions: avoid concomitant use of castor oil with potassium sparing diuretics, potassium supplements.

Contraindications: pregnancy, acute abdominal pain, nausea, vomiting or other symptoms of appendicitis or undiagnosed abdominal pain, intestinal obstruction.

Side effects: abdominal discomfort, nausea, mild cramp, gripping or faintness, excessive irritation of the colon, violent purgation.

Dose and Administration: Oral: Constipation: **Adult:** 15 ml daily; **Child** (< 2 years) 1-5 ml daily; (> 2 years) 5 - 15 ml daily. For total colonic evacuation prior to surgery or radiologic sigmoidoscopic or proctoscopic procedure administered as a single dose about 16 hours before the procedures. **Adult and Child** (≥12 years): 15 - 60 ml; **Child**, 2 - 11 years: 5 -15 ml; (< 2 years) 1 - 5 ml.

Storage: at room temperature in a tight container and in dry place. Protect from freezing.

Note: Drink increased fluid. Take each dose with a full glass of water or other liquid.

Diocetyl sodium Sulphosuccinate (Docusate Sodium)

Tablet, 50 mg, 100 mg

Syrup, 4 mg/ml

Indications: constipation and as an adjunct in abdominal radiological procedure; prophylactically in patients who should

not strain during defecation, such as those with an episiotomy wounds, painful thrombosed hemorrhoids fissures or perianal abscesses, body wall and diaphragmatic hernias, anorectal stenosis, or postmyocardial infarction.

Cautions: do not give with liquid paraffin.

Drug interactions: potassium sparing diuretics, potassium supplement, danthrol, mineral oil, phenolphthalein, aspirin.

Contraindications: symptoms of appendicitis, undiagnosed rectal bleeding, congestive heart failure, hypertension, intestinal obstruction, sensitivity to docusate.

Side effects: undetermined allergies (skin rash), stomach and/or intestinal cramping.

Dose and Administration: Oral: **Adult:** up to 500 mg daily in divided doses; **Child** over 6 months: 12.5 mg 3 times, daily; 2 – 12 years: 12.5 to 25 mg 3 times daily (use pediatric oral solution only).

Note: Take each dose with a full glass of water or other liquid.

Storage: at room temperature, in a dry place and in a tight container.

Glycerin (Glycerol)

Suppository, 1 g, 1.346 g, 2 g, 2.76 g

Indications: constipation, especially in children; see also notes above.

Cautions: avoid habitual use.

Contraindications: as for bisacodyl

Side effects: rectal discomfort such as irritation, burning and pain may occur rarely.

Dose and Administration: Rectal: **Adult:** 2 – 4g suppository; **Child:** 2g suppository; **Infant:** 1g suppository.

Note: The suppositories should be moistened with water before insertion.

Storage: In a cool place, in airtight containers.

Lactulose

Enema

Syrup

Indications: constipation (may take up to 48 hours to act); hepatic encephalopathy (portal systemic encephalopathy).

Cautions: lactose intolerance, diabetic patients (presence of some free galactose and lactose)

Contraindications: as for bisacodyl; galactosaemia, intestinal obstruction, hypersensitivity to lactulose.

Side effects: flatulence, cramps, and abdominal discomfort, nausea & vomiting.

Dose and Administration:Adult: Constipation: Oral: Initially 10-20g (15-30ml) daily in single or 2 divided doses; increased up to 40g (60ml) daily if necessary. Maintenance 7 to 10g (10-15ml) daily.

Hepatic encephalopathy: Oral: initially 60-100g (90-150ml) daily in 3-4 divided doses; doses should be adjusted after 1-2 days to produce 2-3 soft stools daily, or to keep the PH of the stool at about 5.

Child: Constipation: Oral: under 1 year, 2.5ml; 1-5 year, 5ml; 6-12 years, 10ml twice daily, gradually reduced.

Storage: in airtight container preferably at a temperature between 2⁰c and 30⁰c.

Liquid parafin, Heavy

Indication: constipation associated with stricture of colon.

Cautions: avoid prolonged use and caution should be taken in children, pregnant women, elderly patients; caution is also recommended with bedridden patients who may develop lipid pneumonia from aspiration of mineral oil.

Drug interactions: avoid concomitant administration of the oil with fat soluble vitamins (A, D, E, K), carotene, oral

contraceptive, coumarine and indandione derivative anticoagulants.

Contraindications: as for bisacodyl; also colostomy, ileostomy.

Side effects: seepage of mineral oil that may cause soiling of the skin and clothing, anal irritation, pruritis, impair normal rectal reflex mechanism, granulomatous reaction caused by absorption of small quantities of liquid paraffin, lipoid pneumonia.

Dose and Administration: Oral: 5-20ml, when required.

Storage: at room temperature and protect from freezing.

Magnesium sulphate

Crystal

Indications: rapid bowel evacuation in preparations for rectal and bowel examination, and selective colon surgery; to hasten excretion of poisonous substances, except acids or alkalis, from the G.I.T.

Cautions: care should be taken in patients with renal impairment, hepatic impairment, in elderly and debilitated patients.

Drug interactions: coumarin or indandione derivative anticoagulants, digitalis glycoside, chlorpromazine, sodium polystyrene sulfonate, and tetracycline.

Contraindications: as for bisacodyl; acute GI conditions, colostomy, ileostomy, (increased risk of electrolyte or fluid imbalance); dehydration, renal impairment.

Side effects: colic, cramping, diarrhea, gas formation, increased thirst, electrolyte imbalance (confusion, irregular heart beat, muscle cramp, unusual tiredness or weakness).

Dose and Administration: Oral: **Adult:** 5 – 10 gm in a tumberful of water preferably before breakfast (for rapid bowel evacuation).

Child: older than 6 years of age 5 – 10 gms dissolved in 120 ml of water. *Note: take each dose with a full glass of water. Dissolve or mix in water or other liquid before taking.*

Storage: at room temperature in a well-closed container.

Methyl Cellulose

Tablet, 500 mg

Indications: see note above, adjunct in obesity.

Cautions: see notes above: adequate fluid intake should be maintained to avoid intestinal obstruction- it may be necessary to supervise elderly or debilitated patients or those with intestinal narrowing or decreased motility.

Contraindications: dysphagia, difficulty in swallowing, intestinal obstruction, colonic atony, faecal impaction, and infective bowel disease; see also under bisacodyl.

Side effects: flatulence, abdominal distensions, gastro-intestinal obstruction or impaction, hypersensitivity reactions reported.

Dose and Administration: Adult and Child 12 and older: up to 6 g daily given in divided doses of 0.43 - 3 g per dose. **Child 6 - 11 years** of age - up to 3g daily given in divided dose of 0.45 - 1 .5 g per dose.

Storage: at room temperature in a well-closed container.

Psyllium

Powder

Indications: Constipation, especially in diverticular disease and irritable bowel syndrome, and when excessive straining at stool must be avoided.

Cautions: avoid prolonged use; adequate fluid should be taken to avoid intestinal obstruction. Caution on dispensing the powder to avoid sensitization to air born particles of psyllium.

Drug interactions: tetracyclines.

Contraindications: see under bisacodyl; pre-existing faecal impaction, intestinal obstruction or colonic atony.

Side effects: hypersensitivity reactions; esophageal blockage or intestinal impaction.

Dose and Administration: Oral: **Adult and Child** (12 years and older): 30gm given daily in divided doses of 2.5 to 7.5gm per dose; Children 6 to 11 years old - 15gm daily given in divided doses of 2.5-3.75gm per dose.

Storage: at room temperature in a tight container and in a dry place.

Senna

Tablet (total sennosides), 7.5 mg

Indication: constipation and bowel evacuation.

Cautions: Pregnancy, breastfeeding, see also under Cascara Sagrada

Contraindications: see under Cascara Sagrada

Side effects: see notes above.

Dose and Administrations: *Oral:* **Adult:** 15 - 30 mg, as a single dose at bedtime. **Child** (over 6 years of age), one half of the adult dose, and those aged 2 to 6 years are quarter the adult dose.

Note: It is usually effective within 6 to 12 hours.

Storage: at room temperature in a dry place. Protect from freezing

1.6. Medicines Used in Diarrhea

Antidiarrheal medicines are used as adjuncts in the symptomatic treatment of diarrhea, although the main aim in the management of acute diarrhoea is the correction of fluid and electrolyte depletion with rehydration therapy; this is especially important in infants and young children and antidiarrhoeal agents are not generally recommended for this age group. Their use is also limited in chronic diarrhea for treatment aimed at the underlying disorder will often alleviate the diarrhoea.

The main groups of antidiarrhoeal agents are the medicines which reduce intestinal motility such as diphenoxylate, and loperamide. Bulk laxatives (see section 1.5) may also be used in the symptomatic treatment of diarrhoea.

Antimotility drugs (e.g. diphenoxylate, loperamide) are also used for symptomatic treatment of mild or uncomplicated travelers' diarrhoea, including that occurring in adult travelers with HIV infection. The most important measure in the management of travelers' diarrhoea is replacement of lost fluids and electrolytes.

Antispasmodics are occasionally of value in treating abdominal cramp associated with diarrhea but they should not be used for primary treatment. Antispasmodics and antiemetics should be avoided in young children with gastroenteritis because they are rarely effective and have troublesome side effects. Antibacterial medicines are generally unnecessary in simple gastro-enteritis because the complaint usually resolves quickly without them. Adsorbents such as kaolin are not recommended for acute diarrhea.

Antidiarrhoeal agents, especially the adsorbents may interfere with the absorption of other medicines from the gastro-intestinal tract if administered concomitantly. Adsorbents such as kaolin are not recommended for acute diarrhea.

Diphenoxylate with Atropine Sulphate

Tablet, 2.5 mg + 0.05 mg

Indications: acute diarrhoea (adjunctive therapy)

Cautions: inflammatory bowel disease; severe colitis.

Drug interactions: CNS depressants (alcohol, phenobarbitone, opioid analgesics), phenothiazines, tricyclic antidepressants, antimuscaranics, MAO inhibitors.

Contraindications: severe hepatic disease, pseudomembranous colitis and diarrhoea from infective aetiology; elderly and

patients with glaucoma or prostate hypertrophy; children under 4 years.

Side effects: nausea, dizziness, drowsiness, fatigue, sensitivity reactions include angioedema and giant urticaria, headache, euphoria, respiratory and mental depression. Anticholinergic symptoms such as dry mouth, fever, blurred vision; tachycardia and urinary retention may be produced by the atropine in the formulation, especially in children.

Dose and Administration: Oral: **Adult:** Diphenoxylate 5 mg 4 times/day until control achieved (maximum: 20 mg/day), then reduce dose as needed; some patients may be controlled on doses of 5 mg/day. **Child:** some authorities recommend that it should be avoided in children under 12 years. However, in certain circumstances the following doses have been used: 4 - 8 years, 2.5 mg upto 3 times daily, 9 - 12 years, 2.5 mg upto 4 times daily, 13 - 16 years, 5 mg upto 3 times daily.

Storage: store at room temperature and protect from light.

Loperamide

Capsule, 2 mg

Indications: acute and chronic diarrhoea.

Cautions: dehydration, impaired hepatic function; children and the elderly.

Drug interactions: opioid analgesics, CNS depressants (e.g. alcohol).

Contraindications: pseudomembranous colitis, diarrhoea of infective origin, or severe colitis from inflammatory bowel disease, history of allergic reaction to loperamide, for children under 2 years.

Side effects: Abdominal pains, nausea, constipation, dry mouth and blurred vision, CNS reactions such as dizziness, headache and fatigue, hypersensitivity reactions.

Dose and Administration: Oral: **Adult:** Acute diarrhoea: initially 4 mg, followed by 2 mg after each loose stool until diarrhoea is controlled; maximum 16 mg/24 hours. Chronic diarrhoea: usually 4 - 8 mg daily in divided doses. **Child over 2 years:** initially 1 mg/12.5 kg body mass, followed by 0.5 mg /12.5 kg after each loose stool. Alternatively, 0.08 - 0.24 mg/kg/day in 2 - 3 divided doses.

Note: If no improvement has been observed after treatment with 16mg daily for at least 10 days, further administration is unlikely to be of benefit.

Storage: store at room temperature.

Oral Rehydration salt (ORS)

Powder, each sachet for 1 liter contains:

	gm/liter		mmol/liter
sodium chloride	2.6	Na ⁺	75
potassium chloride	1.5	K ⁺	20
sodium citrate	2.9	Cl ⁻	65
anhydrous glucose	13.5	citrate	10
		glucose	75
Total Osmolarity			245

Indications: replacement of fluid and electrolyte loss in diarrhoea.

Cautions: ORS is not appropriate for patients with gastrointestinal obstruction, inability to drink, oliguric or anuric renal failure, or when parenteral rehydration therapy is indicated as in severe dehydration or intractable vomiting.

Side effects: Vomiting can occur after administration of ORS, the risk of hypernatremia or overhydration after administration of ORS is low in patients with normal renal function. Overdosage in patients with renal impairment may lead to hypernatremia and hyperkalaemia.

Dose and Administration: reconstitute one sachet by adding sufficient water to make 1 liter Oral Rehydration Solution. Dose - according to fluid loss, usually 200-400ml solution after ever loose motion, child - 200ml after every loose motion, infant 1 - 1½ times usual feed volume.

Storage: at room temperature.

Zinc Sulphate

Tablet (dispersible), 10mg, 20mg

Oral liquid, 10mg /unit

Indications: zinc deficiency or supplementation in zinc-losing conditions

Cautions: acute renal failure (may accumulate), pregnancy breast feeding

Contraindications: copper deficiency, high-density lipoprotein

Drug interactions: Quinolone antibiotics, tetracycline derivatives, trientine.

Side effects: abdominal pain, dyspepsia, nausea, vomiting, diarrhea, gastric irritation, gastritis; irritability, headache, lethargy

Dose and administration: Zinc supplements should not be given unless there is good evidence of deficiency (hypoproteinaemia spuriously lowers plasma-zinc concentration) or in zinc-losing conditions. Zinc deficiency can occur as a result of inadequate diet or malabsorption; excessive loss of zinc can occur in trauma, burns, and protein-losing conditions. A zinc supplement is given until clinical improvement occurs, but it may need to be continued in severe malabsorption, metabolic disease or in zinc-losing states.

adult and child over 30 kg, 1 tablet in water 1–3 times daily after food; child under 10 kg, ½ tablet daily; 10–30 kg, ½ tablet 1–3 times daily.

1.7. Antiflatulants

Activated Charcoal

Tablet, 125 mg, 250mg

Indications: flatulence, indigestion and intestinal distention.

Cautions: advise patients not to take other medications orally within two hours of the activated charcoal, except when inactivation of the medication is desired.

Drug interactions: avoid simultaneous use of any other medicines with activated charcoal.

Side effects: vomiting, constipation, and pulmonary aspiration, intestinal obstruction (with multiple dose administration); it colours the stool black.

Dose and Administration: Orally with plenty of water chew a tablet every 8 hours daily after meals. *Note: FDA has classified activated charcoal as lacking substantial evidence of efficacy as an antiflatulent or digestive aid.*

Storage: at room temperature, in airtight containers.

Simethicone

Tablet (chewable), 60mg, 80mg, and 95mg

Capsule, 95 mg, 125 mg

Indications: treatment of conditions in which retention of a gas may be a problem. It may be also be used as diagnostic aid as anti-foaming agent during gastroscopy to enhance visualization and prior to radiography of bowel to reduce gas shadows.

Cautions: simethicone is not recommended for the treatment of infant colic because of limited information on its safety in infants and children.

Contraindications: hypersensitivity to simethicone

Side effects: allergic reaction/rash, hives, itching, difficulty breathing, tightness in the chest, swelling of mouth, face, lips, or tongue.

Dose and administration: chewable tablet: oral, 60 to 95 mg four times a day after meals and at bed time or as needed or 150 mg three times a day after meals or as needed. Capsule: oral, 95 or 125mg four times a day after meals and bed time or as needed.*Note: Dose for pediatrics must be individualized by physician.*

Storage: store between 15-30°C, unless otherwise specified by manufacturer. Store in a well-closed container.

1.8. Digestants

Pancreatic enzymes (as pancreatin or pancrelipase) hydrolyse fats to glycerol and fatty acids break down protein into peptides, proteoses and derived substances, and convert starch into dextrins and sugars. They are given by mouth in conditions of pancreatic exocrine deficiency such as pancreatitis and cystic fibrosis.

Pancreatin

Tablet, 325 mg

Indications: replacement therapy in symptomatic treatment of malabsorption syndrom due to cystic fibrosis and other conditions associated with exocrine pancreatic insufficiency

Cautions: fibrotic strictures in the colon with high doses, especially in children, nursing women, pregnancy.

Drug interactions: iron, absorption may be decreased.

Contraindications: hypersensitivity to hog protein.

Side effects: diarrhea or other transient intestinal upset, hyperuricosuria and hyperuricemia, hypersensitivity reactions (e.g. sneezing, lacrimation, rash). Retention of pancreatin preparations in the mouth before swallowing may cause irritation of the mucosa and has resulted in ulceration and stomatitis.

Dose and Administration: Adult: Oral: 1-3 tablets before, during or one hour after meals, with an extra dose taken with any food eaten between meals.

Storage: store at a temperature not exceeding 15°C and in airtight containers.

1.9. Antihaemorrhoidal Agents

Haemorrhoids are enlarged or varicose veins of the tissues at the anus or rectal outlet. They are the most frequent cause of rectal bleeding. Anal and perianal pruritus, soreness and excoriation occur commonly in patient suffering from haemorrhoids, fistulas and proctitis. Careful local toilet with attention to any minor, faecal soiling, adjustment of the diet to avoid hard stools, the use of bulk forming materials such as bran and a high residue diet are helpful.

Soothing preparations containing mild astringents such as bismuth subgallate, zinc oxide, peru balsam and hamamelis with lubricants, vasoconstrictors or mild antiseptics, in the form of topical ointments, creams and suppositories, are used to provide symptomatic relief. Local anesthetics may be included to relieve pain, and corticosteroids may be used when infection is not present; preparations containing either group of medicines are intended only for short term use after exclusion of infections, such as herpes simplex; prolonged use can cause atrophy of the anal skin.

Haemorrhoids in children are rare. Treatment is usually symptomatic and the use of locally applied cream is appropriate for short periods; however, local anaesthetics can cause stinging initially and this may aggravate the child's fear of defecation.

Bismuth Subgallate Compound (Bismuth Subgallate + Bismuth Oxide + Peru Balsam + Zinc Oxide) †

Ointment, 2.25% + 0.87% + 1.875% + 10.75%

Suppository, 5mg + 24mg + 49mg + 296mg

Indications: to relieve anal and perianal pain, itching and soreness associated with hemorrhoids, anal fissures.

Cautions: advise patients to regulate their diet to produce soft stools that pass through the anus with a minimum irritation. Patients should be instructed to take hygienic measures after defecation. See notes above.

Dose and Administration: Rectally, wash and dry the anal area before application. Unless otherwise indicated; Ointment – *Apply rectally* night and morning and after defecation. Suppositories – Insert in to the rectum night and morning and after defecation.

Storage: in a cool place.

Bismuth Subgallate Compound with Hydrocortisone (Bismuth Subgallate + Bismuth Oxide + Peru Balsam + Zinc Oxide + Hydrocortisone acetate + Benzyl Benzoate) †

Ointment, 2.25% + 0.875% + 1.875% + 10.75% + 0.25% + 1.25%

Suppository, 59mg + 24mg + 49mg + 296mg + 10mg + 33mg

Indications: same as Bismuth Subgallate Compound, and anal inflammation in the absence of infection, see notes above.

† Any antihemorrhoidal preparation proven to be therapeutically effective can be used.

† Any antihemorrhoidal preparation proven to be therapeutically effective can be used

Cautions: Same as Bismuth Subgallate Compound. Avoid this preparation in the presence of an infection in the rectal area.

Contraindications: known hypersensitivity to the preparation, untreated infection.

Side effects: worsening of untreated infection, and thinning of the skin structure on prolonged use.

Dose and Administration: Rectally. Wash and dry the ectal area before application. Unless otherwise indicated, Ointments – Apply rectally night and morning and after defecation. Suppositories – Insert into the rectum night and morning and after defecation.

Storage: in a cool place.

Lidocaine + Aluminium Acetate + Zinc Oxide + Hydrocortisone Acetate †

Ointment, 50 mg + 35 mg + 180 mg + 2.5 mg

Suppository, 60 mg + 50 mg + 500 mg + 5 mg.

Indications: for treatment of hemorrhoids. They are suitable for occasional short-term use after exclusion of infection, such as herpes simplex.

Dose and Administration: Ointment – Apply several times daily, short – term use; Suppositories – insert 1 suppository at night and after a bowel movement; short-term use only.

Lignocaine + Tribenoside

Suppository, 40mg + 400mg

Indications: for treatment of rectal Haemorrhoids

Cautions: Severe hepatic impairment, Pregnancy, avoid during 1st trimester, Lactation.

Side effects: Burning sensation, mild pain, increased bowel motility, rash.

Dose and Administration: Insert 1 suppository twice daily until discomfort is relieved, and then reduce to once daily

Prednisolone Caproate + Dibucaine Hydrochloride + Hexachlorophene + Clemizole undecenoate⁴

Ointment, 0.19 % + 0.5 % + 0.5 % + 0.5 % + 1 %

Suppository, 1.3 mg + 1 mg + 2.5 mg + 5 mg.

Indications: short term symptomatic treatment of hemorrhoids.

⁴ Any antihaemorrhoidal preparation proven to be therapeutically effective can be used.

2. UROLOGICAL and RELATED MEDICINES

2.1. Medicine used in benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition affecting men as they age. Stromal and glandular hyperplasia of the prostate gland occurs as a result of the changing hormonal environment in middle-aged men and is present in most men at 45 years of age; about 30% of these men will eventually require treatment if their BPH causes lower urinary tract symptoms. It is increasingly common for surgical treatment to be used only in cases of failure of medical treatment or because of patient preference.

Contraction of smooth muscle in the prostate and bladder neck accounts for up to 40% of bladder outlet resistance. Alpha₁ blockers treat the dynamic component of bladder outlet obstruction. Those available include alfuzosin, prazosin, doxazosin and tamsulosin. They are short acting and are given once or twice daily. The most common side-effects of alphablockers include dizziness, weakness, headaches, and lightheadedness.

Dutasteride and finasteride are specific inhibitors of the enzyme 5 α -reductase, which metabolizes testosterone in to the more potent androgen, dihydrotestosterone. This inhibition of testosterone metabolism leads to reduction in prostate size, with improvement in urinary flow rate and in obstructive symptoms. They are alternatives to alpha-blockers particularly in men with a significantly enlarged prostate.

Dutasteride and finasteride decrease serum concentration of prostate cancer marker such as proste-specific antigen factor; reference value may need adjustment. Both drugs are excreted in semen and use of condom is recommended if sexual partner is pregnant or likely to become pregnant. Women with child bring

2. Urological and Related Medicines

potential should avoid handling crushed or broken tablets of these finasteride and leakage capsules of dutasteride.

Alfuzosin

Tablet, 2.5mg, 5mg, 10mg

Indications: treatment of the functional symptoms of benign prostatic hyperplasia (BPH).

Cautions: not intended for use as an antihypertensive drug. Renal and hepatic impairment, angina, floppy iris syndrome, orthostatic hypotension.

Drug interactions: azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, propofol, protease inhibitors, quinidine, verapamil and other CYP3A4 inhibitors; aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin, rifamycins, and other CYP3A4 inducers, alpha blockers, calcium channel blockers, MAO inhibitors.

Contraindications: Hypersensitivity to alfuzosin or any component of the formulation; moderate or severe hepatic; concurrent use with potent CYP3A4 inhibitors (eg, itraconazole, ketoconazole, ritonavir)

Side effects: dizziness, fatigue/ weakness, headache, abdominal pain, constipation, dyspepsia, nausea, impotence, bronchitis, and pharyngitis, orthostatic hypotension.

Dose and Administration:Adult: *Oral:* 10 mg per day.

Storage: store at room temperature and protect from light and moisture.

Doxazosin

Tablet, 1mg, 2mg, 4mg, 8mg

Indication: Treatment of urinary outflow obstruction and/or obstructive and irritative symptoms associated with benign

2. Urological and Related Medicines

prostatic hyperplasia (BPH), particularly useful in patients with troublesome symptoms who are unable or unwilling to undergo invasive procedures, but who require rapid symptomatic relief; can be used in combination with finasteride; for treatment and management of mild to moderate hypertension.

Cautions: Since doxazosin is alpha₁-selective alpha blockers reduce blood pressure, patients receiving antihypertensive treatment may require reduced dosage and specialist supervision. Caution is required in the elderly and in patients undergoing cataract surgery (risk of intra-operative floppy iris syndrome), angina, orthostatic hypotension, hepatic impair.

Drug interaction: enhanced hypotensive effect with adrenergic neurone blockers, diuretics, ACE inhibitors, calcium channel blockers, other antihypertensive medications, sildenafil, tadalafil, vardenafil, NSAIDs, alcohol, aldesleuk, alprostadil, anxiolytics and hypnotics, baclofen, beta-blockers, hydralazine, MAOIs, antipsychotics, oestrogens, Corticosteroids, levodopa, methyl dopa.

Contraindications: Hypersensitivity to quinazolines (prazosin, terazocin), doxazosin, or any component of the formulation. Alpha-blockers should be avoided in patients with a history of postural hypotension and micturition syncope.

Side effects: Drowsiness, hypotension (notably postural hypotension), syncope, asthenia, dizziness, depression, headache, dry mouth, gastro-intestinal disturbances, oedema, blurred vision, rhinitis, erectile disorders, tachycardia, and palpitations. Hypersensitivity reactions including rash, pruritus and angioedema.

Dose and Administration: Initially 1 mg daily; dose may be doubled at intervals of 1–2 weeks according to response, up to maximum 8 mg daily; usual maintenance 2–4 mg daily. **BPH:** 4-

2. Urological and Related Medicines

8mg/day, maximum dose: 8mg/day. **Hypertension:** maximum dose: 16mg/day. **Elderly:** initial 0.5mg once daily

Note: Syncope may occur usually within 90 minutes of the initial dose.

Storage: Store in a dry place, at room temperature in a well-closed container protected from light.

Dutasteride

Capsule, 0.5mg

Indication: For the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate gland to improve symptoms, and reduce the risk of acute urinary retention and the need for surgery.

Cautions: Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy. Dutasteride and finasteride decrease serum concentration of prostate cancer markers such as prostate-specific antigen; reference values may need adjustment. Dutasteride and finasteride are excreted in semen and use of a condom is recommended if sexual partner is pregnant or likely to become pregnant. No clinical benefit has yet been demonstrated in patients with prostate cancer treated with dutasteride and finasteride. *Women of childbearing potential should avoid handling crushed or broken tablets of finasteride and leaking capsules of dutasteride.*

Drug interaction: Diltiazem, Verapamil

Contraindications: for use in women of childbearing potential; pregnancy, children and adolescents; for patients with known hypersensitivity to dutasteride, other 5 α -reductase inhibitors or any component of the preparation.

Sideeffect: Breast tenderness or enlargement, decrease in sex drive, difficulty ejaculating, and inability to have or maintain an erection, rash, itching, urticaria, localized edema.

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Dose and Administration: The recommended dose dutasteride is 0.5 mg taken orally once a day. The capsules should be swallowed whole and not chewed or opened; as contact with the contents may result in irritation of the oropharyngeal mucosa. Dutasteride may be administered with or without food. Although early improvement in symptoms may be seen, treatment for at least six months may be necessary to assess whether a beneficial response has been achieved. No dosage adjustment is necessary for subjects with renal impairment or elderly. Due to the absence of data in patients with hepatic impairment, no dosage recommendation can be made.

Storage: Store at room temperature; protect from moisture.

Finasteride

Tablet, 5mg

Indications: Finasteride is indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with an enlarged prostate to: cause regression of the enlarged prostate, improve urinary flow and improve the symptoms associated with BPH. Reduce the incidence of acute urinary retention and the need for surgery including transurethral resection of the prostate (TURP) and Prostatectomy.

Cautions: See under dutasteride

Drug interactions: Finasteride is a synthetic analog of testosterone and inhibits an intracellular enzyme responsible for converting testosterone to the potent androgen 5 α -dihydrotestosterone (DHT). Although finasteride appears to interfere with the activation of testosterone to a more active form, presumably blocking the effects of testosterone, it would be illogical to administer finasteride concurrently with testosterone or other androgens.

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Contraindications: Hypersensitivity to any component of this medicine; women who are or may potentially be pregnant; children and adolescents.

Side effect: Impotence, decreased libido, ejaculation disorders, and breast tenderness and enlargement, testicular pain, hypersensitivity reactions (including lip and face swelling, pruritus and rash); male breast cancer.

Dose and Administration: Adult: one 5 mg tablet daily, taken orally with or without food. Finasteride can be administered alone or in combination with the alpha-blocker doxazosin. Although early improvement in symptoms may be seen, treatment for at least six months may be necessary to assess whether a beneficial response has been achieved. Thereafter, treatment should be continued long term. Clinical response occur within 12 weeks to 6 months of initiation of therapy. Therefore, long term administration is recommended for maximal response. No dosage adjustment is required in the elderly or in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 ml/min).

Prazosin Hydrochloride

Tablet, 1 mg, 2 mg, 5 mg

Indications:For treatment of benign prostatic hyperplasia and hypertension, hypertension associated with pheochromocytoma.

Cautions: elderly patients, during pregnancy and breastfeeding, angina pectoris, narcolepsy, and in those sensitive to the medicine. First dose may cause collapse due to hypotension (should be taken on retiring to bed); hepatic or renal function impairment; advice patients not to do activities requiring alertness.

Drug interactions: nifedipine, other antihypertensive agents or nitrates, alcohol, beta blockers and calcium channel blockers.

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Contraindications: heart failure caused by mechanical obstruction, for example aortic or mitral valve stenosis, pulmonary embolism, and restrictive pericardial disease.

Side effects: dizziness, orthostatic hypotension, edema, palpitations, dry mouth, urinary incontinence, angina, dyspnea, and priapism, drowsiness, headache, lack of energy, and nausea.

Dose and Administration: *Oral: Adult:* 0.5 mg 2–3 times daily, the initial dose on retiring to bed or night (to avoid collapse) increased to 1 mg 2 – 3 times daily after 3 – 7 doses further increased if necessary to maximum 20 mg daily. **Child** (under 7 years of age), initially 0.25 mg 2 – 3 times a day adjusted according to response. 7 to 12 years of age, initially 0.5 mg two or three times a day adjusted according to response.

Storage: at room temperature in a well-closed, light – resistant container.

Tamsulosin

Capsule, 0.4mg

Indications: Used in the treatment of signs and symptoms of benign prostatic hyperplasia (reduction in urinary obstruction and relief of associated manifestations such as hesitancy, terminal dribbling of urine, interrupted or weak stream, etc.).

Contraindications: Hypersensitivity to the medicine or any component of the formulation; in patients with a history of postural hypotension and micturition syncope.

Cautions, Drug interactions and Side effects: see under doxazosin

Dose and Administration: 0.4 mg *PO* daily 30 min after the meal each day; if response is not satisfactory in 2–4 weeks, dosage may be increased to 0.8 mg *PO* daily 30 min after the meal each day. If therapy is interrupted for any reason for several days, resume dosing at 0.4 mg *PO* daily.

2. Urological and Related Medicines

Storage: Store at room temperature; protect from moisture.

2.2 Medicines used for Urinary Incontinence

Urinary incontinence is loss of bladder control. Symptoms can range from mild leaking to uncontrollable wetting. It can happen to anyone, but it becomes more common with age. Treatment for urge incontinence generally should include behavior therapy. However, medications can be prescribed as an adjunct to behavior therapy. Indeed, the combination of exercises and medications results in better control of incontinence than either treatment alone. Tolterodine, a selective anticholinergic agent, has relatively more action on cholinergic receptors in the bladder than in the salivary glands and other organs.

2.3. Ant-hyperphosphatemics

Sevelamer hydrochloride

Tablet: 400mg and 800mg

Indication: reduce serum phosphorus in patients with chronic kidney disease who are undergoing hemodialysis (hyperphosphotemia)

Caution: breastfeeding, children younger than 18 years of age, elderly.

Contraindications: hypophosphatemia or bowel obstruction, known hypersensitivity to selvelamer hydrochloride or any ingredient in the formulation.

Drug interaction: ciprofloxacin, antiarrhythmics, anticonvulsants

Side effects: diarrhea, constipation, dyspepsia, flatulence, nausea, vomiting, hypertension, hypotension, thrombosis, infection (nasopharyngitis, bronchitis, upper respiratory infection), cough, dyspnea, headach, back pain.

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Dose and Administration: Serum phosphorus concentration 5.5-7.5mg/dl, should receive an initial sevelamer hydrochloride dosage of 800mg 3 times daily. Serum phosphorus concentration 7.5-9mg/dl, should receive an initial sevelamer hydrochloride dosage of 1.2g 3 times daily (3 tablets of 400mg). Serum phosphorus concentration ≥ 9 mg/dl, should receive an initial sevelamer hydrochloride dosage of 1.6g 3 times daily (two tablets of 800mg).

3. CARDIOVASCULAR MEDICINES

3.1. Medicines used for Congestive Cardiac failure

Angiotensin-converting enzyme (ACE) inhibitors such as captopril, enalapril, fosinopril and lisinopril produce clinical benefit in all stages of chronic heart failure additional to that obtained from diuretics. They relieve symptoms such as dyspnoea and improve exercise tolerance. ACE inhibitors improve survival and reduce the progression of mild or moderate heart failure to more severe stages. ACE inhibitors may also be beneficial in asymptomatic left ventricular dysfunction. ACE inhibitors are recommended in all patients with symptomatic heart failure due to left ventricular systolic dysfunction, including those whose symptoms are controlled with diuretic therapy. ACE inhibitors all appear to have a similar spectrum of adverse effects although at one time some, such as taste disturbance and skin reactions, were attributed to the presence of a sulphhydryl group (as in captopril) but have now also been reported with ACE inhibitors; however, they may be more common with captopril the most common adverse effects are due to the vascular effects of ACE inhibitors and include hypotension, dizziness, fatigue, headache, and nausea and other gastrointestinal disturbances. Other side effects include persistent cough and other upper respiratory tract symptoms, and angioedema. All ACE inhibitors are contraindicated in pregnancy; in patients with hypersensitivity to ACE inhibitors; in known or suspected renovascular disease; aortic stenosis or outflow tract obstruction.

Diuretics have been the mainstay in the treatment of heart failure. They provide very effective symptomatic control in patients with peripheral or pulmonary oedema and rapidly relieve dyspnoea. If symptoms of fluid retention are only mild,

a thiazide diuretic such as hydrochlorthiazide may be adequate. However, diuretics are not a sufficient treatment on their own as clinical stability tends to deteriorate over time.

Cardiac glycosides the benefit of cardiac glycosides such as digoxin in heart failure accompanied by atrial fibrillation is not disputed although their role in patients with sinus rhythm has been debated. There is evidence that withdrawal of digoxin from patients receiving diuretics or ACE inhibitors carries a considerable risk of clinical deterioration if they are stable on such combination therapy. Digoxin, given in addition to diuretics and ACE inhibitors, improved symptoms but had no effect on mortality. Digoxin may therefore have a role in patients who remain symptomatic despite ACE inhibitors, diuretic, and beta-blocker therapy, and in those unable to tolerate ACE inhibitors.

Beta-blockers unless otherwise contraindicated (by asthma, 2nd- or 3rd-degree atrioventricular block, or previous intolerance), are an important addition to ACE inhibitors for chronic systolic dysfunction in most patients, including the elderly, and for diastolic dysfunction in hypertension and hypertrophic cardiomyopathy. They are best started when the patient has no evidence of pulmonary congestion. Some of these drugs improve left ventricular ejection fraction, survival, and other major cardiovascular outcomes in patients with chronic systolic dysfunction, including those with severe symptoms. β -Blockers are particularly useful for diastolic dysfunction because they reduce heart rate, prolonging diastolic filling time, and possibly improve ventricular relaxation. During a severe, acute decompensation, β -blockers should not be started until patients are stabilized and have little evidence of fluid retention. For patients already taking a β -blocker, the dose may be temporarily reduced or, in severe decompensation,

temporarily withheld but restarted and titrated again when patients are stable. For milder decompensations, the β -blocker dose should be continued with a temporary increase in diuretic dose. The beta-blockers bisoprolol and carvedilol are of value in any grade of stable heart failure due to left ventricular systolic dysfunction; nebivolol is licensed for stable mild to moderate heart failure in patients over 70 years. Beta-blocker treatment should be started by those experienced in the management of heart failure, at a very low dose and titrated very slowly over a period of weeks or months. Symptoms may deteriorate initially, calling for adjustment of concomitant therapy.

Phosphodiesterase inhibitors have a dual action being both positive inotropes and vasodilators. Although short-term haemodynamic variables are improved, long-term oral use has been associated either with an unacceptable incidence of adverse effects (amrinone) or with an increased mortality rate (milrinone). Thus, these phosphodiesterase inhibitors have been reserved for heart failure unresponsive to other treatment.

Amrinone Lactate

Injection, 5mg/ml in 20ml ampoule

Indications: is used as a short-term therapy in patients with intractable heart failure. Because of limited clinical experience with the drug, it should be reserved in used for patients under close monitoring.

Cautions: severe aortic or pulmonic valvular disease.

Drug interactions: diuretics (Furosemide), digitalis (digoxin).

Contraindications: gastrointestinal disturbances that may necessitate withdrawal of treatment, hypersensitivity reaction to the medicine. Known hypersensitivity to sulfiting agents

3. Cardiovascular Medicines

(i.e., sulfur dioxide, potassium or sodium bisulfite, potassium or sodium metabisulfite, sodium sulfite)

Side effects: arrhythmias, hypotension, thrombocytopenia, chest pain, fever, hepatotoxicity, and hypersensitivity.

Dose and Administration: Adult and Child: 0.75 mg/kg IV bolus over 2-3 minutes followed by maintenance infusion of 5-10 mcg/kg/minute; IV bolus may need to be repeated in 30 minutes.

Storage: See manufacturers' recommendation.

Captopril

Tablet, 12.5 mg, 25 mg, 50 mg, 100 mg

Indications: treatment of congestive heart failure, management of hypertension, left ventricular dysfunction after myocardial infarction; diabetic nephropathy.

Cautions: impaired renal function, patient with solitary kidney, collagen-vascular disease, patients receiving immunosuppressants or other medicines that cause leukopenia or agranulocytosis, coronary or cerebrovascular disease, severe salt/volume depletion.

Drug interactions: potassium-sparing diuretics or potassium supplements (ACE inhibitors are 'potassium-sparing' agents); aspirin, indomethacin and probably other NSAIDs, antacids, digoxin and lithium, probenecid, food decreases absorption-take 30-60 minutes before meals.

Contraindications: hypersensitivity to ACE inhibitors, idiopathic or hereditary angioedema; known or suspected venovascular disease; aortic or bilateral renal artery stenosis, outflow tract obstruction. ACEIs can cause injury and death to the developing fetus when used in the second and third trimesters. ACEIs should be discontinued as soon as possible once pregnancy is detected.

Side effects: see notes above; slight increase in heart rate, first dose hypotension, dizziness, fainting; rash (maculopapular or urticarial), pruritus; hyperkalemia, neutropenia, proteinuria, increased serum creatinine, cough, hypersensitivity reactions; altered taste sensation.

Note:-In the treatment of heart failure severe first-dose hypotension on introduction of an ACE inhibitor is common in patients on loop diuretics.

Dose and Administration: Dosing: Adult Heart failure: Oral: Initial dose: 6.25-12.5 mg 3 times/day in conjunction with cardiac glycoside and diuretic therapy; initial dose depends upon patient's fluid/electrolyte status. Target dose: 50 mg 3 times per day

Dosing: Pediatric Hypertension: Oral: *Infants:* Initial: 0.15-0.3 mg/kg/dose; titrate dose upward to maximum of 6 mg/kg/day in 1-4 divided doses

Children: Initial: 0.3-0.5 mg/kg/dose; titrate upward to maximum of 6 mg/kg/day in 2-4 divided doses

Older Children: Initial: 6.25-12.5 mg/dose every 12-24 hours; titrate upward to maximum of 6 mg/kg/day

Adolescents: Initial: 12.5-25 mg/dose; titrate to a maximum of 450 mg per day

Dosing: Renal Impairment, Adults: Cl_{cr} 10-50 mL/minute: Administer at 75% of normal dose every 12-18 hours. $Cl_{cr}<10$ mL/minute: Administer at 50% of normal dose every 24 hours.

Prophylaxis after myocardial infarction (in clinically stable patients): Oral:**Adult:** initially 6.25 mg gradually increased over several weeks to 150 mg daily in divided doses.

Storage: at room temperature in a tight container.

Digoxin

Elixir, 0.05 mg/ml

Injection, 0.1 mg/ml in 1 ml ampoule; 0.25 mg/ml in 2 ml ampoule

Tablet, 0.25 mg

Indications: Treatment of mild-to-moderate (or stage C as recommended by the ACCF/AHA) heart failure (HF); atrial fibrillation (rate-control). In treatment of atrial fibrillation (AF), use is not considered first-line unless AF coexistent with heart failure or in sedentary patients.

Cautions: patients with recent myocardial infarction, sick sinus syndrome, hypothyroidism, severe pulmonary disease; elderly patients and in patients with renal function impairment where dosage adjustment is necessary; breast-feeding; electrolyte disturbances; Avoid rapid intravenous administration (nausea and risk of arrhythmias)

Drug interactions: amiodarone, beta-adrenergic blocking agents, (including atenolol, carvedilol, metoprolol and propranolol), calcium channel blocking agents, especially verapamil, potassium-depleting diuretics (such as bumetanide, ethacrynic acid, furosemide, indapamide, mannitol, or thiazide), propafenone, quinidine or quinine, sympathomimetics. Oral aminoglycosides may decrease the serum concentration of digoxin.

Contraindications: hypersensitivity to digoxin or digitoxin, ventricular fibrillations, intermittent complete heart block, second degree AV block, supraventricular arrhythmias caused by wolf – Parkinson white syndrome, hypertrophic obstructive cardiomyopathy toxic effects present from prior administration of any digitalis preparation, ventricular fibrillation.

Side effects: anorexia, nausea, vomiting, lower stomach pain, diarrhea, weakness, blurred or yellow vision, drowsiness, confusion, mental depression, headache and hallucinations, arrhythmias, hypotension, AV block.

Dose and Administration: When changing from oral (tablets or liquid) or I.M. to I.V. therapy, dosage should be reduced by 20% to 25%. **Atrial fibrillation:** (rate control) in patients with heart failure: Loading dose: I.V.: 0.25 mg every 2 hours, up to 1.5 mg within 24 hours; for nonacute situations, may administer 0.5 mg orally once daily for 2 days followed by oral maintenance dose. Maintenance dose: I.V., Oral: 0.125-0.375 mg once daily. **Heart failure:** Daily maintenance dose (*Note: Loading dose not recommended*): Oral: 0.125-0.25 mg once daily; higher daily doses (up to 0.5 mg/day) are rarely necessary. If patient is >70 years of age, has impaired renal function, or has a low lean body mass, low doses (eg, 0.125 mg daily or every other day) should be used. Emergency control of atrial fibrillation, IV infusion over at least 2 hours: **Adult:** Initial total digitalizing dose 0.75–1.5 mg (I.V., I.M.: 0.5-1 mg Daily maintenance dose: Oral: 0.125-0.5 mg once daily (I.V., I.M.: 0.1-0.4 mg once daily. *Note: I.M. not preferred due to severe injection site pain.* **Pediatric:** Atrial dysrhythmias (rate control), heart failure: When changing from oral (tablets or liquid) or I.M. to I.V. therapy, dosage should be reduced by 20% to 25%. See table below.

3. Cardiovascular Medicines

Age	Total Digitalizing Dose (mcg/kg)		Daily Maintenance Dose (mcg/kg)	
	Oral	I.V. or I.M.	Oral	I.V. or I.M.
Preterm infant	20-30	15-25	5-7.5	4-6
Full-term infant	25-35	20-30	6-10	5-8
1 mo - 2 y	35-60	30-50	10-15	7.5-12
2-5 y	30-40	25-35	7.5-10	6-9
5-10 y	20-35	15-30	5-10	4-8
>10 y	10-15	8-12	2.5-5	2-3

Storage: At room temperature in a tight container, protect from freezing.

Enalapril Maleate

Tablet, 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg.

Indications: Treatment of hypertension; treatment of symptomatic heart failure; treatment of asymptomatic left ventricular dysfunction. To delay the progression of nephropathy and reduce risks of cardiovascular events in hypertensive patients with type 1 or 2 diabetes mellitus; hypertensive crisis, diabetic nephropathy, hypertension secondary to scleroderma renal crisis, diagnosis of aldosteronism, idiopathic edema, Bartter's syndrome, postmyocardial infarction for prevention of ventricular failure

Cautions, Drug interactions, Contraindications and Side effects see under captopril and notes above

Dose and Administration: Adult: Oral: **Congestive heart failure:** Oral: Initial: 2.5 mg once or twice daily (usual range: 5-40 mg/day in 2 divided doses); titrate slowly at 1- to 2-week intervals. Target dose: 10-20 mg twice daily.

Storage: See manufacturer's recommendation.

Enalapril Maleate + Hydrochlorothiazide

Tablet, 10 mg + 25 mg

Indications: see under Enalapril maleate

Cautions, Drug interactions, Contraindications; see captopril above and hydrochlorothiazide.

Side effects: see notes above; chest pain, cholecystitis or pancreatitis, hepatic function impairment, hyperuricemia or gout, neutropenia or agranulocytosis, thrombocytopenia, and electrolyte imbalance.

Dose and Administration: *Oral: Congestive heart failure:*

Adult: 1 tablet once or twice per day, as determined by individual titration with the component agents, for a maximum of 20 mg of Enalapril and 50 mg of Hydrochlorothiazide.

Child: as determined by individual titration with the component agents. Enalapril: *Oral*, initially 0.1 mg per kg of body weight per day, the dosage being adjusted as needed and tolerated, up to a maximum of 0.5 mg per Kg of body weight per day. Hydrochlorothiazide: *Oral*, 1 to 2 mg per kg of body weight or 30 to 60 mg per square meter of body surface per day, as a single dose or in two divided doses, the dosage being adjusted according to response.

Hydralazine

Tablet, 10mg, 25mg, 50mg, 100mg

Powder for injection, 20mg/ml in 1 ml ampoule

Indication: Management of moderate-to-severe hypertension. Heart failure; hypertension secondary to pre-eclampsia/eclampsia.

Cautions: I.V. administration: Monitor blood pressure closely following I.V. administration. Response may be delayed and unpredictable in some patients; titrate cautiously to response.

Patient compliance: Patients may be poorly compliant because of frequent dosing.

Drug interactions: May enhance the hypotensive effect of other Antihypertensives. Nonsteroidal Anti-Inflammatory Agents: May diminish the antihypertensive effect of Hydralazine.

Contraindications: Hypersensitivity to hydralazine or any component of the formulation; mitral valve rheumatic heart disease. Hepatic impairment, renal impairment (dosage adjustment). Avoid during first and second trimester, no report on serious harm following use in third trimester.

Side effects: Angina pectoris, orthostatic hypotension, peripheral edema, fluid retention (diuretics needed) tachycardia, vascular collapse, pruritus, rash, urticarial, anorexia, constipation, diarrhea, nausea and vomiting, agranulocytosis, thrombocytopenia, conjunctivitis.

Dose and Administrations: **Congestive heart failure: Oral:** *Initial dose:* 10-25 mg 3-4 times per day. *Adjustment:* Dosage must be adjusted based on individual response. *Target dose:* 225-300 mg/day in divided doses; use in combination with isosorbide dinitrate

Hydralazine +Isosorbide Dinitrate

Tablet, 37.5mg+20mg

Indication: Treatment of heart failure, adjunct to standard therapy,

Cautions, Drug interactions, Contraindications, Side effects: see individual medicine.

Dose and Administrations: Adult, Congestive heart failure:

Oral: Initial: 1 tablet 3 times/day; may titrate to a maximum dose of 2 tablets 3 times/day

Isosorbide Dinitrate

Tablet, 5mg, 10mg, 20mg, 30mg, 40mg, 60mg

Sublingual Tablet, 2.5mg, 5mg, 10mg

Tablet/Capsule(s/r), 40mg

Indication: Isosorbide dinitrate (in combination with cardiac glycosides and diuretics or with hydralazine) effective for the treatment of CHF or other low cardiac output states. Concomitant therapy with isosorbide dinitrate and hydralazine may decrease mortality in patients with CHF; usually reserved for patients who fail to respond to or are intolerant of first-line therapy (e.g., ACE inhibitors) or in combination with such therapy. *Do not use isosorbide dinitrate as monotherapy for CHF.*

Cautions: Severe hypotension (postural) can occur; paradoxical bradycardia and increased angina pectoris can accompany hypotension. Use with caution in volume depletion and moderate hypotension, and use with extreme caution with inferior wall MI and suspected right ventricular infarctions. Nitrates may precipitate or aggravate increased intracranial pressure and subsequently may worsen clinical outcomes in patients with neurologic injury (eg, intracranial hemorrhage, traumatic brain injury).

Drug interactions: May enhance the adverse/toxic effect of other Hypotensive Agents. Phosphodiesterase 5 Inhibitors (e.g., sildenafil) may enhance the vasodilatory effect of Vasodilators (Organic Nitrates). Caution with ethanol (may increase risk of hypotension).

Contraindications: hypersensitivity to isosorbide dinitrate or any component of the formulation; hypersensitivity to organic nitrates; concurrent use with phosphodiesterase-5 (PDE-5) inhibitors (sildenafil, tadalafil, or vardenafil)

Side effects: hypotension, orthostatic hypotension, rebound hypertension, headache, methemoglobinemia

Dose and Administrations: Heart failure (unlabeled use):*Oral:* Immediate release (Note: Use in combination with hydralazine): Initial dose: 20 mg 3-4 times per day; Target dose: 160 mg/day in 4 divided doses

Lisinopril

Tablet 2.5 mg, 5 mg, 10 mg, 20 mg

Indications: Treatment of hypertension, either alone or in combination with other antihypertensive agents; adjunctive therapy in treatment of heart failure (afterload reduction); treatment of acute myocardial infarction within 24 hours in hemodynamically-stable patients to improve survival; treatment of left ventricular dysfunction after myocardial infarction.

Cautions, Drug interactions, Contraindications, Side effects; see notes above and under Captopril.

Dose and Administrations: Adult Heart failure: Oral: Initial: 2.5-5 mg once daily; then increase by no more than 10 mg increments at intervals no less than 2 weeks to a maximum daily dose of 40 mg. Usual maintenance: 5-40 mg/day as a single dose. Target dose: 20-40 mg once daily (ACC/AHA 2009 Heart Failure Guidelines)

Note: If patient has hyponatremia (serum sodium <130 mEq/L) or renal impairment (Cl_{cr} <30 mL/minute or creatinine >3 mg/dL), then initial dose should be 2.5 mg/day

Storage: at room temperature in a well-closed container.

3.2. Antiarrhythmics

Agents used in the management of cardiac arrhythmias form of a diverse group of medicines. Many of them, such as beta blockers, digoxin, lignocaine, magnesium and phenytoin have important actions in addition to their antiarrhythmic properties and thus, as well as being employed in the treatment of cardiac arrhythmias, have a wide range of other clinical applications.

Management of arrhythmias

In general, medicine therapy of serious arrhythmias is unsatisfactory and dangerous. Antiarrhythmics may suppress arrhythmias successfully but paradoxically increase mortality. Cardiac arrhythmias can range from little more than asymptomatic ECG abnormalities through to severe or life-threatening events. In general, pharmacological therapy, particularly chronic therapy, should be instituted only for haemodynamically important, sustained arrhythmias after a search for and correction of any simple precipitating factors and consideration of alternative treatment (e.g. catheter ablation, implantable cardioverter defibrillator). The inappropriate use of an antiarrhythmic for a specific arrhythmia can not only be ineffective but, in view of the proarrhythmic potential of most of them, may even be deleterious.

Antiarrhythmics classes

Class I includes medicines, which directly interfere with depolarization of the cell membrane (membrane-stabilising drugs) by blocking the fast inward current of sodium into cardiac cells; they also have local anaesthetic properties.

Class Ia agents, which prolong action potential duration (APD) and include procainamide, disopyramide and quinidine.

Class Ib agents, shorten APD, includes lidocaine (lignocaine), mexiletine.

Class Ic agents do not affect APD, which include propafenone and flecainide. *This class of medicines is not readily available in Ethiopia.*

Although they are effective antiarrhythmics, the use of many of the class I agents is associated with an increased mortality (compared with placebo).

Class II agents are characterized by beta-blocking activity, leading to a reduction in heart rate, myocardial contractility, and the rate of conduction of impulses through the conducting system, and include propranolol, bretylium and others.

Class III includes those agents which prolong the duration of cardiac action potential, e.g. amiodarone and sotalol.

Class IV agents block the slow inward calcium channel of the SA and AV nodes, e.g. Adenosine, verapamil and diltiazem.

Adenosine

Injection 3mg/ml

Indications: treatment of paroxysmal supraventricular tachycardia (PSVT) including that associated with accessory bypass tracts (Wolff-Parkinson-White syndrome); when clinically advisable, appropriate vagal maneuvers should be attempted prior to adenosine administration; not effective for conversion of atrial fibrillation, atrial flutter, or ventricular tachycardia

Cautions: wide-complex tachycardia, electrolyte imbalance, heart transplant recipient, pulmonary artery hypertension, respiratory disease (e.g., asthma)

Drug interactions: carbamazepine, dipyridamole, theophylline and caffeine (avoid food or drug with caffeine), digoxin, nicotine

Contraindications: hypersensitivity to adenosine or any component of the formulation; second- or third-degree AV

block, sick sinus syndrome, or symptomatic bradycardia (except in patients with a functioning artificial pacemaker); use in patients with atrial fibrillation/flutter with underlying Wolff-Parkinson-White (WPW) syndrome

Side effects: transient new arrhythmia, headache, dizziness, GI discomfort, dyspnea, hypotension, diaphoresis

Dose and Administration: Adult: Paroxysmal supraventricular tachycardia: I.V. (rapid, over 1-2 seconds, via peripheral line; see Note): Initial: 6 mg; if not effective within 1-2 minutes, 12 mg may be given; may repeat 12 mg bolus if needed (maximum single dose: 12 mg). Follow each dose with 20 mL normal saline flush. Note: Initial dose of adenosine should be reduced to 3 mg if patient is currently receiving carbamazepine or dipyridamole, has a transplanted heart or if adenosine is administered via central line. Pharmacologic stress testing: I.V.: Continuous I.V. infusion via peripheral line: 140 mcg/kg/minute for 6 minutes using syringe or volumetric infusion pump; total dose: 0.84 mg/kg. Thallium-201 is injected at midpoint (3 minutes) of infusion. Acute vasodilator testing in pulmonary artery hypertension (*unlabeled use*). I.V.: Initial: 50 mcg/kg/minute increased by 50 mcg/kg/minute every 2 minutes to a maximum dose of 500 mcg/kg/minute or to a maximum dose of 250 mcg/kg/minute; acutely assess vasodilator response.

Child: Rapid I.V. push (over 1-2 seconds) via peripheral line, followed by a normal saline flush: Paroxysmal supraventricular tachycardia: Infants and Children: I.V.: Children <50 kg: Initial: 0.05-0.1 mg/kg (maximum initial dose: 6 mg). If conversion of PSVT does not occur within 1-2 minutes, may increase dose by 0.05-0.1 mg/kg. May repeat until sinus rhythm is established or to a maximum single dose of 0.3 mg/kg or 12 mg. Follow each dose with normal saline flush. Children ≥50 kg: *Refer to adult dosing.* Pediatric advanced life support: Treatment of SVT: I.V.,

I.O.: Initial: 0.1 mg/kg (maximum initial dose: 6 mg); if not effective within 1-2 minutes, administer 0.2 mg/kg (maximum single dose: 12 mg). Follow each dose with ≥ 5 mL normal saline flush.

Storage: Store at controlled room temperature of 15°C to 30°C. Do not refrigerate; crystallization may occur (may dissolve by warming to room temperature).

Amiodarone

Tablet, 100mg, 200 mg, 400mg

Injection, 50mg/ml

Indications: Management of life-threatening recurrent ventricular fibrillation (VF) or hemodynamically-unstable ventricular tachycardia (VT) refractory to other antiarrhythmic agents or in patients intolerant of other agents used for these conditions

Cautions: heart failure and impaired liver function, avoid exposure to sunlight. Arrhythmias, Hepatotoxicity, Proarrhythmic effects, Pulmonary toxicity.

Drug interactions: amiodarone may interact with other drugs for months after treatment is discontinued. It concentrates in the liver and may interfere with the hepatic metabolism of many drugs. Oral anticoagulants, other antiarrhythmics, digoxin, phenytoin; beta blockers, cimetidine and ritonavir.

Contraindications: Hypersensitivity to amiodarone, iodine, or any component of the formulation; severe sinus-node dysfunction; second- and third-degree heart block (except in patients with a functioning artificial pacemaker); bradycardia causing syncope (except in patients with a functioning artificial pacemaker); cardiogenic shock

Side effects: frequent –hyperor hypothyroidism, neurotoxicity (including peripheral neuropathies), photosensitivity, headache,

nausea, vomiting, anorexia, constipation, fatigue and dizziness. Less frequent - pulmonary fibrosis, interstitial or hypersensitivity pneumonitis (include cough, dyspnoea and slight fever), skin discoloration, ocular toxicity, arrhythmias, bradycardia, congestive cardiac failure.

Dose and Administration:Adult: Oral: Lower loading and maintenance doses are preferable in women and all patients with low body weight. Ventricular arrhythmias: Oral: 800-1600 mg/day in 1-2 doses for 1-3 weeks, then when adequate arrhythmia control is achieved, decrease to 600-800 mg/day in 1-2 doses for 1 month; maintenance: 400 mg/day; lower doses are recommended for supraventricular arrhythmias. Pulseless VT or VF: I.V. push, I.O.: Initial: 300 mg rapid bolus; if pulseless VT or VF continues after subsequent defibrillation attempt or recurs, administer supplemental dose of 150 mg. *Note: In this setting, administering undiluted is preferred.* Upon return of spontaneous circulation, follow with an infusion of 1 mg/minute for 6 hours, then 0.5 mg/minute for 18 hours (mean daily doses >2.1 g/day have been associated with hypotension). Breakthrough stable VT or SVT: 150 mg supplemental doses in 100 mL D5W or NS over 10 minutes (mean daily doses >2.1 g/day have been associated with hypotension) I.V. to oral therapy conversion: Use the following as a guide: <1 week I.V. infusion: 800-1600 mg/day; 1 to 3 weeks I.V. infusion: 600-800 mg/day; >3 weeks I.V. infusion: 400 mg.

Note: Conversion from I.V. to oral therapy has not been formally evaluated. Some experts recommend a 1-2 day overlap when converting from I.V. to oral therapy especially when treating ventricular arrhythmias.

Bretylium Tosylate

Injection, 50 mg/ml in 2 ml ampoule

Indications: Bretylium is used in ventricular arrhythmias unresponsive to conventional therapy following acute myocardial infarction. Bretylium has also proven effective in the treatment of premature ventricular contractions, and in the facilitation of countershock in ventricular fibrillation in cases not responding to countershock alone or countershock with other antiarrhythmics

Cautions: avoid in patients with fixed cardiac outputs (i.e., severe aortic stenosis or severe pulmonary hypertension); risk of severe hypotension, digitalized patients, may aggravate digitalis toxicity, geriatrics (hypotension), hyperthermia, hypotension, repeated IM injections in same area may cause atrophy/necrosis, renal impairment, transient hypertension or an increase in arrhythmias possible on administration.

Drug interactions: catecholamines, digoxine, erythromycin, class Ia and class III antiarrhythmics, specific quinolones.

Contraindications: all contraindications are relative to the seriousness of the arrhythmia, digitalis-induced arrhythmias, hypersensitivity to bretylium.

Side effects: hypotension, a transient initial increase in blood pressure and heart rate, a worsening of cardiac arrhythmias, nausea and vomiting, increased frequency of pulmonary ventricular contractions, respiratory depression, exacerbation of digitalis-induced arrhythmias.

Dose and Administration: Adult: I.M.: Ventricular Arrhythmia; Treatment and Prophylaxis: do not dilute prior to injection. Inject 5 to 10 milligrams/kilogram of body weight. The dose may be repeated at 1 to 2 hour intervals if the arrhythmia persists. Thereafter, administer the same dosage every 6 to 8 hours. Intramuscular injection should not be made directly into or near a major nerve and the site of injection should be varied on repeated administration. I.V.: Ventricular

Arrhythmia; Treatment and Prophylaxis Ventricular Fibrillation: Administer undiluted bretylium 5 milligrams/kilogram of body weight by rapid intravenous injection. The usual cardiopulmonary resuscitative measures, including electrical cardioversion, should be employed prior to and following the injection in accordance with good medical practice. If ventricular fibrillation persists, the dosage may be increased to 10 mg/kg body weight and repeated as necessary. The maximum loading dose should not exceed 30 mg/kg.

Storage: store at room temperature

Isoproterenol

Injection, 0.02mg/ml, 0.2mg/ml

Indications: Mild or transient episodes of heart block that do not require electric shock or pacemaker therapy; serious episodes of heart block and Adams-Stokes attacks (except when caused by ventricular tachycardia or fibrillation); cardiac arrest until electric shock or pacemaker therapy is available; bronchospasm during anesthesia; adjunct to fluid and electrolyte replacement therapy and other drugs and procedures in the treatment of hypovolemic or septic shock and low cardiac output states (eg, decompensated heart failure, cardiogenic shock).

Cautions: elderly, diabetics, renal or cardiovascular disease, distributive shock, seizure disorder or hyperthyroidism.

Drug interactions: sympathomimetic agents, general anesthetics.

Contraindications: hypersensitivity, angina, pre-existing cardiac arrhythmias, tachycardia.

Side effects: bradycardia, tachycardia, headache, nervousness, nausea, vomiting, dyspnea.

Dose and Administration: I.V: Cardiac arrhythmias: Adult: Bradyarrhythmias, AV nodal block, or refractory torsade de pointes: Continuous I.V. infusion: Usual range: 2-10 mcg/minute; titrate to patient response.

Brugada syndrome with electrical storm (unlabeled use): I.V. bolus: Initial: 1-2 mcg, followed by a continuous infusion of 0.15-0.3 mcg/minute for 1 day; may repeat sequence if ventricular tachycardia/fibrillation recurs.

Child: Bradyarrhythmias, AV nodal block, or refractory torsade de pointes: Continuous I.V. infusion: Usual range: 0.05-2 mcg/kg/minute; titrate to patient response. Patients may exhibit dose-dependent vasodilation due to unopposed beta2-agonism elicited by isoproterenol.

Storage: store at room temperature.

Lidocaine hydrochloride

Injection, 5 mg/ml, 10 mg/ml, 20 mg/ml in 20 ml vial

Indications: acute treatment of ventricular arrhythmias from myocardial infarction or cardiac manipulation, cardiac catheterization and those caused by digitalis intoxication

Cautions: lower dosage in congestive heart failure, bradycardia, renal and hepatic impairment, marked hypoxia, severe respiratory depression, following cardiac surgery and in elderly.

Drug interactions: other antiarrhythmics (e.g., amiodarone), anticonvulsants, cimetidine, beta-blockers, saquinavir

Contraindications: sino-atrial disorder, any grade of atrioventricular block or any other type of conduction disturbances, severe myocardial depression, acute porphyria or hypovolaemia, history of hypersensitivity to amide type local anesthetics; pregnancy & children-safe use is not established.

Side effects: dizziness, paraesthesia, drowsiness, confusion, apnoea, respiratory depression, coma, seizures, and convulsions, hypotension, arrhythmias, heart block, cardiovascular collapse and brady cardia (may lead to cardiac arrest), nystagmus often an early sign of lidocaine overdose.

Dose and Administration: Antiarrhythmic: Adult: VF or pulseless VT (after defibrillation attempts, CPR, and vasopressor administration) if amiodarone is not available: I.V., intraosseous (I.O.): Initial: 1-1.5 mg/kg. If refractory VF or pulseless VT, repeat 0.5-0.75 mg/kg bolus every 5-10 minutes (maximum cumulative dose: 3 mg/kg). Follow with continuous infusion (1-4 mg/minute) after return of perfusion. Reappearance of arrhythmia during constant infusion: 0.5 mg/kg bolus and reassessment of infusion (Zipes, 2000).

Hemodynamically stable monomorphic VT: I.V.: 1-1.5 mg/kg; repeat with 0.5-0.75 mg/kg every 5-10 minutes as necessary (maximum cumulative dose: 3 mg/kg). Follow with continuous infusion of 1-4 mg/minute (or 14-57 mcg/kg/minute).

Child: I.V., intraosseous (I.O.): Note: For use in VF or pulseless VT if amiodarone is not available; give after defibrillation attempts, CPR, and epinephrine: Loading dose: 1 mg/kg (maximum: 100 mg); follow with continuous infusion; may administer second bolus of 0.5-1 mg/kg if delay between bolus and start of infusion is >15 minutes. Continuous infusion: 20-50 mcg/kg/minute. Per the manufacturer, do not exceed 20 mcg/kg/minute in patients with shock, hepatic disease, cardiac arrest, or CHF.

Storage: store at room temperature.

Metoprolol

Injection, 1 mg/ml, 05ml/ml

Tablet, 50 mg, 100 mg, 200 mg (s/r.)

Indications: Treatment of angina pectoris, hypertension, or hemodynamically-stable acute myocardial infarction. Treatment of angina pectoris or hypertension; to reduce mortality/hospitalization in patients with heart failure (stable NYHA Class II or III) already receiving ACE inhibitors, diuretics, and/or digoxin.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under propranolol.

Dose and Administration:Adult: Atrial fibrillation/flutter (ventricular rate control), supraventricular tachycardia (SVT) (acute treatment; unlabeled use; Antman, 2004; Fuster, 2006; Neumar, 2010): I.V.: 2.5-5 mg every 2-5 minutes (maximum total dose: 15 mg over a 10-15 minute period). Note: Initiate cautiously in patients with concomitant heart failure; avoid in patients with decompensated heart failure.

Maintenance: Oral (immediate release): 25-100 mg twice daily. Hypertension/ventricular rate control: I.V. (in patients having nonfunctioning GI tract): Initial: 1.25-5 mg every 6-12 hours; titrate initial dose to response. Initially, low doses may be appropriate to establish response; however, although not routine, up to 15 mg administered as frequently as every 3 hours has been employed in patients with refractory tachycardia. Myocardial infarction: Acute: I.V.: 5 mg every 2 minutes for 3 doses in early treatment of myocardial infarction; thereafter, give 50 mg orally every 6 hours beginning 15 minutes after last I.V. dose and continue for 48 hours; then administer a maintenance dose of 100 mg twice daily. Note: Do not initiate this regimen in those with signs of heart failure, a low output state, increased risk of cardiogenic shock, or other contraindications (eg, second- or third-degree heart block). If initial I.V. dosing is not tolerated, may give 25-50 mg orally (depending on degree of intolerance) every 6 hours beginning

15 minutes after the last I.V. dose or as soon as clinical condition permits.

Storage: at room temperature

Mexiletin Hydrochloride

Capsules, 50 mg, 200 mg

Injection, 25 mg/ml, in 10 ml ampoule

Indications: ventricular arrhythmias, prevention of recurrent cardiac arrests, suppression of paroxysmal ventricular contractions.

Cautions: patients with sinus node dysfunction, conduction defect, bradycardia, hypotension, cardiogenic shock, or cardiac or hepatic failure.

Drug interactions: opioid analgesics, atropine, phenytoin, rifampicin, cimetidine, lignocaine, phenobarbital.

Contraindications: hypersensitivity to mexiletin.

Side effects: nausea, vomiting, heart burn, tremor, confusion, dizziness, and visual disturbances, hypotension, sinus bradycardia, conduction defects and exacerbation of arrhythmias.

Dose and Administration: Adult: Oral: Initial: 200 mg every 8 hours (may load with 400 mg if necessary); adjust dose every 2-3 days; usual dose: 200-300 mg every 8 hours; maximum: 1.2 g/day (some patients respond to every 12-hour dosing). When switching from another antiarrhythmic, initiate a 200 mg dose 6-12 hours after stopping former agents, 3-6 hours after stopping procainamide. IV injection: 100 to 250 mg at a rate of 25 mg per minute, followed by an infusion at a rate of 250 mg over 1 hour, 250 mg over the next 2 hours, and then at about 0.5 mg per minute for maintenance, according to patient response.

Storage: store in airtight containers.

Phenytoin (Diphenylhydantoin sodium)

Powder for injection, 250mg in vial

Indication: Phenytoin and phenytoin sodium are administered orally. Phenytoin sodium also may be administered by slow IV injection for the treatment of status epilepticus and by slow IV or IM injection for the prophylaxis and treatment of seizures during neurosurgery. Ref Because parenteral administration of phenytoin is associated with more frequent and severe complications, the oral route is preferred for maintaining therapeutic concentrations of the drug during nonemergency situations; patients receiving the drug parenterally should routinely be assessed for feasibility of oral therapy.

Caution, contraindication, drug interaction, side effects (see under antiepileptics)

Dose and Administration: IV injections of phenytoin sodium should be made directly into a large vein through a large-gauge needle or IV catheter. The drug must be injected slowly at rates not exceeding 50 mg/minute in adults and 1–3 mg/kg per minute in pediatric patients. Each injection of phenytoin sodium should be followed by administration of sodium chloride injection through the same needle or IV catheter to reduce local venous irritation caused by the alkalinity of the injection solution. Subcutaneous and perivascular injection of phenytoin sodium should be avoided.

Procainamide hydrochloride

Injection, 100 mg/ml, 10-ml ampoule

Tablet, 250 mg,

Indications: Treatment of supraventricular arrhythmias. *Note: In the treatment of atrial fibrillation, use only when preferred treatment is ineffective or cannot be used. Use in paroxysmal atrial tachycardia when reflex stimulation or other measures are ineffective.*

Cautions: elderly, renal and hepatic impairment, asthma, pregnancy; breastfeeding, blood dyscrasias, drug induced lupus erythematosus

Drug interactions: other antiarrhythmics, anticholinergics, cimetidine, trimethoprim.

Contraindications: Hypersensitivity to procainamide, procaine, other ester-type local anesthetics, or any component of the formulation; complete heart block; second-degree AV block or various types of hemiblock (without a functional artificial pacemaker); SLE; torsade de pointes

Side effects: nausea, vomiting, diarrhoea, anorexia, severe hypotension, ventricular fibrillation, pericarditis, rashes, pruritus, urticaria, flushing, fever, and angioedema, depression, dizziness, and psychosis; blood disorders include leukopenia, haemolytic anemia and agranulocytosis after prolonged treatment; lupus erythematosus-like syndrome.

Dose and Administration: Adult: Dose must be titrated to patient's response. Antiarrhythmic: I.M.: 50 mg/kg/day divided every 3-6 hours or 0.5-1 g every 4-8 hours. I.V.: Loading dose: 15-18 mg/kg administered as slow infusion over 25-30 minutes or 100 mg/dose at a rate not to exceed 50 mg/minute repeated every 5 minutes as needed to a total dose of 1 g. Hemodynamically stable monomorphic VT or pre-excited atrial fibrillation. Loading dose: Infuse 20-50 mg/minute or 100 mg every 5 minutes until arrhythmia controlled, hypotension occurs, QRS complex widens by 50% of its original width, or total of 17 mg/kg is given. Follow with a continuous infusion of 1-4 mg/minute. *Note: Not recommended for use in ongoing ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) due to prolonged administration time and uncertain efficacy.*

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Maintenance dose: 1-4 mg/minute by continuous infusion. Maintenance infusions should be reduced by one-third in patients with moderate renal or cardiac impairment and by two-thirds in patients with severe renal or cardiac impairment. Oral: Sustained release formulation: Maintenance: 50 mg/kg/24 hours given in divided doses every 6 hours. **Child:** Must be titrated to patient's response: Arrhythmias: I.M.: 20-30 mg/kg/day divided every 4-6 hours; maximum: 4 g/day. I.V.: Load: 3-6 mg/kg/dose over 5 minutes not to exceed 100 mg/dose; may repeat every 5-10 minutes to maximum of 15 mg/kg/load. Maintenance as continuous I.V. infusion: 20-80 mcg/kg/minute; maximum: 2 g/24 hours.

Storage: store in airtight containers and at room temperature. Protect from light.

Propranolol

Injection, 1 mg/ml in 1 ml ampoule

Tablet, 10 mg, 40 mg

Indications: Management of hypertension; angina pectoris; pheochromocytoma; essential tremor; supraventricular arrhythmias (such as atrial fibrillation and flutter, AV nodal re-entrant tachycardias), ventricular tachycardias (catecholamine-induced arrhythmias, digoxin toxicity); prevention of myocardial infarction; migraine headache prophylaxis; symptomatic treatment of hypertrophic subaortic stenosis (hypertrophic obstructive cardiomyopathy)

Cautions: peripheral arterial insufficiency, first degree atrioventricular block, major surgery, renal & hepatic impairment, diabetes, myasthenia gravis, pregnancy. Avoid abrupt withdrawal.

Drug interactions: chlorpromazine, phenothiazines, thioxanthenes, lidocaine, cimetidine, hepatic enzyme inducers,

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(barbiturates, phenytoin, rifampicin), non-steroidal anti-inflammatory agents, digoxin, verapamil, neuromuscular blocking agents, anaesthetic agents, insulin or oral antidiabetic agents.

Contraindications: Hypersensitivity to propranolol, beta-blockers, or any component of the formulation; uncompensated congestive heart failure (unless the failure is due to tachyarrhythmias being treated with propranolol), cardiogenic shock, severe sinus bradycardia or heart block greater than first-degree (except in patients with a functioning artificial pacemaker), severe hyperactive airway disease (asthma or COPD).

Side effects: heart failure, heart block, hypotension, bronchospasm, fatigue and coldness of the extremities, headache, depression, dizziness, confusion and sleep disturbances, dry mouth, nausea, vomiting, diarrhea, impotence or decreased libido.

Dose and Administration: Oral: Adult: Tachyarrhythmias: Oral: 10 to 30 mg/dose every 6-8 hours. I.V.: 1 to 3 mg/dose slow IVP; repeat every 2-5 minutes up to a total of 5 mg; titrate initial dose to desired response or 0.5 to 1 mg over 1 minute; may repeat, if necessary, up to a total maximum dose of 0.1 mg/kg. *Note: Once response achieved or maximum dose administered, additional doses should not be given for at least 4 hours.* Thyroid storm: Oral: 60-80 mg every 4 hours; may consider the use of an intravenous shorter-acting beta-blocker (ie, esmolol). I.V.: 0.5-1 mg administered over 10 minutes every 3 hours. Thyrotoxicosis: Oral: 10-40 mg/dose every 6-8 hours; may also consider administering extended or sustained release formulations. Variceal hemorrhage prophylaxis (*unlabeled use*) Oral: Primary prophylaxis: Initial: 20 mg twice daily; adjust to maximal tolerated dose. *Note: Risk factors for hemorrhage*

include Child-Pugh class B/C or variceal red wale markings on endoscopy. Secondary prophylaxis: Initial: 20 mg twice daily; adjust to maximal tolerated dose 10 to 30mg/dose every 6-8 hours. **Child:** Initial: 0.5 to 1mg/kg/day in divided doses every 6-8 hours; titrate dosage upward every 3-7 days; usual dose: 2-6mg/kg/day; higher doses may be needed; do not exceed 16mg/kg/day or 60mg/day. **IV:** Adult: 1mg/dose slow IV injection; repeat every 5 minutes up to a total of 5mg. **Child:** 0.01-0.1mg/kg/dose slow IV injection over 10 minutes; maximum dose: 1mg for infants; 3mg for children.

Storage: store at room temperature

Quinidine sulphate

Tablet, 200 mg

Indications: Quinidine sulfate salts: Conversion and prevention of relapse into atrial fibrillation and/or flutter; suppression of ventricular arrhythmias. Note: Due to proarrhythmic effects, use should be reserved for life-threatening arrhythmias. Moreover, the use of quinidine has largely been replaced by more effective/safer antiarrhythmic agents and/or nonpharmacologic therapies (eg, radiofrequency ablation).

Cautions: hepatotoxicity, hypersensitivity reactions, proarrhythmic effects: disease-related concerns, atrial fibrillation/flutter, conduction disturbances: electrolyte imbalance, G6PD deficiency, heart failure, concurrent drug therapy issues (e.g. digoxin), elderly, do not interchange the different salt products.

Drug interactions: digoxin, amiodarone, rifampicin, Phenobarbital & phenytoin, nelfinavir & ritonavir, sodium bicarbonate, carbonic anhydrase inhibitors, other antiarrhythmics, phenothiazines, anticholinergics, reserpine, and anticonvulsants.

Contraindications: complete heart block, digitalis overdosage.

Side effects: the elderly are particularly susceptible to adverse nervous system effects and diarrhea, abdominal cramps, bitter taste, nausea and vomiting. Hypersensitivity reactions may occur, monitor patient after first dose. Acute hypotension, cinchonism and, in severe toxicity, photophobia, confusion, systemic lupus erythematosus and psychosis may occur.

Dose and Administration: Adult: Oral: Initial test dose of 200 mg to detect hypersensitivity to quinidine. *Note: Dosage expressed in terms of the salt: 267 mg of quinidine gluconate = 200 mg of quinidine sulfate.*

Antiarrhythmic: Oral: Immediate release formulations: Quinidine sulfate: Initial: 200-400 mg/dose every 6 hours the dose may be increased cautiously to desired effect. Extended release formulations: Quinidine sulfate: Initial: 300 mg every 8-12 hours; the dose may be increased cautiously to desired effect. Quinidine gluconate: Initial: 324 mg every 8-12 hours; the dose may be increased cautiously to desired effect.

Storage: store at room temperature and protect from light.

Sotalol

Tablet, 80mg, 120mg, 160mg, 240mg

Indications: Treatment of documented ventricular arrhythmias (ie, sustained ventricular tachycardia), that in the judgment of the physician are life-threatening; maintenance of normal sinus rhythm in patients with symptomatic atrial fibrillation and atrial flutter who are currently in sinus rhythm.

Contraindications: Hypersensitivity to sotalol or any component of the formulation; bronchial asthma; sinus bradycardia; second- or third-degree AV block (unless a functioning pacemaker is present); congenital or acquired long QT syndromes; cardiogenic shock; uncontrolled heart failure.

Dose and Administration: Adult: Baseline QTc interval and creatinine clearance must be determined prior to initiation. Sotalol should be initiated and doses increased in a hospital with facilities for cardiac rhythm monitoring and assessment. Proarrhythmic events can occur after initiation of therapy and with each upward dosage adjustment. Conversion from oral sotalol to I.V. sotalol:

- 80 mg oral equivalent to 75 mg I.V.
- 120 mg oral equivalent to 112.5 mg I.V.
- 160 mg oral equivalent to 150 mg I.V.

Ventricular arrhythmias:I.V.: Note: The effects of the initial I.V. dose must be monitored and the dose titrated either upward or downward, if needed, based on clinical effect, QTc interval, or adverse reactions. Substitution for oral sotalol: Initial dose: 75 mg infused over 5 hours twice daily.Dose adjustment: If the frequency of relapse does not reduce and excessive QTc prolongation does not occur, may increase to 112.5 mg twice daily. For ventricular arrhythmias, may increase dose every 3 days in increments of 75 mg/day.Dose range: Usual therapeutic dose: 75-150 mg twice daily; maximum dose: 300 mg twice daily.Hemodynamically stable monomorphic VT, ongoing (*unlabeled use*): 1.5 mg/kg over 5 minutes. *Note: Clinical trial employed standard dose of 100 mg.*Oral: Initial: 80 mg twice daily; dose may be increased gradually to 240-320 mg/day; allow 3 days between dosing increments (to attain steady-state plasma concentrations and to allow monitoring of QTc intervals). Usual range: Most patients respond to 160-320 mg/day in 2-3 divided doses. Maximum: Some patients, with life-threatening refractory ventricular arrhythmias, may require doses as high as 480-640 mg/day; prescribed ONLY when the potential benefit outweighs the increased of adverse events.

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Atrial fibrillation or atrial flutter: I.V.: Note: The effects of the initial I.V. dose must be monitored and the dose titrated either upward or downward, if needed, based on clinical effect, QTc interval, or adverse reactions. Substitution for oral sotalol: Initial dose: 75 mg infused over 5 hours twice daily. Dose adjustment: If the frequency of relapse does not reduce and excessive QTc prolongation does not occur, may increase to 112.5 mg twice daily. For ventricular arrhythmias, may increase dose every 3 days in increments of 75 mg/day. Dose range: Usual therapeutic dose: 112.5 mg twice daily; maximum dose: 150 mg twice daily.

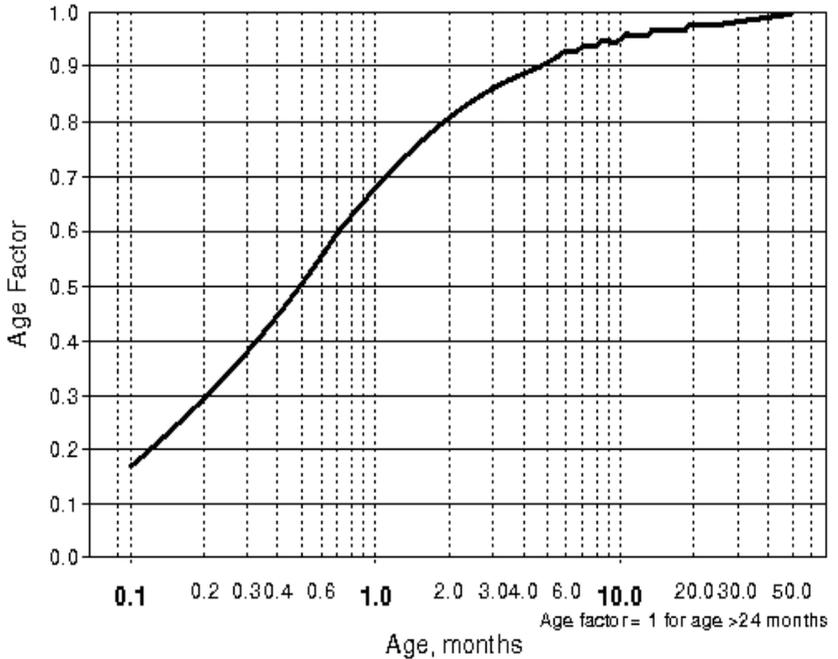
Dosing: Pediatric: Baseline QTc interval and creatinine clearance must be determined prior to initiation. Sotalol should be initiated and doses increased in a hospital with facilities for cardiac rhythm monitoring and assessment. Proarrhythmic events can occur after initiation of therapy and with each upward dosage adjustment.

Note: The safety and efficacy of sotalol in children have not been established
Supraventricular arrhythmias: Oral: *Note: Dosing per manufacturer, based on pediatric pharmacokinetic data; wait at least 36 hours between dosage adjustments to allow monitoring of QTc intervals.*

Children ≤ 2 years: Dosage should be adjusted (decreased) by plotting of the child's age on a logarithmic scale; see graph or refer to manufacturer's package labeling. Age factor nomogram:
Children > 2 years: Initial: 90 mg/m²/day in 3 divided doses; may be incrementally increased to a maximum of 180 mg/m²/day

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Age Factor Nomogram



Adapted from U.S. Food and Drug Administration.
<http://www.fda.gov/cder/foi/label/2001/2115s3lbl.PDF>

Verapamil Hydrochloride

Injection, 2.5 mg/ml in 2 ml ampoule

Tablets, 40 mg, 80 mg, 120 mg

Indications: Oral: Treatment of hypertension; angina pectoris (vasospastic, chronic stable, unstable); supraventricular tachyarrhythmia (PSVT, atrial fibrillation/flutter [rate control]); I.V.: Supraventricular tachyarrhythmia (PSVT, atrial fibrillation/flutter [rate control])

Cautions: first-degree atriovertricular block; acute phase of myocardial infarction; renal and hepatic impairment; children, pregnancy, breast-feeding, muscular dystrophy, aortic stenosis

Drug interactions: beta blocking-agents; antiarrhythmics, other highly protein-bound agents, carbamazepine, grape fruit juice, digoxin, lithium & cyclosporine and calcium salts.

Contraindications: Hypersensitivity to verapamil or any component of the formulation; severe left ventricular dysfunction; hypotension (systolic pressure <90 mm Hg) or cardiogenic shock; sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker); second- or third-degree AV block (except in patients with a functioning artificial ventricular pacemaker); atrial flutter or fibrillation and an accessory bypass tract (Wolff-Parkinson-White [WPW] syndrome, Lown-Ganong-Levine syndrome), Additional contraindications include concurrent use of I.V. beta-blocking agents; ventricular tachycardia.

Dose and Administration: Adult Chronic atrial fibrillation (rate-control), PSVT prophylaxis: Oral: Immediate release: 240-480 mg/day in 3-4 divided doses; Usual dose range (Fuster, 2006): 120-360 mg/day in divided doses. SVT I.V.: 2.5-5 mg over 2 minutes; second dose of 5-10 mg (~0.15 mg/kg) may be given 15-30 minutes after the initial dose if patient tolerates, but does not respond to initial dose; maximum total dose: 20-30 mg. Dosing: Pediatric SVT: *Note: Verapamil is no longer included in the Pediatric Advanced Life Support (PALS) tachyarrhythmia algorithm.*

Children: 1-15 years: I.V.: 0.1-0.3 mg/kg/dose over 2 minutes; maximum: 5 mg/dose, may repeat dose in 30 minutes if inadequate response; maximum for second dose: 10 mg.

3.3. Antilipemic agents

Antilipemic agents are used to modify blood lipid concentrations in the management of hyperlipidaemias and for the reduction of cardiovascular risk. The principal groups of lipid regulating medicines are the statins, fibrates, bile-acid binding resins, nicotines, and omega-3-triglycerides.

Statins: are inhibitors of 3-hydroxy-3-methyl glutaryl co enzyme A (HMG-CoA) reductase, the rate determining enzyme for cholesterol synthesis. These agents include simvastatin, rosuvastatin, atorvastatin, fluvastatin and lovastatin. They are potent reducers of plasma LDL cholesterol and triglyceride. They are indicated in severe hypercholesterolaemia, and may also be effective in some cases of mixed hyperlipidaemia and even in mild hypertriglyceridaemia. They are regarded as the medicines of choice for the management of most dyslipidaemias. The commonest side effects of therapy with statins are gastrointestinal disturbances. Myalgia, muscle enzyme release, or both has been reported, especially in patients taking statins concurrently with ciclosporin, fibric acid derivatives, or nicotinic acid.

Fibrates inhibits the synthesis of cholesterol and bile acids, and enhance the secretion of cholesterol in bile. These agents include gemfibrozil, clofibrate, bezafibrate and fenofibrate. The main effect is to reduce triglycerides by reducing the concentration of VLDL; they also increase HDL-cholesterol and have variable effects on LDL-cholesterol. They are used mainly in patients with hypertriglyceridaemia. The most common side effects of fibrates therapy are gastrointestinal disturbances including anorexia, nausea, and gastric discomfort. Fibrates therapy may be associated with myositis, myopathy, rarely rhabdomyolysis and gallstones.

Bile-acid binding agents such as cholestyramine are basic anion-exchange resins that bind bile acids in the gut, preventing their enterohepatic recycling and causing the hepatocyte to upregulate LDL receptors to obtain cholesterol for compensatory increases in bile acid synthesis. It is not absorbed and is effectively and safely combined with other agents in the treatment of hypercholesterolaemia. As cholestyramine reduces absorption, other medication should be taken at least an hour before, or delayed for at least four hours after administration of the resin.

Atorvastatin

Tablet, 10 mg, 20mg, 40mg, 80mg

Indications: Treatment of dyslipidemias or primary prevention of cardiovascular disease (atherosclerotic) as detailed below: Primary prevention of cardiovascular disease (high-risk for CVD): To reduce the risk of MI or stroke in patients without evidence of heart disease who have multiple CVD risk factors or type 2 diabetes. Treatment reduces the risk for angina or revascularization procedures in patients with multiple risk factors. Secondary prevention of cardiovascular disease: To reduce the risk of nonfatal MI, nonfatal stroke, revascularization procedures, hospitalization for heart failure, and angina in patients with evidence of coronary heart disease.

Treatment of dyslipidemias: To reduce elevations in total cholesterol (C), LDL-C, apolipoprotein B, and triglycerides in patients with elevations of one or more components, and/or to increase low HDL-C as present in Fredrickson type IIa, IIb, III, and IV hyperlipidemias, heterozygous familial and nonfamilial hypercholesterolemia, and homozygous familial hypercholesterolemia. Treatment of heterozygous familial hypercholesterolemia (HeFH) in adolescent patients (10-17

years of age, females >1 year postmenarche) having LDL-C ≥ 190 mg/dL or LDL-C ≥ 160 mg/dL with positive family history of premature cardiovascular disease (CVD) or with two or more CVD risk factors.

Cautions: hepatic disease or elevated serum transaminases.

Drug interactions: alcohol, warfarin, cholestyramine, digoxin, drug which inhibit cytochrome P450 isoenzyme 3A4 (cyclosporin, macrolides, azoles, protease inhibitor; they increase risk of myopathy), fibrates, nicotinic acid, propranolol.

Contraindications: known hypersensitivity to the drug; active liver disease or unexplained persistently raised serum-aminotransferase concentrations, pregnancy.

Side effects: abdominal pain, constipation, diarrhea, flatulence, nausea, dyspepsia; myalgia associated with muscle stiffness or weakness, or elevations of creatine kinase; plasma transaminase elevation; headache, insomnia, skin rash, peripheral neuropathy and a hypersensitivity syndrom with angioedema. Rhabdomyolysis with renal failure has occurred. Incidence and severity of myopathy are increased by drug interactions-see above.

Dose and Administration: Adult: Primary prevention: Note: Doses should be individualized according to the baseline LDL-cholesterol concentrations, the recommended goal of therapy, and patient response; adjustments should be made at intervals of 2-4 weeks. **Hypercholesterolemia (heterozygous familial and nonfamilial) and mixed hyperlipidemia (Fredrickson types IIa and IIb):** Oral: Initial: 10-20 mg once daily; patients requiring >45% reduction in LDL-C may be started at 40 mg once daily; range: 10-80 mg once daily. **Homozygous familial hypercholesterolemia:** Oral: 10-80 mg once daily. **Secondary prevention: Clinically evident coronary heart disease:** Oral: Initial: 80 mg once daily; adjust based on patient tolerability

and recommended goal LDL-C. **Intensive lipid-lowering after an ACS event regardless of baseline LDL (unlabeled use):** Oral: Initial: 80 mg once daily; adjust based on patient tolerability and recommended goal LDL-C (Cannon, 2004; Pederson, 2005; Schwartz, 2001). **Noncardioembolic stroke/TIA (unlabeled use):** Oral: Initial: 80 mg once daily; adjust based on patient tolerability and recommended goal LDL-C.

Dosage adjustment for atorvastatin with concomitant medications: Clarithromycin, itraconazole, fosamprenavir, ritonavir (plus darunavir, fosamprenavir, or saquinavir): Use lowest effective atorvastatin dose (not to exceed 20 mg daily), Nelfinavir: Use lowest effective atorvastatin dose (not to exceed 40 mg daily)

Pediatric Note: *Doses should be individualized according to the baseline LDL-cholesterol concentrations, the recommended goal of therapy, and patient response; adjustments should be made at intervals of 4 weeks*

HeFH: Children 10-17 years (females >1 year postmenarche): Oral: 10 mg once daily (maximum: 20 mg/day). **Dosage adjustment for atorvastatin with concomitant medications:** Clarithromycin, itraconazole, fosamprenavir, ritonavir (plus darunavir, fosamprenavir, lopinavir, or saquinavir): Lowest effective atorvastatin dose (not to exceed 20 mg/day) should be used. Nelfinavir: Lowest effective atorvastatin dose (not to exceed 40 mg/day) should be used.

Storage: store in well-closed, light -resistant containers at 5 – 30°C

Cholestyramine

Powder, 4 g in 9g sachet

Indications: Adjunct in the management of primary hypercholesterolemia; pruritus associated with elevated levels of bile acids; regression of arteriosclerosis.

Cautions: patients with constipation and phenylketoneuria, risk of vitamin deficiencies in prolonged use.

Drug interactions: fat-soluble vitamins, warfarin, digoxin, thiazides, barbiturates, aspirin, tetracyclines and thyroxine.

Contraindications: complete biliary and bowel obstruction, active peptic, ulcer disease; sensitivity to tartrazine.

Side effects: frequently unpalatable or associated with bloated feeling, nausea, vomiting, constipation occurs frequently, headache and dizziness, (<1%). May aggravate hypertriglyceridaemia; see also notes above.

Note: constipation, most common side effect of cholestyramine, may be, countered by increased fiber and water intake

Dose and Administration: Oral: **Adult:** **Dyslipidemia:** Oral: Initial: 4 g 1 to 2 times/day; increase gradually over ≥ 1 month intervals; maintenance: 8-16 g/day divided in 2 doses; maximum: 24 g/day

Child: over 6 years, 240 mg/kg/day in divided doses has been suggested.

Storage: store in airtight containers and at room temperature.

Ezetimibe

Tablet, 10mg

Indications: Use in combination with dietary therapy for the treatment of primary hypercholesterolemia (as monotherapy or in combination with HMG-CoA reductase inhibitors); homozygous sitosterolemia; homozygous familial hypercholesterolemia (in combination with atorvastatin or simvastatin); mixed hyperlipidemia (in combination with fenofibrate).

Drug interactions: cholestyramine, ciclosporine

Contraindications: moderate to severe hepatic impairment; children under 10 years of age.

Side effects: Common - headache, abdominal pain and diarrhoea, rash & angioedema. Also, when combined with a statin, constipation, flatulence, nausea, increased ALT/AST, myalgia and rhabdomyolysis.

Dose and Administration: Adult: Oral: 10 mg daily. Children: ≥ 10 years, 10 mg daily.

Fenofibrate

Tablets, (micronised) 160 mg

Indications: Adjunct to dietary therapy for the treatment of adults with elevations of serum triglyceride levels (types IV and V hyperlipidemia); adjunct to dietary therapy for the reduction of low density lipoprotein cholesterol (LDL-C), total cholesterol (total-C), triglycerides, and apolipoprotein B (apo B), and to increase high density lipoprotein cholesterol (HDL-C) in adult patients with primary hypercholesterolemia or mixed dyslipidemia (Fredrickson types IIa and IIb).

Cautions: liver function tests recommended every 3 months for first year (discontinue treatment if significantly raised); Renal impairment: reduce dose to 134 mg daily if eGFR less than 60 mL/minute/1.73 m²; reduce dose to 67 mg daily if eGFR less than 20 mL/minute/1.73 m²; avoid if eGFR less than 15 mL/minute/1.73 m²; myositis-like syndrome, especially if renal function is impaired. Also, combination of a fibrate with a statin increases the risk of muscle effects (especially rhabdomyolysis)

Contraindications: gall bladder disease; pancreatitis (unless due to severe hypertriglyceridaemia); photosensitivity to ketoprofen; Hepatic impairment (avoid in severe liver disease), Pregnancy, Breast-feeding

Druginteraction: Ciclosporin, Colchicine, Coumarins, Daptomycin, Ezetimibe, Insulin, Phenindione, Statins, Sulfonylureas

Side effects: gastro-intestinal disturbances, anorexia; less commonly cholestasis, weight gain, dizziness, headache, fatigue, drowsiness, renal impairment, raised serum creatinine (unrelated to renal impairment), erectile dysfunction, myotoxicity (with myasthenia or myalgia)—special risk in renal impairment (see Cautions), urticaria, pruritus, photosensitivity reactions.

Dose and Administration:Adult: oral, 160 mg daily (not appropriate for children or in renal impairment)

Fluvastatin

Capsule, 20mg, 40mg

Tablet, 80mg

Indications: To be used as a component of multiple risk factor intervention in patients at risk for atherosclerosis vascular disease due to hypercholesterolemia. Adjunct to dietary therapy to reduce elevated total cholesterol (total-C), LDL-C, triglyceride, and apolipoprotein B (apo-B) levels and to increase HDL-C in primary hypercholesterolemia and mixed dyslipidemia (Fredrickson types IIa and IIb); to slow the progression of coronary atherosclerosis in patients with coronary heart disease; reduce risk of coronary revascularization procedures in patients with coronary heart disease.

Cautions: previous, liver disease or heavy ethanol use. Treatment in patients < 18 years of age is not recommended.

Drug interactions: cimetidine, omeprazole, ranitidine and ritonavir, erythromycin, gemfibrozil, digoxin, amiodarone, fluoxetine, phenytoin, warfarin and others.

Contraindications: hypersensitivity reaction, active liver disease, unexplained persistent elevations of serum transaminases, pregnancy, breast-feeding.

Side effects: headache, fatigue, insomnia, dyspepsia, diarrhea, abdominal pain, nausea, urinary tract infection, myalgia, sinusitis, bronchitis.

Dose and Administration:Adult: Oral: Patients requiring \geq 25% decrease in LDL-C: 40mg capsule or 80mg extended release tablet once daily in the evening; may also use 40mg capsule twice daily

Patients requiring $<$ 25% decrease in LDL-C: 20mg capsule once daily in the evening.

Note: Dosing range: 20-80 mg/day; adjust dose based on response to therapy; maximum response occurs within 4-6 weeks.

Storage: store at 25⁰C. Protect from light.

Gemfibrozil

Capsule, 300 mg

Indications: treatment of hypertriglyceridemia in WHO types IV and V hyperlipidemia for patients who are at great risk for pancreatitis and who have not responded to dietary interventions.

Cautions: hyperthyroidism, gall bladder disorders, peptic ulcer, hyperalbuminaemic states and cardiovascular disease.

Drug interactions: warfarin, HMG CoA reductase inhibitors, phenytoin, sulphonylureas, and cholestyramine.

Contraindications: hypersensitivity to fibrates; renal or hepatic failure; primary biliary cirrhosis; gallstones.

Side effects: gastrointestinal disturbances, myalgia/myosis like syndrome, eczema, rash headache, dizziness, blurred vision; transient leucopenia may occur; see also notes above.

Dose and Administration: Adult: Oral: Initially 300 mg twice daily, increased to 600 mg twice daily, 30 minutes before the morning and evening meals. Dosage range, 0.9-1.5 g daily in 2 divided doses.

Storage: store in airtight containers and at room temperature.

Lovastatin

Tablet, 20 mg

Indications: Adjunct to dietary therapy to decrease elevated serum total and LDL cholesterol concentrations in primary hypercholesterolemia. Primary prevention of coronary artery disease (patients without symptomatic disease with average to moderately elevated total and LDL-cholesterol and below average HDL cholesterol); slow progression of coronary atherosclerosis in patients with coronary heart disease and reduce the risk of myocardial infarction, unstable angina, and coronary revascularization procedures. Adjunct to dietary therapy in adolescent patients (10-17 years of age, females >1 year postmenarche) with heterozygous familial hypercholesterolemia having LDL >189 mg/dL, or LDL >160 mg/dL with positive family history of premature cardiovascular disease (CVD), or LDL >160 mg/dL with the presence of at least two other CVD risk factors.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under simvastatin.

Dose and Administration: Adult: Oral: an initial dose of 10 to 20 mg daily in the evening with food, increased, if necessary, at intervals of 4 weeks or more to 80 mg daily in single or divided doses. In patients taking immunosuppressant drugs an initial dose of 10 mg daily is recommended; the daily dose should not exceed 20 mg.

Orlistat

Capsule, 120mg

Indication: Management of obesity, including weight loss and weight management, when used in conjunction with a reduced-calorie and low-fat diet; reduce the risk of weight regain after prior weight loss; indicated for obese patients with an initial body mass index (BMI) ≥ 30 kg/m² or ≥ 27 kg/m² in the presence of other risk factors (eg, diabetes, dyslipidemia, hypertension).

Cautions: Epilepsy; pregnancy; breast-feeding; impair absorption of fat soluble vitamins, children; If a multivitamin supplement is required, it should be taken at least 2 hours after orlistat dose or at bedtime.

Drug Interactions: Acarbose, Amiodarone, antiepileptics, ciclosporin, coumarins, levothyroxine.

Contraindications: Orlistat is contraindicated in patients with chronic malabsorption syndrome or cholestasis, and in patients with known hypersensitivity to Orlistat or to any component of this product.

Side effects: oily leakage from rectum, flatulence, faecal urgency, liquid or oily stools, faecal incontinence, abdominal distension and pain (gastro-intestinal effects minimised by reduced fat intake), tooth and gingival disorders; respiratory infections; fatigue, anxiety, headache; menstrual disturbances, urinary-tract infection; hypoglycaemia; rarely rectal bleeding, hypothyroidism; very rarely diverticulitis, cholelithiasis, hepatitis, and bullous eruptions; oxalate nephropathy .

Dose and Administration: one capsule (120 mg) three times daily. Adult over 18 years: 120 mg taken immediately before, during, or up to 1 hour after each main meal (up to max. 360 mg daily); continue treatment beyond 12 weeks only if weight loss since start of treatment exceeds 5% (target for

initial weight loss may be lower in patients with type 2 diabetes): administered orally with each main meal containing fat; if a meal is missed by the patient or the meal contains no fat, that dose may be omitted. Patients should be on a reduced-calorie diet with approximately 30% of the calories from fat. Protein, carbohydrate, and fat intake should be balanced over 3 main meals. May decrease the absorption of some fat-soluble vitamins (A, D, E, K) and beta-carotene. To ensure adequate nutrition, patients should take a multivitamin supplement that contains fat-soluble vitamins. The multivitamin supplement should be taken orally once per day at least two hours before or after administration (i.e. bedtime).Maximum Dosage Limits:

- Adults: 360 mg/day PO.
- Elderly: 360 mg/day PO.
- Adolescents \geq 12 years: 360 mg/day PO.

Storage: Store at room temperature

Rosuvastatin

Tablet, 5mg, 10mg, 20mg, 40mg

Indication: Treatment of dyslipidemias: Used with dietary therapy for hyperlipidemias to reduce elevations in total cholesterol (TC), LDL-C, apolipoprotein B, nonHDL-C, and triglycerides (TG) in patients with primary hypercholesterolemia (elevations of 1 or more components are present in Fredrickson type IIa, IIb, and IV hyperlipidemias); increase HDL-C; treatment of primary dysbetalipoproteinemia (Fredrickson type III hyperlipidemia); treatment of homozygous familial hypercholesterolemia (FH); to slow progression of atherosclerosis as an adjunct to diet to lower TC and LDL-C. Heterozygous familial hypercholesterolemia (HeFH): In adolescent patients (10-17 years of age, females >1 year postmenarche) with HeFH having LDL-C >190 mg/dL or LDL

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>160 mg/dL with positive family history of premature cardiovascular disease (CVD), or ≥ 2 other CVD risk factors.

Primary prevention of cardiovascular disease: To reduce the risk of stroke, myocardial infarction, or arterial revascularization procedures in patients without clinically evident coronary heart disease or lipid abnormalities but with all of the following: 1) an increased risk of cardiovascular disease based on age ≥ 50 years old in men and ≥ 60 years old in women, 2) hsCRP ≥ 2 mg/L, and 3) the presence of at least one additional cardiovascular disease risk factor such as hypertension, low HDL-C, smoking, or a family history of premature coronary heart disease.

Secondary prevention of cardiovascular disease: To slow progression of atherosclerosis

Cautions: In patients with risk factors for myopathy or rhabdomyolysis (including personal or family history of muscular disorders or toxicity), Hepatic impairment, renal impairment, pregnancy, breast feeding. Safety and efficacy have not been established in children.

Drug Interactions: Antacids (magnesium), atazanavir, coumarins, darunavir, erythromycin, ethinylestradiol, fasamprenavir, indinavir, lopinavir, nelfinavir, norgestrel, Chlchicine, cyclosporine, fibrate, gemfibrozil, tipranavir, ritonavir, phenindione, saquinavir, daptomycin, nicotic acid, niacin, warfarin, cholestyramine and colestipol, alcohol.

Contraindications: known hypersensitivity to any component of this product; active liver disease or with unexplained persistent elevations of serum transaminases.

Sideeffects: Headache, dizziness, depression, rash, abdominal pain, constipation, nausea, vomiting, diarrhea, anemia, pain in the muscles (myalgia), weakness or loss of strength (asthenia), presence of protein in the urine.

Dosage and Administration: Dosing: Adult

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Note: Doses should be individualized according to the baseline LDL-cholesterol levels, the recommended goal of therapy, and patient response; adjustments should be made at intervals of 4 weeks or more.

Hyperlipidemia, mixed dyslipidemia, hypertriglyceridemia, primary dysbetalipoproteinemia, slowing progression of atherosclerosis: Oral: *Initial dose:* General dosing: 10 mg once daily; 20 mg once daily may be used in patients with severe hyperlipidemia (LDL >190 mg/dL) and aggressive lipid targets
Conservative Dosing: Patients requiring less aggressive treatment or predisposed to myopathy (including patients of Asian descent): 5 mg once daily. *Titration:* After 2 weeks, may be increased by 5 to 10 mg once daily; dosing range: 5 to 40 mg/day (maximum dose: 40 mg once daily).

Note: The 40 mg dose should be reserved for patients who have not achieved goal cholesterol levels on a dose of 20 mg/day, including patients switched from another HMG-CoA reductase inhibitor.

Homozygous familial hypercholesterolemia (FH): Oral: Initial: 20 mg once daily (maximum dose: 40 mg/day). **Dosage adjustment with concomitant medications:** Oral: *U.S. labeling:* Cyclosporine: Rosuvastatin dose should not exceed 5 mg/day. Gemfibrozil: Avoid concurrent use; if unable to avoid concurrent use, rosuvastatin dose should not exceed 10 mg/day. Atazanavir/ritonavir or lopinavir/ritonavir: Rosuvastatin dose should not exceed 10 mg/day. *Canadian labeling:* Cyclosporine: Concomitant use is contraindicated

Gemfibrozil: Rosuvastatin dose should not exceed 20 mg/day.

Dosage adjustment for hematuria and/or persistent, unexplained proteinuria while on 40 mg/day: Reduce dose and evaluate causes.

Dosing: Pediatric *Note: Doses should be individualized according to the baseline LDL-cholesterol levels, the recommended goal of therapy, and patient response; adjustments should be made at intervals of 4 weeks or more.*

Heterozygous familial hypercholesterolemia (HeFH):

U.S. labeling: Children 10-17 years (females >1 year postmenarche): Oral: 5-20 mg once daily; maximum: 20 mg/day. *Dosage adjustment for rosuvastatin with concomitant cyclosporine, atazanavir/ritonavir or lopinavir/ritonavir:* Refer to adult dosing.

Canadian labeling: Oral: 5-10 mg once daily; maximum: 10 mg/day. Dosing: Renal Impairment Mild to moderate impairment: No dosage adjustment required.

$Cl_{cr} < 30 \text{ mL/minute/1.73 m}^2$: Initial: 5 mg/day; do not exceed 10 mg once daily. Dosing: Hepatic Impairment *U.S. labeling:* Active hepatic disease, including unexplained persistent transaminase elevations: Use is contraindicated. *Canadian labeling:* Active hepatic disease or unexplained persistent transaminase >3x *ULN: Use is contraindicated.* Mild to moderate impairment: No dosage adjustment required. Severe impairment: Initial: 5 mg/day; do not exceed 20 mg once daily.

Storage: Store it at room temperature.

Simvastatin

Tablets, 5mg, 10 mg, 20 mg, 40 mg

Indications: Used with dietary therapy for the following: Secondary prevention of cardiovascular events in hypercholesterolemic patients with established coronary heart disease (CHD) or at high risk for CHD: To reduce cardiovascular morbidity (myocardial infarction, coronary/noncoronary revascularization procedures) and mortality; to reduce the risk of stroke.

Hyperlipidemias: To reduce elevations in total cholesterol (total-C), LDL-C, apolipoprotein B, triglycerides, and VLDL-C, and to increase HDL-C in patients with primary hypercholesterolemia (elevations of 1 or more components are

present in Fredrickson type IIa, IIb, III, and IV hyperlipidemias); treatment of homozygous familial hypercholesterolemia. Heterozygous familial hypercholesterolemia (HeFH): In adolescent patients (10-17 years of age, females >1 year postmenarche) with HeFH having LDL-C \geq 190 mg/dL or LDL-C \geq 160 mg/dL with positive family history of premature cardiovascular disease (CVD), or 2 or more CVD risk factors in the adolescent patient.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under Atrovastatin

Dose and Administration: Adult: Oral: initially 10mg at night, adjusted, if required, at intervals of 4 weeks or more. Maximum 80 mg/day. Severe renal impairment (creatinine clearance <30 ml/min): 10 mg/day. If higher doses are necessary, implement with caution.

Ursodeoxycholic Acid

Capsule, 250mg

Indication: The medicine reduces cholesterol absorption and is used to dissolve (cholesterol) gallstones in patients who want an alternative to surgery.

Cautions: Pregnancy, breast-feeding, hepatic impairment

Drug Interactions: Ciclosporin, antacids, colestipol, colestyramine, oestrogens, clofibrate, clomifene, conjugated estrogens, diethylstilbestrol, estradiol, ethnyl estradiol, fenofibrate, gemfibrozil.

Contraindications: Ursodeoxycholic acid will not dissolve calcified cholesterol stones, radiopaque stones, or radiolucent bile pigment stones. Hence, patients with such stones are not candidates for ursodeoxycholic acid; Patients with compelling reasons for cholecystectomy including unremitting acute cholecystitis, non-functioning gall bladder, inflammatory

diseases and other conditions of the small intestine, cholangitis, biliary obstruction, gallstone pancreatitis, or colon and liver which interfere with entero-hepatic circulation of bile salts are not candidates for Ursodeoxycholic acid therapy; Allergy to bile acids.

Side-effects: nausea, vomiting, diarrhoea; gallstone calcification; pruritus.

Dose and Administration: Dissolution of gallstones, 8–12 mg/kg daily as a single dose at bedtime or in two divided doses, for up to 2 years; treatment is continued for 3–4 months after stones dissolve.

Storage: Store at room temperature.

3.4. Medicines used for Angina/Ischemic Heart Disease

Angina pectoris is a syndrome that arises from reduced myocardial oxygen supply. The prominent symptom is transient precordial distress ranging from discomfort to severe pain. The three main types of angina are: stable angina: unstable angina, and Prinzmetal's angina. These should not be regarded as discrete groups as more than one type is usually present in the patient with angina.

Treatment depends on the type of angina and includes drug therapy (nitrates, beta blockers and calcium channel blockers), percutaneous coronary interventions, and coronary artery bypass surgery. Antithrombotics are used in unstable angina and include anticoagulants and antiplatelets.

Glyceryl trinitrate and other organic nitrates have a vasodilator effect with venodilatation predominating over dilatation of the arterioles and they have a useful role in angina. Sublingual Glyceryl trinitrate is one of the most effective drugs for providing rapid symptomatic relief of angina, but its effect lasts only for 20 to 30 minutes. Duration of action may be

prolonged by modified - release and transdermal preparations (but tolerance may develop)

A sublingual tablet of isosorbide dinitrate is more stable in storage than glyceryl trinitrate and is useful in patients who require nitrates infrequently; it has a slower onset of action, but effects persist for several hours.

Beta-blockers, such as atenolol, block beta-adrenergic receptors in the heart, and thereby decrease heart rate and myocardial contractility and oxygen consumption, particularly during exercise. Beta-blockers are first-line therapy for patients with effort-induced chronic stable angina; they improve exercise tolerance, relieve symptoms, reduce the severity and frequency of angina attacks, and increase the anginal threshold. Beta-blockers should be withdrawn gradually to avoid precipitating an anginal attack; they should not be used in patients with underlying coronary vasospasm (prinzmetal angina). The different beta-blockers appear to be equally effective in stable angina, although it has been suggested that those with intrinsic sympathomimetic activity should be avoided.

A calcium-channel blocker, such as verapamil, is used as an alternative, particularly in patients unable to tolerate beta-blockers. Calcium-channel blockers interfere with the inward movement of calcium ions through the slow channels in heart and vascular smooth muscle cell membranes, leading to relaxation of vascular smooth muscle. Calcium-channel blockers are used to improve exercise tolerance in patients with chronic stable angina due to coronary atherosclerosis or with abnormally small coronary arteries and limited vasodilator reserve. They can also be used in patients with unstable angina with a vasospastic origin, such as Prinzmetal angina, and in patients in whom alterations in cardiac tone may influence the

angina threshold. Care is required in selecting an appropriate medicine since the properties of dihydropyridine calcium-channel blockers (such as nifedipine) and rate-limiting calcium channel blockers (diltiazem and verapamil) are not the same. Studies comparing long-acting calcium-channel blockers (verapamil or modified-release nifedipine) with beta-blockers have shown similar outcomes in terms of symptom control and cardiovascular events. However, dihydropyridines may cause tachycardia and are less suitable than rate limiting calcium-channel blockers for monotherapy; they should not be used with out beta-blockers in unstable angina. Short-acting preparations of nifedipine have been associated with increased mortality and are not recommended.

Atenolol

Tablets, 50 mg, 100 mg

Indications: angina, Chronic Stable Angina: Unstable Angina/Non-ST-Elevation Myocardial Infarction.

Cautions, Drug interactions, Contraindications, Side effects; see section 3.2 under propranolol.

Dose and Administration: Oral: Angina: **Adult Angina pectoris:** Oral: 50 mg once daily; may increase to 100 mg/day. Some patients may require 200 mg/day.

Child: 0.8 to 1.5 mg/kg/day (maximum 2 mg/kg/day)

Storage: store at room temperature and protect from light.

Diltiazem Hydrochloride

Tablets, 60 mg, 90 mg, 120 mg, 90 mg (s/r), 120 mg (s/r)

Indications: angina (including Prinzmetal's angina), hypertension, supraventricular arrhythmias.

Cautions, Drug interactions, Contraindications and Side effects; see section 3.2 under verapamil

Dose and Administration: Oral: **Adult:** Angina: Immediate release: usual starting dose: 30mg 4 times/day; usual range: 180-360 mg/day in divided doses. Extended release: 180mg once daily; may increase at 7-14 day intervals (maximum recommended dose: 360mg/day).

Note: Do not crush long sustained release dosage forms.

Storage: store at room temperature.

Glyceryl trinitrate (Nitroglycerine)

Capsule (extended release), 2.5 mg, 6.5mg, 9mg

IV infusion, 0.1mg/ml, 0.2mg/ml, 0.4mg/ml

Injection, 5mg/ml

Ointment, 2%

Transdermal Patch, 0.1mg/hr, 0.2mg/hr, 0.4mg/hr

Transdermal Spray, 0.4mg/dose

Tablet (sublingual), 0.3mg, 0.4mg, 0.5 mg, 0.6mg

Tablet (Sustained released), 2.5 mg

Controlled release tablet, 2.6mg

Indications: prophylaxis and treatment of angina.

Cautions: severe hepatic or renal impairment; hypothyroidism, malnutrition, or hypothermia, recent history of myocardial infarction; conditions that cause dry mouth.

Drug interactions: alcohol, antihypertensive, vasodilators and sildenafil.

Contraindications: hypersensitivity to nitrates; hypertensive conditions and hypovolaemia; hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis; marked anaemia, head trauma, cerebral haemorrhage, closed - angle glaucoma.

Side effects: Flushing of the face, dizziness, tachycardia, and throbbing headache. Large doses cause vomiting, restlessness, blurred vision, hypotension (which can be severe), syncope and

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rarely cyanosis, and methaemoglobinaemia; impairment of respiration and bradycardia may ensue. Contact dermatitis (topical glyceryl trinitrate preparations), localized burning sensation (sublingual tablets). Tolerance may develop from uninterrupted, repeated use.

Note: tolerance may be managed by nitrate withdrawal (12-36 hours) and reinstatement with the same agent. Doses may need to be reviewed as tolerance develops.

Dose and Administrations: Adult: Sublingual: 0.3 to 0.6 mg repeated at five-minute intervals for the maximum of 3 doses in 15 minutes, may also use prophylactically 5-10 minutes prior to activities which may provoke an attack. **Oral:** 2.5 to 9mg 2-4 times/day (up to 26 mg 4 times/day). **Ointment:** topical to the skin, 15 to 30 mg of nitroglycerin (contained in 2.5 to 5cm [1 to 2 inches] of ointment as squeezed from the tube) every eight hours during the day and at bedtime. If angina occurs between doses, frequency of application may be increased to every six hours. **Buccal:** Initial: 1mg every 3-5 hours while awake (3times/day); titrate dosage upward if angina occurs with tablet in place. **IV:** 5mcg/minute, increase by 5mcg/minute every 3-5 minutes to 20mcg/minute; if no response at 20mcg/minute increase by 10mcg/minute every 3-5 minutes, up to 200mcg/minute. **Patch, transdermal:** initial: 0.2 to 0.4 mg/hour titrates to doses of 0.4-0.8mg/hour. **Spray:** 1to2 sprays into mouth under tongue every 3 to 5 minutes for maximum of three doses in 15 minutes. *Dosage has not been established for pediatric use.*

Note1:Sublingual tablet: Instruct patient to sit or lie down upon first indication of incoming angina pain and to place tablet under tongue or in buccal pouch (hypotensive effect of drug is intensified in the upright position). Instruct patient to allow tablet to dissolve naturally and not to swallow until drug is entirely dissolved. Advise patient

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with dry mouth to take a sip of water or place 1ml saline under the tongue before taking the nitroglycerin tablet.

Note 2: Sustained-release tablet or capsule Take on an empty stomach (1 hour before or 2 hours after meals), with a full glass of water, and swallowes whole. Sustained release form helps to prevent anginal attack, it is not intended for immediate relief of angina. Do not crush or chew.

Note 3: Transdermal ointment: Ointment is applied in a thin, even layer covering an area of the same size (measuring at least 2 by 3 inches) at each use, but it is not to be rubbed or massaged into the skin. The site of ointment application may be the non-hairy skin of the chest, stomach, front of the thighs, or any other accessible areas of clean, dry skin. Application to the chest is commonly preferred since the patient also benefits psychologically from applying medication to the area where the pain is experienced. Keep ointment container tightly closed and store in cool place.

Storage: nitroglycerin tablets for sublingual use may easily lose half their potency in 24 hours if stored incorrectly. Tablets should be kept in the original container, which should be kept tightly Closed and closed immediately after use. Pateints should keep the container in a cool place, e.g. handbag or outer clothing Pocket. Discard 60 days after opening. No more than 100 tablets should be dispensed at one time

Isosorbide dinitrate

Tablets (sublingual), 5 mg, 10 mg

Indications: relief of acute anginal attacks and for management of long-term angina pectoris; congestive cardiac failure.

Cautions, Drug interactions, Contraindications and Side effects; see under glyceryl trinitrate.

Note: as with other long acting nitrates, tolerance develops rapidly.

Dose and Administration: Adult: Sublingually:Angina (acute attack): 2.5 to 10 mg, if relief is not attained after a single dose, additional doses may be given at 5-10 minute intervals; no more

than 3 doses should be given in a 15-30 minute period. Angina prophylaxis: 2.5 - 10 mg 4-6 hourly. Congestive cardiac failure: 40mg 4 times daily. However, as 6 hourly administrations may promote tolerance, 12 hourly dosage is preferable, alternatively dosing with a nitrate-free night restores tolerance.

Storage: store at room temperature.

Isosorbide mononitrate

Tablet, 10mg, 20mg, 25mg(m/r), 40mg(m/r), 60mg(m/r)

Capsule(m/r), 40mg, 50mg

Indications: prophylaxis of angina; adjunct in congestive heart failure

Cautions: pregnancy, renal and hepatic impairment, hypothyroidism; malnutrition; hypothermia; recent history of myocardial infarction; heart failure due to obstruction; hypoxaemia or other ventilation and perfusion abnormalities; susceptibility to angle-closure glaucoma; metal-containing transdermal systems should be removed before magnetic resonance imaging procedures, cardioversion, or diathermy; avoid abrupt withdrawal

Drug interactions: enhanced hypotensive effect when given with ACE inhibitors, Adrenergic neurone blockers, alcohol, Alpha- blockers, Alprostadil, general anaesthetics, angiotensine II receptor Antagonists

Contraindications: hypersensitivity to isosorbide mononitrate or organic nitrates, hypotensive conditions and hypovolaemia; hypertrophic cardiomyopathy; aortic stenosis; cardiac tamponade; constrictive pericarditis; mitral stenosis; toxic pulmonary oedema; raised intracranial pressure due to cerebral haemorrhage or head trauma; marked anaemia, avoid concomitant use with Sildenafil, Tadalafil and verdinafil (hypotensive effects will be enhanced).

Side effects:Headache, rash, dizziness, upset stomach, flushing

Dose and Administration: Adult: Oral: 20mg 8-12 hourly. 20-120mg/day in divided doses has been used.

Storage: store at room temperature

Metoprolol

Injection, 1mg/ml, 5mg/ml

Tablets, 50mg, 100 mg, 200mg(s/r)

Indications, Cautions, Drug interactions, Contraindications,

Side effects and Storage; see section 2.2, under metoprolol.

Dose and Administration:Oral:Angina: 50-100mg 2to 3 times daily.

Nifedipine

Capsule,5mg,10mg,20mg,30mg (s/r); 20mg (soft gelatin)

Tablet, 10 mg, 20 mg,30mg, 40mg, 60mg, 90mg(m/r)

Indications: used alone or in combination with other agents for treatment of hypertension and angina pectoris, Raynaud's phenomenon.

Cautions: aortic stenosis or hypertrophic obstructive cardiomyopathy (may worsen cardiac failure or increase outflow track obstruction); angina (may worsen symptoms); nursing mother, renal & hepatic impairment.

Drug interactions: other antihypertensives, beta blockers (*use with special caution*), digoxin, medicines that inhibit cytochromeP4503A4 (cimetidine, erythromycine, fluoxetine, protease inhibitors, ketoconazole, itraconazole, fluconazole), medicines that induce cytochromeP450 3A4 (carbamzepine, phenobarbital etc.), rifampicin, tacrolimus, valproic acid.

Contraindications: hypotension, unstable angina or acute myocardial infarction (increased infarct rate and mortality) in

the absence of current beta blockade; cardiogenic shock. Avoid sudden withdrawal.

Side effects: peripheral edema (swelling at ankles, feet, or lower legs), dizziness or light – headedness, flushing or feeling of warmth, headache, nausea, congestive heart failure or pulmonary edema (breathing difficulty, coughing, or wheezing), tachycardia, constipation, unusual tiredness or weakness, palpitation, increased frequency of micturation, eye pain, gum hyperplasia, depression.

Dose and Administration: Oral: **Adult** Dosage adjustments should occur at 7 to 14 days interval to allow for adequate assessment of new dose; when switching from immediate release to sustained release formulations, use same total daily dose. Chronic stable or vasospastic angina: Oral: Immediate release: Initial: 10 mg 3 times/day; usual dose: 10-20 mg 3 times/day; coronary artery spasm may require up to 20-30 mg 3-4 times/day. Single doses >30 mg and total daily doses >120 mg are rarely needed; maximum: 180 mg/day. *Note: Do not use for acute anginal episodes; may precipitate myocardial infarction.* Extended release: Initial: 30 or 60 mg once daily; maximum: 120-180 mg/day. **Child:** dosage has not been established

Storage: store between 15 and 25°C in a tight, light-resistant container.

Nimodipine

Tablet, 30mg

Injection, 1mg/5ml

Indication: Prevention and treatment of ischaemic neurological deficits following aneurysmal subarachnoid haemorrhage

Cautions: Hepatic impairment, renal impairment, pregnancy, breast-feeding, cerebral oedema or severely raised intracranial pressure; hypotension, heart attack, unstable angina.

Drug interactions: Rifampicin, calcium-channel blockers, antihypertensive, azole antifungals, hypnotics, alcohol, general anaesthetics, antipsychotics, anxiolytics & cimetidine, corticosteroids, muscle relaxant (non-depolarising), NSAIDs, oestrogens, ritonavir, sodium nitroprusside, theophylline, tizanidine.

Contraindications: Hypersensitivity to nimodipine or any component of the formulation

Side-effects: Hypotension, variation in heart-rate, flushing, headache, gastro-intestinal disorders, abdominal discomfort, nausea, sweating and feeling of warmth; thrombocytopenia and rash.

Dose and Administration: Subarachnoid hemorrhage: Oral: 60 mg every 4 hours for 21 days, start therapy within 96 hours after subarachnoid hemorrhage.

Treatment, by intravenous infusion via central catheter, initially 1 mg/hour (up to 500 micrograms/hour if bodyweight is less than 70 kg or if blood pressure unstable), increased after 2 hours to 2 mg/hour if no severe fall in blood pressure; continue for at least 5 days (maximum 14 days); if surgical intervention during treatment, continue for at least 5 days after surgery; maximum total duration of nimodipine use is 21 days. Dosage in renal and hepatic impairment: the initial dosage of nimodipine in such patients should be reduced to 30mg every 4 hours and blood pressure and heart rate monitored closely.

Storage: Store it at room temperature and away from excess heat and moisture.

Pentaerythritol Tetranitrate

Capsule, 80 mg

Tablet, 10 mg, 20 mg

Indications: angina pectoris.

Dose and Administration: Oral: Adult: up to 240mg daily, in divided doses, before a meal.

Propranolol

Tablet, 10 mg, 40 mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 3.2 under propranolol.

Dose and Administration: Adult: Oral: Post-MI mortality reduction: Oral: 180-240 mg/day in 3-4 divided doses. Stable angina: Oral: 80-320 mg/day in doses divided 2-4 times/day. Initial: 80 mg once daily; maximum dose: 320 mg once daily

Trimetazidine

Controlled release tablet, 35mg

Indications: Long-term treatment of angina pectoris

Dose and Administration: Adult: oral: 35mg twice daily, in the morning and evening with meals.

3.5. Antihypertensives

Management of hypertension

Since treatment for hypertension is often life-long, it is important to integrate the treatment of hypertension into an overall program of management of associated risk factors and conditions, particularly in elderly patients who often have multiple associated disorders. Mild hypertension is defined as 140 to 159 mmHg systolic blood pressure and 90 to 99 mmHg diastolic blood pressure. Moderate hypertension 160 to 180 mmHg systolic and 100 to 109 mmHg diastolic and severe

hypertension more than 180 mmHg systolic and more than 110 mmHg diastolic.

Lifestyle changes should be introduced for all patients; they include weight reduction, reduction in alcohol intake, reduction of dietary sodium, stopping tobacco smoking, and reduction in saturated fat intake. The patient should eat a healthy nutritious diet including adequate fruit and vegetables and should exercise regularly. These measures alone may be sufficient in mild hypertension with no target organ damage, but patients with moderate to severe hypertension will also require specific antihypertensive therapy.

Drug treatment of hypertension: The goal of treatment is to obtain the maximum tolerated reduction in blood pressure. Five classes of medicine are used for first-line treatment of hypertension: Diuretics, Beta - adrenoceptor antagonists (beta blockers), Angiotensin-converting enzyme (ACE) inhibitors, calcium-channel blockers and alpha-adrenoceptor blocking medicines (alpha blockers). All five classes are effective in reducing blood pressure; thiazide diuretics and beta-blockers have been shown to reduce mortality due to cardiovascular complications of hypertension other classes of medicines may be used in certain situations.

Thiazide diuretics, such as Hydrochlorothiazide have been used as first-line antihypertensive therapy and are particularly indicated in the elderly. They have few adverse effects in low doses, but in large doses they may cause a variety of unwanted metabolic effects (principally potassium depletion), reduced glucose tolerance, ventricular ectopic beats and impotence; they should be avoided in gout. These effects can be reduced by keeping the dose as low as possible; higher doses do not produce an increased reduction in blood pressure. Thiazides are inexpensive and when used in combination, can enhance the

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effectiveness of many other classes of antihypertensive medicine.

Beta adrenoceptor antagonist (beta-blockers) such as propranolol are effective in all grades of hypertension, and are particularly useful in angina and following myocardial infarction; they should be avoided in asthma, chronic obstructive pulmonary disease, and heart block.

Angiotensin-converting enzyme inhibitors (ACE inhibitors) such as captopril are effective and well tolerated by most patients (see also section 2.1). They can be used in heart failure, left ventricular dysfunction and diabetic nephropathy, but should be avoided in renovascular disease and in pregnancy. The most common adverse effect is a dry persistent cough.

Calcium Channel blockers such as Nifedipine are effective antihypertensives. Particularly for isolated systolic hypertension and in the elderly when thiazides cannot be used. Short acting formulations of nifedipine should be avoided as they may evoke reflex tachycardia and cause large variations in blood pressure.

Alpha-adrenoceptor blocking medicines (alpha-blockers) such as prazosin are effective in lowering blood pressure but remain too expensive to be considered as first line therapy in many countries. They are particularly useful in prostatism, but should be avoided in urinary incontinence. They are usually used in combination with other antihypertensives, the first dose being given at bedtime, as profound hypotension may occur.

Medicines acting on the Central nervous system are also effective antihypertensive medicines. In particular, methyldopa is effective in the treatment of hypertension in pregnancy, and may also be used in asthma and heart failure. Reserpine is also used because of its effectiveness and low cost. It should be used in combination with diuretics and prescribed in much lower

doses than were formerly used. Combining antihypertensive medicines often produces a beneficial additive effect.

Hypertension in pregnancy

Medicine therapy for chronic hypertension during pregnancy remains controversial. If diastolic blood pressure is greater than 95 mmHg. Methyldopa is the safer medicine. Beta-blockers should be used with caution in early pregnancy. Since they may retard fetal growth they are effective and safe in the third trimester. ACE inhibitors are contraindicated in pregnancy since they may damage fetal and neonatal blood pressure control and renal function. Women who are taking these medicines and become pregnant should have their antihypertensive therapy changed immediately. Pre-eclampsia and eclampsia. If pre-eclampsia or severe hypertension occurs beyond the 36th week of pregnancy, delivery is the treatment of choice. For acute severe hypertension in pre-eclampsia or eclampsia, intravenous hydralazine can be used.

Amiloride and Hydrochlorothiazide

(Potassium-sparing diuretic; antihypertensive)

Oral solution, 5mg+50mg/5ml

Tablet, 2.5mg + 25 mg, 5mg + 50mg

Indications: hypertension, especially when a potassium-sparing diuretic effect is desired.

Cautions: possibility of hypokalemia or hyperkalemia.

Drug interactions: chlorpropamide, carbenoxolone, see also hydrochlorothiazide.

Side effects: hyponatraemia, constipation, allergic reactions, cholecystitis or pancreatitis, gout or hyperuricemia, hepatic function impairment, thrombocytopenia.

Dose and Administration: Oral: **Adult:** start with 5mg+50mg per day, then may be increased to 10mg+100mg per day if needed; given in a single dose.

Storage: at room temperature.

Amlodipine

Tablet 2.5 mg, 5 mg, 10 mg

Indications: Treatment of hypertension; treatment of symptomatic chronic stable angina, vasospastic (Prinzmetal's) angina (confirmed or suspected); prevention of hospitalization due to angina with documented CAD (limited to patients without heart failure or ejection fraction <40%).

Cautions, Drug interactions, Contraindications, Side effects; see under Nifedipine below.

Dose and Administration:Hypertension: Oral: **Adult:** Initial dose 2.5 mg twice daily (1.25 mg twice daily in elderly, hepatic or renal impairment); increased if necessary after 3 - 4 weeks to 5 mg twice daily (exceptionally up to 10 mg twice daily); maintenance 2.5 or 5 mg once daily may be sufficient

Storage: at room temperature in a tight, light resistant container.

Atenolol

Tablet, 50mg, 100mg

Indication: treatment of hypertension, alone or in combination with other agents; management of angina pectoris, postmyocardial infarction patients.

Contraindication: Hypersensitivity to atenolol or any component of the formulation; sinus bradycardia; node dysfunction; heart block greater than first degree(except in patients with a functioning artificial pacemaker); cardiogenic

shock; uncompensated cardiac failure; pulmonary edema; pregnancy and breast feeding mother.

Drug interaction: digoxin, verapamil, diltiazem, alpha-blockers(prazosin, terazosin), alpha-adrenergic stimulants(epinephrine, phenylephrine), insulin, oral hypoglycemic, clonidine, beta-blockers, reserpine, aluminum salts, barbiturates, calcium salts, cholestyramine, colestipol, NSAID, penicillins, rifampin, salicylates and sulfinpyrazone.

Dosage and administration: Dosing: Adult Hypertension:

Oral: 25-50 mg once daily, may increase to 100 mg/day. Doses >100 mg are unlikely to produce any further benefit. **Pediatric:**

Hypertension: Oral: Children: 0.5-1 mg/kg/dose given daily; range of 0.5-1.5 mg/kg/day; maximum dose: 2 mg/kg/day up to 100 mg/day. **Renal Impairment:** Cl_{cr} 15-35 mL/minute:

Administer 50 mg/day maximum. Cl_{cr} <15 mL/minute: Administer 50 mg every other day maximum.

Side effects: Persistent bradycardia, hypotension, chest pain, edema, heart failure, dizziness, fatigue, insomnia, lethargy, confusion, headache, nightmares, constipation, diarrhea, nausea, impotence, cold extremities.

Storage: store between 15 and 30°C, in a well-closed container, unless otherwise specified by manufacturer. Protect from light.

Candesartan

Tablet, 4mg, 8mg, 16mg, 32mg

Indications: alone or in combination with other antihypertensive agents in treating essential hypertension.

Cautions: pre-existing renal insufficiency.

Drug interactions: concurrent use with potassium sparing diuretics (amiloride, spironolactone, triamterene), trimethoprim, avoid garlic.

Contraindications: hypersensitivity to candesartan; bilateral renal artery stenosis; pregnancy (2nd and 3rd trimesters)

Side effects: worsening of renal function in patients dependent on rennin-angiotensin-aldosterone system. tachycardia, dizziness, lightheadedness, drowsiness, headache, anxiety, depression, somnolence, fever, rash, hyperglycemia, hyperuricemia, dyspepsia, gastroenteritis, hematuria, dyspnea, pharyngitis, and epistaxis.

Dose and Administration: Dosing: Adult Hypertension: Oral: Dosage must be individualized. Initial: 16 mg once daily; titrate to response (within 2 weeks, antihypertensive effect usually observed); usual range: 8-32 mg/day in 1-2 divided doses; maximum daily dose: 32 mg/day.

Pediatric Hypertension: Oral: Children 1 to <6 years: Initial: 0.2 mg/kg/day in 1 to 2 divided doses; titrate to response (within 2 weeks, antihypertensive effect usually observed); usual range: 0.05 to 0.4 mg/kg/day; maximum daily dose: 0.4 mg/kg/day.

Children 6 to <17 years: <50 kg: Initial: 4 to 8 mg/day in 1 to 2 divided doses; titrate to response (within 2 weeks, antihypertensive effect usually observed); usual range: 2 to 16 mg/day; maximum daily dose: 32 mg/day.

>50 kg: Initial: 8-16 mg/day in 1-2 divided doses; titrate to response (within 2 weeks, antihypertensive effect usually observed); usual range: 4-32 mg/day; maximum daily dose: 32 mg/day.

Renal Impairment: Children 1 to <17 years: *No dosage adjustment provided in manufacturer's labeling.* Children with GFR <30 mL/minute/1.73 m² should not receive candesartan.

Adults: No initial dosage adjustment necessary; however, in patients with severe renal impairment ($Cl_{cr} < 30$)

mL/minute/1.73m²) AUC and C_{max} were approximately doubled after repeated dosing.

Hepatic Impairment: Mild impairment: No initial dosage adjustment necessary. Moderate impairment: Consider initiation at lower dosages (AUC increased by 145%). Severe impairment: No dosage adjustment provided in manufacturer's labeling.

Candesartan and Hydrochlorothiazide

Tablet, 16mg+ 12.5mg, 32mg+12.5mg

Indications: Treatment of hypertension; combination product should not be used for initial therapy

Contraindication: with severe hepatic impairment and/or cholestasis.

Dose and Administration: Dosing: **Adult** Hypertension, replacement therapy: Oral: Combination product can be substituted for individual agents; maximum therapeutic effect would be expected within 4 weeks. Usual dosage range: Candesartan: 16-32 mg/day, given once daily or twice daily in divided doses. Hydrochlorothiazide: 12.5 to 25 mg once daily

Geriatric: Refer to adult dosing. **Renal Impairment:** Serum levels of candesartan are increased and the half-life of hydrochlorothiazide is prolonged in patients with renal impairment. Contraindicated with severe renal impairment (Cl_{cr}<30 mL/minute). **Hepatic Impairment:** Use with caution with moderate hepatic impairment.

Captopril

Tablet 12.5 mg, 25 mg, 50 mg, 100 mg

Indications, Cautions, Drug interactions, Contraindications, Side effect; see section 3.1 and notes above

Dose and Administrations: *Note: Titrate dose according to patient's response; use lowest effective dose.*

Adult: Acute hypertension (urgency/emergency): Oral: 12.5-25 mg, may repeat as needed (may be given sublingually, but no therapeutic advantage demonstrated). **Hypertension: Oral:** Initial dose: 25 mg 2-3 times/day (a lower initial dose of 12.5 mg 3 times/day may also be considered [VA Cooperative Study Group, 1984]); may increase by 12.5-25 mg/dose at 1 to 2 week intervals up to 50 mg 3 times/day; add thiazide diuretic, unless severe renal impairment coexists then consider loop diuretic, before further dosage increases or consider other treatment options; maximum dose: 150 mg 3 times/day. Usual dose range (JNC 7): 25-100 mg/day in 2 divided doses.

Geriatric: Refer to adult dosing. In the management of hypertension, consider lower initial doses and titrate to response.

Pediatric: Hypertension: Oral: *Infants:* Initial: 0.15-0.3 mg/kg/dose; titrate dose upward to maximum of 6 mg/kg/day in 1-4 divided doses. *Children:* Initial: 0.3-0.5 mg/kg/dose; titrate upward to maximum of 6 mg/kg/day in 2-4 divided doses. *Older Children:* Initial: 6.25-12.5 mg/dose every 12-24 hours; titrate upward to maximum of 6 mg/kg/day. *Adolescents:* Initial: 12.5-25 mg/dose; titrate to a maximum of 450 mg/day

Dosing: Renal Impairment *Manufacturers recommendations:* Reduce initial daily dose and titrate slowly (1 to 2 weeks intervals) with smaller increments. Slowly back titrate to determine the minimum effective dose once the desired therapeutic effect has been reached. *Alternative recommendations:* Adults: Cl_{cr} 10-50 mL/minute: Administer at 75% of normal dose every 12-18 hours. Cl_{cr} <10 mL/minute: Administer at 50% of normal dose every 24 hours.

Captopril + Hydrochlorothiazide

Tablet, 50 + 25 mg

See section 3.1.underCaptopril and Hydrochlorthiazide

Carvedilol

Tablet, 3.125 mg, 6.25 mg, 12.5 mg, 25 mg

Indications: hypertension; mild to moderate congestive heart failure as an adjunct to standard therapy.

Cautions: sinus bradycardia and partial heart block.

Drug interactions: as for other beta-blockers.

Contraindications: as for other beta-blockers, hepatic impairment.

Side effects: as for other beta-blockers; see atenolol, liver function abnormalities.

Dose and Administration: Hypertension: Oral: **Adult:** Initially 12.5 mg once daily; increased after 2 days to 25 mg once daily; may be increased at intervals of at least 2 weeks up to a maximum of 50mg/day in single or divided doses.**Elderly:** 12.5mg once daily, titrated at intervals of at least 2 weeks upto 25mg/day.

Storage: store at room temperature.

Clonidine Hydrochloride

Injection, 0.15 mg/ml in 1 ml ampoule

Tablet, 0.025 mg, 0.15 mg

Indications: management of mild to moderate hypertension either used alone or in combination with other antihypertensives.

Cautions: cardiovascular disease, ischaemic heart disease including myocardial infarction, renal impairment, occlusive peripheral vascular disorders such as raynaud's disease, or those with a history of depression; gradual withdrawal is needed.

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Note: it causes drowsiness and patients should not drive or operate machinery where loss of attention could be dangerous. IV injection of clonidine should be given slowly. Patients should be warned of the risk of missing a dose or stopping the medicine as sudden discontinuation may cause rebound hypertension.

Drug interactions: Alcohol and other CNS depressants, tricyclic antidepressants, opiate analgesics, beta-blockers.

Contraindications: hypersensitivity to clonidine or any component of the formulation.

Side effects: drowsiness, dry mouth, dizziness, and headache, constipation, depression, anxiety, fatigue, nausea, anorexia, parotid pain, sleep disturbances, vivid dreams, impotence, loss of libido, urinary retention or incontinence, slight orthostatic hypotension, and itching, or burning sensation in the eye, fluid retention, and sudden withdrawal of clonidine may produce rebound hypertension.

Dose and Administration:**Hypertension:** Oral**Adult:** initial dose: 0.1 mg twice daily (maximum recommended dose 2.4mg/day); usual dose range 0.1 to 0.8mg/day in 2 divided doses.

Child: initial dose 5 to 10 mcg/kg/day in divided doses every 8 to 12 hours, increase gradually at 5 to 7 day interval to 25 mcg/kg/day in divided doses every 6 hours, maximum:

0.9mg/day.**Acute Hypertension Urgency:** Oral**Adult:** initial dose 0.1-0.2 mg; may be followed by additional doses of 0.1mg every hour, if necessary, to a maximum total dose of 0.6mg.

Storage: at room temperature in tightly closed container.

Diazoxide

Injection, 15 mg/ml in 20 ml ampoule

Indications: hypertensive crisis, commonly used with a diuretic such as furosemide.

Caution: impaired cardiac or cerebral circulation and in patients with aortic coarctation, arteriovenous shunt, heart failure; impaired renal function, diabetes mellitus; during labour, history of gout, uremia.

Drug interactions: hyperglycaemic, hyperuricaemic, other antihypertensive or vasodilators; phenytoin.

Contraindications: hypersensitivity to diazoxide or to other thiazides, cerebral bleeding, eclampsia.

Side effects: hypotension, hyperglycaemia, heart failure, nausea, anorexia, and other gastrointestinal disturbances, mild hyperuricaemia, extrapyramidal symptoms, eosinophilia, dizziness, tinnitus and blurred vision; hypersensitivity reaction such as rashes, leucopenia, & fever.

Dose and Administration: IV: **Adult and Child:** 1 to 3 mg/kg up to a maximum of 150mg in a single injection; repeat dose in 5-15 minutes until blood pressure adequately reduced; repeat administration at intervals of 4 to 24 hours; monitor the blood pressure closely; do not use longer than 10 days.

Enalaprilat

Injection, 1.25 mg/ml

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 3.1 under Enalaprilat and notes above.

Dose and Administration: Hypertension: I.V: **Adult:** (over at least five minutes), 1.25 mg every six hours.

Enalapril Maleate

Tablet, 2.5mg, 5mg, 10mg, 20mg, 40mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.1 under Enalapril maleate and notes above.

Dose and Administrations: Hypertension: Oral: **Adult:**

Used alone, initially 5 mg once daily. If used in addition to diuretic in elderly patients, or in renal impairment, initially 2.5 mg daily, usual maintenance dose 10 mg - 20 mg once daily, in severe hypertension may be increased to maximum 40 mg once daily.

Enalapril Maleate and Hydrochlorothiazide

Tablet, 10 mg + 25 mg

Indications: hypertension; symptomatic heart failure (adjunct) prevention of symptomatic heart failure in patients with asymptomatic left ventricular dysfunction

Cautions, Drug interactions, dose, Contraindications, see section under Enalapril Maleate and Hydrochlorothiazide

Fosinopril

Tablet, 10mg, 20mg

Indications: Treatment of hypertension, either alone or in combination with other antihypertensive agents; treatment of heart failure (HF)

Cautions, Drug interactions, Contraindications, Side effects; see under captopril.

Dose and Administration: Dosing: **Adult Hypertension:**

Oral: Initial: 10 mg/day; increase to a maximum dose of 80 mg/day. Most patients are maintained on 20-40 mg/day. May need to divide the dose into two if trough effect is inadequate. Discontinue the diuretic, if possible 2-3 days before initiation of therapy. Resume diuretic therapy carefully, if needed.

Dosing: Pediatric Hypertension: Children ≥ 6 years and >50 kg: Oral: Initial: 5 to 10 mg once daily (maximum: 40 mg/day).

Renal Impairment: None need since hepatobiliary elimination

compensates adequately diminished renal elimination. **Hepatic Impairment:** Decrease dose and monitor effects

Hydralazine

Injection, 20 mg /ml in 1 ml ampoule

Tablet, 25 mg, 50 mg

Indications: moderate to severe hypertension (low doses used in combination therapy, especially with beta blockers).

Cautions: pregnancy, breast-feeding, in elderly patients, in patients with hepatic or renal impairment, with coronary artery disease.

Drug interactions: other antihypertensive medicines, nitrates, diazoxide.

Contraindications: coronary artery disease, rheumatic heart disease (mitral valvular), cerebrovascular disease or accident, idiopathic systemic lupus erythematosus, severe tachycardia, high output heart failure, myocardial insufficiency due to mechanical obstruction.

Side effects: tachycardia, palpitations, nausea, vomiting, diarrhoea, anorexia, fluid retention, headache, systemic lupus erythematosus like syndrome, fever, changes in blood count, peripheral neuritis.

Dose and Administration: Dosing: Adult **Hypertension:** Oral: Initial: 10 mg 4 times/day; increase by 10-25 mg/dose every 2-5 days (maximum: 300 mg/day); usual dose range (JNC 7): 25-100 mg/day in 2 divided doses. **Acute hypertension:** I.M., I.V.: Initial: 10-20 mg/dose every 4-6 hours as needed, may increase to 40 mg/dose; change to oral therapy as soon as possible.

Pre-eclampsia/eclampsia: I.M., I.V.: 5 mg/dose then 5-10 mg every 20-30 minutes as needed.

Geriatric: Oral: Initial: 10 mg 2-3 times/day; increase by 10-25 mg/day every 2-5 days.

Pediatric:Hypertension: Oral: Initial: 0.75-1 mg/kg/day in 2-4 divided doses; increase over 3-4 weeks to maximum of 7.5 mg/kg/day in 2-4 divided doses; maximum daily dose: 200 mg/day

Acute hypertension: I.M., I.V.: 0.1-0.2 mg/kg/dose (not to exceed 20 mg) every 4-6 hours as needed, up to 1.7-3.5 mg/kg/day in 4-6 divided doses

Renal Impairment: Cl_{cr} 10 to 50 mL/minute: Administer every 8 hours. Cl_{cr} <10 mL/minute: Administer every 8 to16 hours in fast acetylators and every 12-24 hours in slow acetylators.

Hemodialysis effects: Supplemental dose is not necessary.

Peritoneal dialysis effects: Supplemental dose is not necessary.

Storage: at room temperature. Protect from freezing.

Hydrochlorothiazide

Tablet, 25mg

Indication: management of mild to moderate hypertension; treatment of edema in congestive heart failure and nephritic syndrome.

Contraindications: Hypersensitivity to the medicine or any component of the formulation; thiazides, or sulfonamide-derived drugs; anuria; renal decompensation, pregnancy

Drug-interactions: furosemide, other loop diuretics, ACE-inhibitor, beta-blockers, cyclosporine, digoxin,lithium, neuromuscular blocking agents, cholestyramine, colestipol,NSAIDs.

Dosage and administration: Oral (effect of medicine may be decreased when used every day):Children : <6 months: 2-3 mg/kg/day in 2 divided doses and >6 months: 2mg/kg/day in divided doses.**Adult:** Edema: 25-100mg/day in 1-2 doses; maximum: 200mg/day. **Hypertension:** 12.5-50mgmg/day: minimal increase in response and more electrolyte disturbances

are seen with doses > 50mg/day. **Elderly:** 12.5-25mg once daily (in pediatric patients, chlorothiazide may be preferred over hydrochlorothiazide as there are more dosage formulations (eg. suspension available)).

Indapamide

Film coated tablet 1.25mg, 2.5mg

Indications: Management of mild to moderate hypertension

Cautions: Diabetes, gout, and systemic lupus erythematosus, renal impairment, nephrotic syndrome, hyperaldosteronism, and malnourishment, mild to moderate hepatic impairment, in patients with moderate or high cholesterol concentrations; also acute porphyria.

Drug interactions: Furosemid and other loop diuretics, ACE-inhibitors, cyclosporine, thiazide type diuretics, digoxin, lithium, oral hypoglycemic, cholestyramine, colestipol and NSAIDs.

Contra-indications: refractory hypokalaemia, hyponatraemia and hypercalcaemia, symptomatic hyperuricaemia, severe hepatic impairment, renal impairment if glomerular filtration rate (GFR) is less than 30 mL/minute/1.73 m², and Addison's disease; also hypersensitivity to sulfonamides and thiazides
Pregnancy, Breast-feeding, anuria.

Side-effects; mild gastro-intestinal disturbances, postural hypotension, altered plasma-lipid concentrations, metabolic and electrolyte disturbances including hypokalaemia, hyponatraemia, hypomagnesaemia, hypercalcaemia, hyperglycaemia, hypochloreaemic alkalosis, hyperuricaemia, and gout. Less common side-effects include blood disorders such as agranulocytosis, leucopenia, and thrombocytopenia, and impotence. Pancreatitis, intrahepatic cholestasis, cardiac arrhythmias, headache, dizziness, paraesthesia, visual

disturbances, and hypersensitivity reactions (including pneumonitis, pulmonary oedema, photosensitivity, and severe skin reactions) have also been reported. Also palpitation, diuresis with doses above 2.5 mg daily

Dose and Administration: 1.25mg in the morning may increase to 5mg/day by increments of 1.25-2.5mg; consider adding another antihypertensive and decreasing the dose if response is not adequate.

Note: Administer early in day to avoid nocturia.

Irbesartan

Tablet, 75mg, 150mg, 300mg

Indications: treatment of hypertension alone or in combination with other antihypertensives.

Cautions: safety and efficacy have not been established for pediatric patients < 6 years of age.

Drug interactions: potassium salts, co-trimoxazole, ACE inhibitors, potassium sparing diuretics, amiodarone, fluoxetine, glipizide, phenytoin, rosiglitazone, warfarin, sertraline.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: Dosing: Adult **Hypertension:** Oral: 150 mg once daily; patients may be titrated to 300 mg once daily. **Note:** Starting dose in volume-depleted patients should be 75 mg. **Nephropathy in patients with type 2 diabetes and hypertension:** Oral: Target dose: 300 mg once daily.

Geriatric: Refer to adult dosing.

Pediatric:Hypertension: Oral: <6 years: *Safety and efficacy have not been established.* ≥6-12 years: Initial: 75 mg once daily; may be titrated to a maximum of 150 mg once daily; 13-16 years: Refer to adult dosing.

Renal Impairment: No dosage adjustment necessary with mild to severe impairment unless the patient is also volume depleted.

Isradipine

Tablet, 2.5 mg

Indications: treatment of hypertension.

Cautions, Drug interactions, Contraindication, Side effects; see under Nifedipine.

Dose and Administration: Mild to moderate hypertension: Oral:**Adult:** 2.5 mg twice daily; may be increased after 4 weeks up to 5 mg twice daily. Hepatic or renal function impairment, and the elderly; initially 1.25 mg twice daily.

Labetalol Hydrochloride

Tablets, 50 mg, 100 mg, 200 mg, 300mg, 400 mg

Injection, 5mg/ml, 1000mg/20ml

Indications: Treatment of mild-to-severe hypertension; I.V. for severe hypertension (eg, hypertensive emergencies).

Cautions: as for other beta-blockers, and also, hepatic disease or treated heart failure.

Drug interactions: alcohol and anaesthetics; agents inhibiting or inducing liver enzymes, other antihypertensives.

Contraindications: second or third degree atrioventricular block, symptomatic heart failure, sinus bradycardia, or cardiogenic shock; asthma, severe bronchospasm, history of allergy.

Side effects: as for beta blockers; and it has also alpha blocking activity which contributes to its adverse effects such as orthostatic hypotension, impaired male sexual function to a greater extent than with beta blockade alone; muscle weakness, tremor, urinary retention, hepatitis and jaundice.

Dose and Administration:Adult: Hypertension: Oral: Initial: 100 mg twice daily, may increase as needed every 2-3 days by 100 mg twice daily (titration increments not to exceed 200 mg twice daily) until desired response is obtained; usual dose: 100-400 mg twice daily may require up to 2.4 g/day.

Acute hypertension (hypertensive emergency/urgency): *I.V. bolus:* Per the manufacturer: Initial: 20 mg I.V. push over 2 minutes; may administer 40-80 mg at 10-minute intervals, up to 300 mg total cumulative dose; as appropriate, follow with oral antihypertensive regimen. *I.V. infusion (acute loading):* Per the manufacturer: Initial: 2 mg/minute; titrate to response up to 300 mg total cumulative dose (eg, discontinue after 2.5 hours of 2 mg/minute); usual total dose required: 50-200 mg; as appropriate, follow with oral antihypertensive regimen

Arterial hypertension in acute ischemic stroke *I.V. to oral conversion:* Upon discontinuation of *I.V. infusion*, may initiate oral dose of 200 mg followed in 6-12 hours with an additional dose of 200-400 mg. Thereafter, dose patients with 400-2400 mg/day in divided doses depending on blood pressure response.

Pediatric: *Note: Due to limited documentation of its use, labetalol should be initiated cautiously in pediatric patients with careful dosage adjustment and blood pressure monitoring.*

Hypertension: Oral: Hypertension (*unlabeled use*): Initial: 1 to 3 mg/kg/day, in 2 divided doses; maximum: 10 to 12 mg/kg/day, up to 1200 mg/day. *I.V.:* Intermittent bolus doses of 0.3-1 mg/kg/dose have been reported. Pediatric hypertensive emergencies: Initial continuous infusions of 0.4-1 mg/kg/hour with a maximum of 3 mg/kg/hour have been used; administration requires the use of an infusion pump.

Lisinopril

Tablet 2.5 mg, 5 mg, 10 mg, 20 mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 3.1 and notes above

Dose and Administration: Hypertension, initially 2.5 mg daily including patients with renal impairment, the elderly or those who receiving a diuretic; if possible, the diuretic should be withdrawn 2 or 3 days before Lisinopril is started and resumed later if required and usual maintenance dose 10 - 20 mg daily, maximum 40 mg daily.

Lisinopril and Hydrochlorothiazide

Tablet, 10mg + 12.5mg

Indications: treatment of hypertension

Dose and Administration: Adult: Oral: Dosage is individualized; doses >80mg/day lisinopril or > 50mg/day hydrochlorothiazide are not recommended.

Losartan

Tablet, 25mg, 50mg, 100mg

Indications: Treatment of hypertension (HTN); treatment of diabetic nephropathy in patients with type 2 diabetes mellitus (noninsulin dependent, NIDDM) and a history of hypertension; stroke risk reduction in patients with HTN and left ventricular hypertrophy (LVH).

Drug interactions: potassium sparing diuretics or potassium supplements.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Side effects: dizziness, headache, skin rash, urticaria, cough, myalgia, GI effect, angio edema, hyperkalaemia.

Dose and Administration: Adult: Hypertension: Oral: Usual starting dose: 50 mg once daily; can be administered once or twice daily with total daily doses ranging from 25-100 mg.

3. Cardiovascular Medicines

Usual initial doses in patients receiving diuretics or those with intravascular volume depletion: 25 mg once daily. Nephropathy in patients with type 2 diabetes and hypertension: Oral: Initial: 50 mg once daily; can be increased to 100 mg once daily based on blood pressure response. Stroke reduction (HTN with LVH): Oral: 50 mg once daily (maximum daily dose: 100 mg); may be used in combination with a thiazide diuretic.

Pediatric: Hypertension: Oral: Children 6-16 years: 0.7 mg/kg once daily (maximum: 50 mg/day); doses >1.4 mg/kg (maximum: 100 mg) have not been studied.

Renal Impairment: Children: Use is not recommended if GFR <30 mL/minute/1.73 m². Adults: No adjustment necessary. **Hepatic Impairment:** Adults: Reduce the initial dose to 25 mg/day

Methyldopa

Tablet, 250 mg, 500mg

Indications: hypertension in pregnancy, moderate to severe hypertension.

Cautions: renal or hepatic impairment, or with a history of haemolytic anaemia, liver disease, or depression; Parkinsonism.

Drug interactions: alcohol, CNS depression producing medications, monoamine oxidase inhibitors including furazolidine, paragyline, procarbazine; cocaine, norepinephrine, phenylepinephrine, anaesthetics, and lithium, diuretics, other antihypertensives, antipsychotics.

Contraindications: depression, active liver disease, phaeochromocytoma, haemolytic anemia.

Side effects: dry mouth, sedation, depression, drowsiness, diarrhoea, fluid retention, failure of ejaculation, liver damage, haemolytic anaemia, lupus erythematosus like syndrome,

parkinsonism, rashes, nasal stuffiness edema (swelling of feet or lower legs), gynaecomastia.

Dose and Administration: Oral:**Adult:** 250mg 2-3 times daily gradually increased at intervals of two or more days to maximum daily dose 3gm.

Elderly: 120mg twice daily initially, gradually increased, maximum daily dose 2gm.

Storage: at room temperature.

Metoprolol Tartrate

Injection, 1mg/ml, 5mg/ml

Tablets, 50mg, 100 mg, 200mg(s/r)

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.2 under metoprolol.

Dose and Administration: Oral:**Adult:**initial dose 100mg daily, increased weekly according to response to 400mg daily. Maintenance dose 100 to 200mg daily.

Elderly: 25mg daily, usual range 25-300mg/day.

Nicardipine

Injection, 0.1mg/ml

Indications: used alone or in combination with other agents for treatment of hypertension and chronic stable angina pectoris.

Cautions: hepatic dysfunction, renal dysfunction, pregnancy, breastfeeding mother, cardiac heart failure, pheochromocytoma, patient with portal hypertension, avoid systemic hypotension when administering the drug to patients who have sustained an acute cerebral infarction or hemorrhage.

Drug interactions: Cimitidine, digoxin, Fentanyl anesthesia, cyclosporine, azole antifungals, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, nefazodone, propofol, protease inhibitors, quinidine, telithromycin, verapamil,

aminoglutethimide, carbamazepine, nevirapine, Phenobarbital, phenytoin, rifamycins.

Contraindications: It is contraindicated in patients with known hypersensitivity to the medicine and also in patients with advanced aortic stenosis, severe hypotension, cardiogenic shock, ventricular tachycardia.

Side effects: Hypotension, headache, tachycardia, palpitation, peripheral edema, nausea, vomiting, weakness.

Dose and Administration: Acute Hypertension: Initial: 5mg/hour increased by 2.5mg/hour every 15 minutes to a maximum of 15mg/hour; consider reduction to 3mg/hour after response is achieved. Monitor and titrate to lowest dose necessary to maintain stable blood pressure. Substitution for oral therapy (approximate equivalents): 20mg every 8 hours oral, equivalent to 0.5mg/hour IV infusion; 30mg every 8 hours oral, equivalent to 1.2mg/hour IV infusion; 40mg every 8 hours oral, equivalent to 2.2mg/hour IV infusion.

Storage: Store at room temperature 20° to 25°C

Nifedipine

Capsule, 5 mg, 10 mg, 20 mg 30mg (s/r)

Tablet, 10 mg, 20 mg, 30mg, 40mg, 60mg, 90mg(m/r)

Indications: used alone or in combination with other agents for treatment of hypertension and angina pectoris, Raynaud's phenomenon.

Cautions: aortic stenosis or hypertrophic obstructive cardiomyopathy (may worsen cardiac failure or increase outflow tract obstruction); angina (may worsen symptoms); nursing mother, renal & hepatic impairment.

Drug interactions: other antihypertensives, beta blockers (use with special caution), digoxin, medicines that inhibit cytochrome P450 3A4 (cimetidine, erythromycin, fluoxetine,

protease inhibitors, ketoconazole, itraconazole, fluconazole), medicines that induce cytochrome P450 3A4 (carbamazepine, phenobarbital e.t.c.), rifampicin, tacrolimus, valproic acid.

Contraindications: hypotension, unstable angina or acute myocardial infarction (increased infarct rate and mortality) in the absence of current beta blockade; cardiogenic shock. Avoid sudden withdrawal.

Side effects: peripheral edema (swelling at ankles, feet, or lower legs), dizziness or light – headedness, flushing or feeling of warmth, headache, nausea, congestive heart failure or pulmonary edema (breathing difficulty, coughing, or wheezing), tachycardia, constipation, unusual tiredness or weakness, palpitation, increased frequency of micturation, eye pain, gum hyperplasia, depression.

Dose and Administration: Oral:**Adult:** 10 to 20mg three times daily up to 180mg/day or 30 to 90mg sustained release once per day.**Child:** dosage has not been established

Note: Short acting preparation is not recommended for the management of hypertension.

Storage: store between 15 and 25°c in a tight, light-resistant container.

Phenoxybenzamine Hydrochloride

Capsule, 10 mg

Indications: symptomatic management of pheochromocytoma, treatment of hypertensive crisis caused by sympathomimetic amines.

Cautions: renal impairment, cerebral or coronary arteriosclerosis, elderly, heart failure and ischaemic heart disease, it aggravates the symptoms of respiratory infections.

Drug interactions: beta-blockers, sildenafil, tadalafil, and adrenaline

Contraindications: instances when fall in blood pressure would be dangerous; compensated congestive failure.

Side effects: postural hypotension, tachycardia, shock, headache, confusion, fatigue, dry mouth, dizziness, miosis, nasal congestion, inhibition of ejaculation.

Dose and Administration: Oral:Pheochromocytoma:

Adult: initial: 10mg twice daily, increase by 10mg every other day until optimum dose is achieved; usual range: 20-40mg 2-3 times/day.**Child:** initial: 0.2mg/kg (maximum: 10mg) once daily, increase by 0.2mg/kg increments; usual maintenance dose: 0.4-1.2mg/kg/day every 6-8 hours, higher doses may be necessary.

Storage: store at room temperature.

Phentolamine mesilate

Injection, 10 mg/ml in 1ml

Indications: Diagnosis of pheochromocytoma and treatment of hypertension associated with pheochromocytoma or other forms of hypertension caused by excess sympathomimetic amines; treatment of dermal necrosis after extravasation of drugs with alpha-adrenergic effects (ie, dopamine, epinephrine, norepinephrine, phenylephrine).

Cautions: gastritis or peptic ulcer.

Drug interactions: adrenaline, ethanol, sildenafil, and tadalafil.

Contraindications: as phenoxybenzamine & also angina pectoris or other evidence of ischemic heart disease.

Side effects: tachycardia, angina pain, arrhythmia, flushing, sweating, feeling of apprehension, orthostatic hypotension, dizziness, nausea, vomiting, diarrhea, nasal congestion, pulmonary hypertension, myocardial infarction & cerebrovascular spasm or occlusion.

Dose and Administration: Surgery for pheochromocytoma hypertension: I.M. I.V.: **Adult: Treatment of alpha-adrenergic agonist drug extravasation:** SubQ: Infiltrate area with a small amount (e.g. 1 ml) of solution (made by diluting 5 to 10 mg in 10 ml of NS) within 12 hours of extravasation; in general, do not exceed 0.1 to 0.2 mg/kg (5 mg total); typically doses of ≤ 5 mg are effective; a case using 50 mg for a large extravasation has been reported.

Diagnosis of pheochromocytoma: I.M., I.V.: 5 mg Surgery for pheochromocytoma: Hypertension: I.M., I.V.: 5 mg given 1 to 2 hours before procedure and repeated as needed every 2-4 hours Hypertensive crisis: I.V.: 5-20 mg Treatment of pralidoxime-induced hypertension: I.V.: 5 mg.

Child: 0.05-0.1mg/kg/dose given 1-2 hours before procedure; repeat as needed every 2-4 hours until hypertension is controlled; maximum single dose: 5mg.

Storage: store powder for injection at room temperature. Reconstituted solution is stable for 48 hours at room temperature and 1 week when refrigerated.

Prazosin Hydrochloride

Tablet, 1 mg, 2 mg, 5 mg

Indications: hypertension, hypertension associated with pheochromocytoma.

Cautions: elderly patients, during pregnancy and breastfeeding, angina pectoris, narcolepsy, and in those sensitive to the drug. First dose may cause collapse due to hypotension (should be taken on retiring to bed); hepatic or renal function impairment; advice patients not to do activities requiring alertness.

Drug interactions: nifedipine, other antihypertensive agents or nitrates, alcohol, beta blockers and calcium channel blockers.

Contraindications: heart failure caused by mechanical obstruction, for example aortic or mitral valve stenosis, pulmonary embolism, and restrictive pericardial disease.

Side effects: dizziness, orthostatic hypotension, edema, palpitations, dry mouth, urinary incontinence, angina, dyspnea, and priapism, drowsiness, headache, lack of energy, and nausea.

Dose and Administration: Oral:**Adult:** 0.5 mg 2–3 times daily, the initial dose on retiring to bed or night (to avoid collapse) increased to 1 mg 2 – 3 times daily after 3 – 7 doses further increased if necessary to maximum 20 mg daily.**Child** (under 7 years of age), initially 0.25 mg 2 – 3 times a day adjusted according to response. 7 to 12 years of age, initially 0.5 mg two or three times a day adjusted according to response.

Storage: at room temperature in a well-closed, light – resistant container.

Propranolol

Injection, 1mg/ml in 1ml ampoule

Tablet, 10mg, 40mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.2 under propranolol.

Dose and Administration: Hypertension: Oral: 80mg twice daily increased at weekly intervals as required, maintenance 160-320mg daily.I.V. injection: 1.3mg administered at a rate not to exceed 1mg/minute, repeated after two minutes and again after four hours if necessary (for Antiarrhythmic).

Ramipril

Capsule, 1.25mg, 2.5mg, 5mg, 10mg

Indications: treatment of hypertension, either alone or in combination with other antihypertensive agents.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: Oral: **Adult:** 2.5-5mg once daily, maximum: 20mg/day.

Reserpine

Tablet, 0.1mg, 0.25mg

Injection, 1mg/ml in 1ml ampoule

Indications: mild to moderate hypertension.

Cautions: debilitated or elderly patients, during breastfeeding, in those patients with cardiac arrhythmias, myocardial infarction, severe cardiac damage, renal insufficiency, gallstones, epilepsy, or allergic conditions such as bronchial asthma.

Note: Advice patients not to operate machineries or drive vehicles

Drug interactions: diuretic and hypotensive agents, cardiac glycosides or quinidine, monoamine oxidase inhibitors, CNS depressants.

Contraindications: mental depression, active peptic ulcer, with ulcerative colities and in patients receiving electroconvulsive therapy.

Side effects: nasal congestion, CNS symptoms including depression, drowsiness, lethargy, nightmares, diarrhoea, abdominal cramp; nausea, vomiting and anorexia, respiratory distress, cyanosis, breast enlargement and galactorrhoea, gynaecomastia, decreased libido, impotence, sodium retention, oedema, weight gain, miosis, dry mouth, sialorrhoea, dysuria, rashes, thrombocytopenia purpura..

Dose and Administration: Oral: **Adult:** initially 0.05 - 0.125mg once daily; this may be increased gradually to an accepted maximum of 0.25mg daily. The lowest effective dose should be used. **Child:** 0.005 to 0.02mg per kg of body weight a

day in one or two divided daily doses. *Note: Take with meals or milks.*

Storage: at room temperature, in tight, light-resistant containers.

Sodium Nitroprusside

Powder for injection, 50 mg in ampoule.

Indications: Management of hypertensive crises; acute decompensated heart failure (HF); used for controlled hypotension to reduce bleeding during surgery.

Cautions: impaired pulmonary function; hypothyroidism; renal impairment; ischaemic heart disease; impaired cerebral circulation; hyponatraemia; raised intracranial pressure; elderly; hypothermia; monitor blood pressure and blood-cyanide concentration, also blood –thiocyanate concentration if given for more than 3 days; avoid sudden withdrawal (reduce infusion over 15 - 30 minutes to avoid rebound effects); pregnancy; breast feeding.

Drug interactions: other antihypertensives; acetazolamide, alcohol.

Contraindications: severe hepatic impairment; compensatory hypertension; severe vitamin B12 deficiency; hereditary optic atrophy or increased intracranial pressure

Side effects: nausea and vomiting, headache, apprehension, restlessness, palpitations, dizziness and abdominal pain, convulsions, confusion and hyperreflexia.

Dose and Administration: Hypertensive crisis: IV infusion:

Adult: Initially 0.3 mcg/kg/minute; usual maintenance dose 0.5 - 6 mcg/kg/minute; maximum dose 8mcg/kg/minutes; stop infusion if no response after 10 minutes at maximum dose. Lower doses in patients already being treated with antihypertensives.

Storage: store at room temperature.

Tolazoline

Injection, 25mg/ml in 10ml ampoule

Indications: persistent pulmonary vasoconstriction and hypertension of the newborn (persistent fetal circulation), peripheral vasospastic disorders.

Caution: mitral stenosis. *Note: pretreatment of infants with antacid may prevent gastrointestinal bleeding*

Drug interactions: ischaemic heart disease, hypotension or after a cerebrovascular accident; peptic ulcer disease.

Side effects: piloerection, headache, flushing, tachycardia, cardiac arrhythmias, tingling, chilliness, shivering, sweating, nausea, vomiting, diarrhoea, and epigastric pain, orthostatic hypotension or marked hypertension with large doses; peptic ulcer disease, oliguria, haematuria, myocardial infarction, gastrointestinal haemorrhage, thrombocytopenia and other blood dyscrasias.

Dose and administration: **Adult:** peripheral vasospastic disorder: IM, IV, SC: 10-50mg 4 times/day.

Neonates: Initial: IV: 1-2mg/kg over 10-15minutes via scalp vein or upper extremity; Maintenance: 1 to 2mg/kg/hour; use lower maintenance doses in patients with decreased renal function.

Valsartan

Tablet, 40mg, 80mg, 160mg, 320mg

Indications: treatment of hypertension alone or in combination with other antihypertensives. Treatment of heart failure.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: Oral: **Adult:** Initial: 80 mg once daily; maximum recommended dose: 320mg/day
Heart failure: initial: 40mg twice daily; titrate dose to 80-160 mg twice daily, maximum daily dose 320mg. Note: Do not use with ACE inhibitors and beta blockers.

Valsartan +Hydrochlorothiazide

Tablet, 80mg+12.5mg, 160mg+12.5mg, 160mg+25mg, 320mg+12.5mg, 320mg+25mg

Indication: inadequately controlled hypertension with single therapy of either valsartan or hydrochlorothiazide; or patients adequately controlled hypertension with hydrochlorothiazide experiencing hypokalemia.

Cautions: hepatic problem, driving or other activities need alertness, surgery, alcohol use, sunlight, diabetic patients

Contraindications: Pregnancy, breast feeding, hypersensitivity to valsartan, hydrochlorothiazide or other sulfonamide derived substances, anuria. Risk benefit should be evaluated for the following cases: Congestive heart failure, atherosclerosis or hyperlipidemia, diabetes mellitus, gout, hepatic function impairment, renal function impairment

Drug interactions: barbiturates, opioid analgesics, oral antidiabetic agents or insulin, NSAIDs, corticosteroids, lithium, tubocurarine

Side effects: dizziness, fatigue, pharyngitis, headache, viral infection, abdominal pain, allergic reaction, hypotension, jaundice, anxiety neutropenia, cough, impotence, libido photosensitivity

Dose and administration: adult: oral: the usual starting dose for patients taking usual dose of valsartan as a single therapy and uncontrolled blood pressure is 80mg/12.5mg valsartan/hydrochlorothiazide combination therapy and the usual starting

dose for patients taking 25 mg hydrochlorothiazide as a single therapy with uncontrolled blood pressure or patients taking hydrochlorothiazide experiencing hypokalemia is 80mg/12.5mg valsartan/ hydrochlorothiazide once daily. Titrate the dose to 160 mg/25 mg valsartan/ hydrochlorothiazide combination once daily if the blood pressure remains uncontrolled.

Verapamil

Injection, 2.5 mg/ml in 2ml ampoule

Tablets, 40 mg, 80 mg, 120 mg

Cautions, contraindication, side effects: See section 3.2. Under Verapamil

Dosing: Adult Hypertension: Oral: Initial: 80 mg or 160 mg once daily (in patients who are not volume depleted); dose may be increased to achieve desired effect; maximum recommended dose: 320 mg/day

Pediatric: Hypertension: Oral: Children 6-16 years: Initial: 1.3 mg/kg once daily (maximum: 40 mg/day); dose may be increased to achieve desired effect; doses >2.7 mg/kg (maximum: 160 mg) have not been studied.

Renal Impairment: $Cl_{cr} \geq 30$ mL/minute: No dosage adjustment necessary. $Cl_{cr} < 30$ mL/minute: *No dosage adjustment provided in manufacturer's labeling; safety and efficacy has not been established.*

3.6. Diuretics

Diuretics promote the excretion of water and electrolytes by the kidneys. They are used in the treatment of heart failure or in hepatic, renal, or pulmonary disease when salt and water retention has resulted in oedema or ascites. Diuretics are also used, either alone, or in association with other agents, in the treatment of hypertension. Low dose diuretics are

recommended first-line therapy in uncomplicated cases of hypertension, especially in black patients and elderly patients with isolated systolic hypertension. High doses are not recommended because of biochemical repercussions, including an adverse lipid profile, hyperuricaemia and impaired glucose control.

The principal groups of diuretics are Low-ceiling diuretics, 'Loop' or 'high - ceiling' diuretics, potassium sparing diuretics, osmotic diuretics, mercurial diuretics and carbonic anhydrase inhibitors. Low-ceiling diuretics: The thiazides, e.g. hydrochlorothiazide, are used as initial therapy for mild congestive heart failure and mild to moderate hypertension. Low doses are well tested in mild hypertension and in systolic hypertension, and should not exceed 25mg. The low-ceiling diuretics do not induce a diuresis at low creatinine clearances.

In hypertension, diuretics may be used alone or in combination with potassium-sparing diuretics or other antihypertensive agents. They are also used for the management of oedema associated with nephritic syndrome, liver cirrhosis (usually preceded by spironolactone) and heart failure, idiopathic hypercalciuria, nephrogenic diabetes insipidus (where they have an antidiuretic effect) and to help prevent osteoporosis.

High-ceiling diuretics: loop diuretics, e.g. furosemide, are used in the initial therapy of severe heart failure. Furosemide is effective in high doses even if there is severe impairment of renal function. Furosemide is similar chemically to the thiazide diuretics. It has prompt onset of diuretic action and acts primarily by inhibiting chloride and sodium reabsorption over the entire length of the thick ascending limb of the loop of henle. The intravenous route is very fast-acting in emergency situations such as pulmonary oedema. In such circumstances it

has an acute haemodynamic effect, i.e. venodilation with reduced venous return.

The oral form may be used for hypertension, either alone or in combination with other antihypertensive agents, but the thiazide-type diuretics are preferred unless there is renal impairment or cardiac failure.

Potassium-sparing diuretics: these include the aldosterone antagonists, e.g. spironolactone, which should only be used where specifically indicated.

Others are amiloride and triamterene. Amiloride inhibits sodium reabsorption in the distal tubule and is a weak diuretic when administered alone. It also has some antihypertensive activity. Its potassium and magnesium-sparing properties are useful if combined with a potassium-depleting diuretic, e.g. hydrochlorothiazide. It is the drug of choice in Liddle's syndrome and is an alternative to spironolactone in patients with primary aldosteronism, who experience adverse effects.

The adverse effects of diuretic therapy are mainly due to the fluid and electrolyte imbalance induced by the drugs. Hyponatraemia is an adverse effect of all diuretics. The risk of hypokalaemia, which may occur with both thiazide and loop diuretics, depends more on the duration of action than on potency and is thus greater with thiazides than with loop diuretics (when given in equipotent doses). Potassium-sparing diuretics can cause hyperkalaemia. Other electrolyte disturbances include hypercalcaemia (thiazides), hypocalcaemia (loop diuretics) and hypomagnesaemia (thiazide and loop diuretics).

Symptoms of fluid and electrolyte imbalance include dry mouth, thirst, gastrointestinal disturbances (including nausea, vomiting), weakness, lethargy, drowsiness, restlessness, seizures, confusion, headache, muscle pains or cramps,

hypotension (including postural hypotension), oliguria, arrhythmias.

The elderly are more susceptible to electrolyte imbalance than younger patients; treatment should begin with a lower initial dose of the diuretic (commonly about 50 % of the adult dose) and then adjusted carefully according to renal function, plasma electrolytes and diuretic response.

Amiloride

Tablet, 5mg

Indications: counteracts potassium loss induced by other diuretics in the treatment of hypertension or oedematous conditions including CHF, hepatic cirrhosis, and hypoaldosteronism.

Cautions: diabetes mellitus, elderly, pregnancy and breast-feeding.

Drug interactions: ACE inhibitors, potassium supplements and salt substitutes, NSAIDs.

Contraindications: hyperkalaemia, renal failure, and hypersensitivity; see also Hydrochlorothiazide

Side effects: except for hyperkalaemia serious adverse effects are uncommon; nausea, anorexia, abdominal pain and flatulence, headache, weakness and dizziness. Rarely - visual disturbances, blood dyscrasias, skin rashes, pruritus, bladder spasm, muscle cramps and jaundice.

Dose and Administration: Edema: Oral: **Adult:** 5-10mg/day (up to 20mg). **Elderly:** initial: 5mg once daily or every other day.

Storage: store at room temperature

Amiloride and Hydrochlorothiazide

Oral solution, 5mg + 50mg/5ml

Tablet, 2.5mg + 25mg; 5mg + 50mg

See section 2.5 under Amiloride and hydrochlorthiazide

Furosemide

Elixir, 10 mg/ml

Injection, 10 mg/ml in 2 ml ampoule

Tablet, 40 mg, 80mg

Indications: edema of cardiac, hepatic or renal origin, oliguria due to renal failure; mild to moderate hypertension, usually in combinations with other antihypertensive agents and as adjunct in the treatment of hypertensive crisis and for the treatment of hypercalcemia.

Cautions: children, elderly patients, pregnancy (not used to treat hypertension in pregnancy) and breast feeding; hypotension; correct hypovolaemia before using in oliguria. It may cause hypokalaemia and hyponatraemia, aggravates diabetes mellitus and gout, liver failure, renal impairment, prostatic enlargement, porphyria.

Drug interactions: antigout, potassium-depleting agents, cephalosporins, NSAIDs, thiazide diuretics.

Contraindications: patients with precomatose states associated with liver cirrhosis, renal failure with anuria.

Side effects: hyponatraemia, hypokalaemia, hypomagnesaemia, hypochloroemic alkalosis, increased calcium excretion, hypotension, less commonly nausea, gastro-intestinal disturbances, hyperuricemia and gout, hyperglycemia, temporary increase in plasma cholesterol and triglyceride concentrations, photosensitivity and bone marrow depression, pancreatitis, tinnitus and deafness, orthostatic hypotension as a result of massive diuresis (dizziness or light-headedness when getting up from sitting position).

Dose and Administration:Edema: Oral:**Adult:** initially 40 mg daily on rising, maintenance, 20 mg daily or 40 mg on alternate days, may be increased to 80 mg daily in resistant oedema;

Child: 1 to 3 mg/Kg body weight daily (maximum 40 mg daily).Acute Pulmonary edema: Slow IV injection:

Adult: 20 to 50 mg, if necessary increase by 20 mg steps every 2 hours; if effective single dose is more than 50 mg, consider using slow intravenous infusion at a rate not exceeding 4 mg/minute.

Child: 0.5 to 1.5 mg/kg body weight daily (maximum 20 mg daily).Oliguria (glomerular filtration rate less than 20 ml/minute): Slow IV infusion of a rate not exceeding 4mg/minute:**Adult:** initially 250 mg over 1 hour; if urine output not satisfactory during hour after first dose, infuse 500 mg over 2 hours then, if no satisfactory response during hour after second dose, infuse 1 g over 4 hours; if no response after third dose, dialysis probably necessary.**Hypertension:**Oral: initially 40mg two times a day; the dosage being adjusted according to patient's need. IV: hypertensive crisis in patients with normal renal function, IV 40 to 80mg. Hypertensive crisis accompanied by pulmonary edema or acute renal failure IV 100-200 mg.**Antihypercalcemic:**Oral: 120mg a day a single dose or divided into two or three doses; IM or IV: **Adult:** 80-100mg in severe cases, the dosage being repeated if necessary every one to two hours until the desired response is obtained. In less severe cases smaller doses may be given every two or four hours. **Child:** IM or IV: 25 to 50mg, the dosage being repeated if necessary every four hours until the desired response is obtained.

Storage: Store at room temperature in a well closed container, protect from freezing and light.

Hydrochlorothiazide

Tablet, 25 mg

Indications: oedema, hypertension and cardiac failure.

Cautions: paediatrics, elderly patients, during pregnancy and breast-feeding, heart failure, aggravates diabetes and gout, and may exacerbate systemic lupus erythematosus, dyslipidaemia.

Drug interactions: lithium, antidiabetic agents, hypotensive agents, NSAIDs, drugs causing potassium depletion, digoxin, cholestyramine.

Contraindications: refractory hypokalaemia, hyponatraemia, hypercalcaemia, severe renal and hepatic impairment, and symptomatic hyperuricemia, Addison's disease, anuria.

Side effects: postural hypotension and mild gastrointestinal effects, impotence (reversible), hypokalaemia, hypomagnesaemia, hyponatraemia, hypercalcaemia, hypochloraemic alkalosis, hyperuricemia, gout, hyperglycemia, and increased in plasma cholesterol concentrations, less commonly rashes, photosensitivity, blood disorders (including neutropenia and thrombocytopenia), pancreatitis, intrahepatic cholestasis, hypersensitivity reaction.

Dose and Administration: Hypertension: Oral: **Adult:** 12.5, 25 mg daily; elderly initially 12.5 mg daily.

Edema: Oral: **Adult:** initially 25 mg daily on rising increasing to 50 mg daily if necessary, elderly initially 12.5 mg daily.

Severe Oedema in patients unable to tolerate loop diuretics: Oral: **Adult:** up to 100 mg either daily or on alternate days (maximum 100 mg daily).

Nephrogenic diabetes insipidus: Oral: **Adult:** initially up to 100 mg daily.

Mannitol

Injection, 25 % in 50 ml, 20 % in 250 ml, 10 % in 500 ml

Indications: oliguria due to acute renal failure; reduction of intracranial pressure - cerebral oedema; reduction of intraocular pressure - for angle closure glaucoma.

Cautions: extravasation causes inflammation and thrombophlebitis.

Drug interactions: digitalis glycosides, lithium.

Contraindications: cardiac failure, pulmonary oedema, well established anuria caused by severe renal disease or impaired renal functions who do not respond to a test dose, severe dehydration, metabolic edema, intracranial bleeding.

Side effects: chest pain or fast heartbeat, chills or fever, head ache, convulsions, difficulty in urination, electrolyte imbalance (confusion, irregular heartbeat, muscle cramps or pain, numbness, tingling, pain or weakness in hands or feet), pulmonary congestion, thrombophlebitis (redness or swelling or pain at injection site).

Dose and Administrations: Test dose (to assess adequate renal function), by intravenous infusion, as a 20 % solution, 200 mg/kg body weight infused over 3-5 minutes, repeat test dose if urine output less than 30 - 50 ml/hour; if response inadequate after second test dose, re-evaluate patient. **Raised intracranial or intraocular pressure:** I.V infusion: as a 20 % solution infused over 30 - 60 minutes, 0.25 - 2g/kg body weight. **Cerebral Oedema:** I.V infusion: as a 20 % solution infused rapidly, 1g/kg body weight.

Storage: at room temperature protect from freezing.

Metolazone

Tablet, 2.5 mg, 5 mg, 10 mg

Indications: management of mild to moderate hypertension; treatment of edema in congestive heart failure and nephritic syndrome, impaired renal function.

Cautions: as for Hydrochlorothiazide.

Drug interactions: furosemide, see also under hydrochlorothiazide.

Contraindications: as for hydrochlorothiazide.

Side effects: as for hydrochlorothiazide, and also palpitation, chest pain, and chills.

Dose and Administration: Oral: **Adult:** Edema: 5-20mg/dose every 24 hours. Hypertension: 2.5-5mg/dose every 24 hours.

Storage: store at room temperature.

Spironolactone

Tablet, 25 mg, 100 mg

Syrup, 5mg 10mg, 25mg, 50mg, 100mg/5ml

Indications: oedema and ascites in cirrhosis of the liver, malignant ascites, nephritic syndrome, congestive heart failure; primary hyperaldosteronism.

Cautions: renal and hepatic function impairment, diabetes mellitus, pregnancy, breast feeding, elderly, monitor electrolytes (discontinue if hyperkalaemia)

Drug interactions: Angiotensin - converting enzyme (ACE) inhibitors, cyclosporin, diuretics, potassium containing medications, potassium supplements or substances containing high levels of potassium, lithium, digoxin, NSAIDs, warfarin.

Contraindications: hyperkalaemia, hyponatraemia, pregnancy and breast-feeding, Addison's disease.

Side effects: gastro-intestinal disturbances; impotence, gynaecomastia, menstrual irregularities; lethargy, headache, confusion; rashes, hyperkalaemia (discontinue), hyponatraemia, hepatotoxicity, osteomalacia, and blood disorders reported.

Dose and Administration: Oral: **Oedema: Adult:** 100 - 200 mg daily, increased if necessary to 400 mg daily in resistant oedema, usual maintenance dose 75 - 200 mg daily. **Child:**

initially 3 mg/kg body weight daily in divided doses. **Primarily hyperaldosteronism: Adult:** diagnosis, 400 mg daily for 3 - 4 weeks; preoperative management, 100 - 400 mg daily; if not suitable for surgery, lowest effective dose for long term maintenance. **Adjunct in severe heart failure: Adult:** usually 25 mg daily. *Note: Take with meals or milk.*

Storage: at room temperature in a tight, light - resistant container

3.7. Sclerosing Agents

Sclerosants are used in the management of varicosities including varicose veins and oesophageal varices when their capacity to damage veins is apparently put to good use. The mechanisms by which injection sclerotherapy works are not completely understood but are thought to involve damage to the intima, intraluminal thrombosis, and intravascular fibrous organisation. Sclerosants used include: ethanolamine oleate, sodium tetradecyl sulphate and sodium morrhuate.

Ethanolamine Oleate

Injection, 5 % in 2 ml ampoule

Indications: treatment of varicose veins and oesophageal varices.

Cautions: fatal anaphylactic shock has been reported following administration; use with caution and decrease dose in patients with significant liver dysfunction, with concomitant cardiorespiratory disease, or in the elderly or critically ill.

Contraindications: varicose veins of the legs in patients with thrombosis or a tendency to thrombosis; acute phlebitis, marked arterial, cardiac, or renal disease; local or systemic infections; or uncontrolled metabolic disorders such as diabetes mellitus. Known hypersensitivity to the agent or oleic acid.

Side effects: irritant to skin and mucus membranes; local injection may cause sloughing, ulceration, and in severe cases, necrosis and pain may occur at the site of injection. Patients receiving treatment for oesophageal varices may develop pleural effusion or infiltration. Hypersensitivity reactions have been reported.

Dose and Administration: IV: **Adult:** Varicose veins: 2 to 5 ml of a 5 % solution of ethanolamine oleate is injected into empty isolated sections of veins, divided between 3 or 4 sites. Injection into full veins is also possible. Oesophageal varices: 1.5 to 5 ml of a 5 % solution per varix to a maximum total dose of 20 ml per treatment session.

Storage: protect from light.

SodiumMorrhuate

Injection, 5% in 5ml ampoule

Indications: treatment of small, uncomplicated varicose veins of the lower extremities.

Cautions: should only be administered when adequate facilities, drugs (e.g. epinephrine, antihistamines, corticosteroids), and personnel are available for the treatment of anaphylactic reactions.

Contraindications: hypersensitivity reactions to the medicine or to the fatty acids of cod liver oil. thrombophlebitis; arterial disease, varicosities caused by abdominal and pelvic tumors, uncontrolled diabetes mellitus, thyrotoxicosis, tuberculosis, neoplasms, asthma, sepsis, blood dyscrasias, acute respiratory or skin diseases; and in bedridden patients.

Side effects: thrombosis, valvular incompetency, vascular collapse, drowsiness, headache, dizziness, urticaria, nausea, vomiting, burning at the site of injection, severe extravasation effects, asthma, anaphylaxis, weakness.

Dose and Administration: IV: **Adult:** Small veins: 50-100mg (1-2ml or 5% injection). Large veins: 150-200 mg (3-5ml or 5% injection).

Storage: store at room temperature and protect from light.

Sodium Tetradecyl Sulphate

Injection, 1%, 3 %

Indications: varicose veins, management of bleeding oesophageal varices.

Cautions, Contraindications and Side effects; as for ethanalamine oleate.

Dose and Administration: IV: Test dose: 0.5ml given several hours prior to administration of larger dose; 0.5-2ml (preferred maximum: 1ml) in each vein, maximum: 10ml per treatment session; 3% solution reserved for large varices.

Storage: store at a temperature not exceeding 25°C. Protect from light.

3.8. Medicines used in vascular shock

Shock is a complex clinical syndrome of multiple aetiologies but the common factor in all types of shock is a failure of the circulatory system to maintain cellular perfusion and function. Cardiac shock usually results from acute failure of the heart, leading to an inadequate stroke volume and reduced cardiac output. It has a number of causes, but is most commonly associated with acute myocardial infarction.

Successful correction of hypovolaemia may alleviate hypotension in some cases, but cardiac output may remain depressed and signs of impaired organ perfusion may persist, necessitating additional therapy.

In cardiogenic shock cardiac output is usually low but peripheral resistance is high and drugs that have predominantly inotropic effects are most suitable.

Dopamine or dobutamine are often chosen. Dopamine has been widely used in all forms of shock, often in combination with other inotropes. At low doses it causes peripheral vasodilation, which was thought to protect renal perfusion; however, any clinical benefit is unclear and at higher doses it causes vasoconstriction and is useful where hypotension is not significant. Noradrenaline causes peripheral vasoconstriction and should be reserved for severe hypotension. It is particularly useful in septic shock where the cardiac output is usually high but peripheral resistance is low. Adrenaline has also been used alone but renal artery vasoconstriction may limit its use, and it has also been reported to cause lactic acidosis. In cardiogenic shock associated with myocardial infarction, specific therapy to restore myocardial perfusion is also indicated.

Adrenaline (Epinephrine)

Injection, 0.1 %, 1:1000 1mg/ml

Indications: Anaphylactic shock, cardiac arrest; bronchospasms; open angle (chronic simple) glaucoma; added to local anaesthetics.

Cautions: hyperthyroidism, hypertension, diabetes mellitus, ischaemic heart disease, arrhythmias, cerebrovascular disease, and elderly, cerebral arteriosclerosis, parkinson's , rapid IV infusion may cause death from cerebrovascular hemorrhage or cardiac arrhythmias.

Drug interactions: other sympathomimetic agents (additive effects), alpha-adrenergic blocking agents, anaesthetics

(volatile), beta blockers, digoxin, theophylline, tricyclic antidepressants, monoamine oxidase inhibitors.

Contraindications: asymmetric septal hypertrophy, pheochromocytoma, tachyarrhythmias.

Side effects: tachycardia and arrhythmia, hypertension, hypotension, tremor, anxiety, sweating, nausea, vomiting, weakness, dizziness, pulmonary oedema, headache, peripheral vasoconstriction.

Dose and Administration: The 1:1000 (1mg/ml) concentration of epinephrine injection must be diluted before administering intravenously. **Adult:** vasopressor-intravenous infusion, 1mcg per minute. The dose may be titrated up to 2 to 10 microgram per minutes for desired hemodynamic response.

Storage: at room temperature. Protect from light and freezing.

Dobutamine

Powder for injection, 250 mg

Indications: inotropic support in cardiogenic shock, acute myocardial infarction, post-cardiac surgery and septic shock after adequate volume replacement; management of refractory cardiac failure.

Cautions: pregnancy, severe hypotension, hypovolaemia should be corrected before treatment.

Drug interactions: beta-blocking agents; anaesthetic agents (eg, halothane); MAO inhibitors.

Contraindications: idiopathic hypertrophic cardiomyopathy with outflow obstruction.

Side effects: palpitations, ectopic heartbeats and, rarely, ventricular tachycardia, angina, increase in systolic blood pressure (10 - 20 mmHg, in most patients, but may be more dramatic, particularly in the presence of preexisting

hypertension), nausea, vomiting, headache, paraesthesia and dyspnoea may occur.

Dose and Administration: Adult: IV infusion: initially, 2.5-10 mcg/kg/minute, increasing gradually in increments of 2.5 mcg/kg/minute up to 15 mcg/kg /minute. Usually not > 20 mcg/kg/ minute are needed. May be infused for up to 72 hours, provide the patient is carefully monitored; thereafter intermittently.

Storage: store at room temperature.

Dopamine Hydrochloride

Injection, 40 mg/ml

Indications: cardiogenic shock in infarction or cardiac surgery, renal failure or septicaemia after adequate volume replacement; short-term management of refractory cardiac failure and treatment of acute hypotension.

Cautions: hypovolaemia; low dose in shock due to acute myocardial infarction, hypoxia, hypercapnia, and metabolic acidosis before or at some time as starting treatment, history of peripheral vascular disease, elderly.

Note: hypovolaemia should be corrected before dopamine is used in shocked patients.

Drug interactions: halogenated anaesthetics (such as cyclopropane, halothane); monoamine oxidase inhibitors, betablockers, digoxin, ergotamine/ergotamine, tricyclic antidepressants.

Contraindications: tachyarrhythmias, ventricular fibrillation, ischaemic heart disease, Pheochromocytoma; hyperthyroidism.

Side effects: nausea and vomiting, peripheral vasoconstriction, hypotension with dizziness, fainting, flushing, tachycardia, ectopic beats, palpitations, anginal pain; headache dyspnoea, hypertension.

Dose and Administration: Cardiogenic shock: I.V infusion into large vein: **Adult:** initially 2 - 5 micrograms/Kg/minutes; gradually increased by 5 - 10 micrograms/Kg/minutes according to blood pressure, cardiac output and urine output; seriously ill patients up to 20 - 50 micrograms/Kg minutes. **Child:** IV same as for adults.

Storage: at room temperature protect from freezing.

Isoprenaline (Isoproterenol) hydrochloride

Injection, 0.02 mg/ml, 0.2mg/ml

Indications: severe bradycardia, unresponsive to atropine; short-term emergency treatment of heart block; ventricular arrhythmias secondary to atrioventricular nodal block.

Cautions, Drug interactions, Contraindications and Side effects; as for adrenaline above.

Dose and Administration:Adult: Emergency treatment: Slow IV bolus: 0.01 to 0.06 mg (10 - 60 mcg), with subsequent doses ranging from 0.01 to 0.2 mg. IV infusion: initially 1 mcg/minute, adjusted according to response. **Child:** IM or SC: 0.2 mg as a single dose. IV: 0.02 mg as a single dose. IV infusion: 0.2 mg (1ml) in 200 ml 5 % dextrose water; rate depends on size of patient and situation.

Storage: store in tight, light-resistant containers.

Levarterenol (Noradrenaline) Tartarate

Tartrate Injection, 8mg/ml in 1ml ampoule

Injection, 1:1000

Indications: treatment of shock which persists after adequate fluid volume replacement.

Cautions: never use leg veins for infusion sites, monitor blood pressure closely and adjust infusion rate, hypoxia or hypercapnia.

Drug interactions: tricyclic antidepressants, MAO inhibitors, antihistamines, beta-blockers (nonselective), ergot alkaloids, reserpine, and methyldopa, alpha-blockers.

Contraindications: hypersensitivity to the drug, pregnancy, during anesthesia with cyclopropane or halothane anesthesia (risk of ventricular arrhythmias)

Side effects: bradycardia, arrhythmia, peripheral ischemia, headache, anxiety, and dyspnea, skin necrosis, respiratory difficulty.

Dose and Administration: Vasopressor: **Adult:** initial, I.V infusion, 0.5 to 1mcg (base) per minute; the dosage being adjusted gradually to achieve desired blood pressure. Maintenance: Intravenous infusion, 2 to 12 mcg (base) per minute. **Child:** IV, 0.1mcg (base) per kg of body weight per minute; the dosage being adjusted gradually to achieve desired blood pressure, up to 1mcg per kg of body weight per minute.

Note: Noradrenaline is administered only by intravenous infusion. Subcutaneous or intramuscular administration is not recommended because of the potent vasoconstrictor effect of norepinephrine.

Storage: store at room temperature.

Phenylephrine Hydrochloride

Injection, 10 mg/ml in 1 ml ampoule

Indications: treatment of vascular failure, unresponsive to adequate fluid volume replacement, in shock, shock like states, drug induced hypotension, or hypersensitivity.

Cautions: late pregnancy and during labour, diabetes mellitus, cerebral arteriosclerosis, bradycardia, elderly patients.

Drug interactions: alpha adrenergic blocking agents such as labetalol; phenoxy benzamine; phentolamine; prazosin, anaesthetics, tricyclic antidepressant, ergotamine, B-blockers, MAO inhibitors

Contraindications: hypertension, hyperthyroidism or myocardial disease or tachycardia.

Side effects: chest discomfort, pain, dizziness, nervousness, restlessness, trembling, troubled breathing, unusual paleness, and unusual weakness.

Dose and Administration:Adult: IM, SC: 2-5 mg/dose every 1-2 hours as needed (initial dose should not exceed 5 mg). IV. bolus: 0.1-0.5 mg/dose every 10 -15 minutes as needed (initial dose should not exceed 0.5 mg). **Child:** IM, SC: 0.1mg/kg/dose every 1-2 hours as needed (maximum: 5 mg). IV. bolus: 5-20 mcg/kg/dose every 10-15 minutes as needed. IV. infusion: 0.1-0.5 mcg/kg/minute.

Storage: at room temperature and protect from light and freezing.

3.9. Thrombolytic agent

Antithrombic enzymes convert plasminogen to plasmin, which inturn degrades fibrin thrombi and fibrinogen. The most generally accepted indication for the use of antithrombic enzymes is in the treatment of selected cases of acute myocardial infarction. Other indications include acute severe pulmonary thromboembolism; acute arterial thrombosis and thromboembolism; severe deep-vein thrombosis; and clearance of arteriovenous catheters and cannulae. Thrombolytic agents should not be used to treat superficial thrombophlebitis.

Alteplase

Powder for injection, 50mg, 100mg /vial

Indications: management of acute occulsiive myocardial infarction for the lysis of thrombi in coronary arteries; management of acute massive pulmonary embolism (PE) in adults.

Cautions: refractory hypertension, traumatic resuscitation, non-compressible vascular punctures, transient ischaemic attack (TIA) in preceding 6 months, warfarin therapy, recent retinal laser treatment.

Drug interactions: aminocaproic acid, oral anticoagulants, heparin, non steroidal ant inflammatory medicines, nitroglycerin.

Contraindications: cerebrovascular accident, or history of recent major trauma, surgery or head injury (within the preceding month); gastrointestinal bleeding within the last month; dissecting aneurysm, intracranial aneurysm, active bleeding or known bleeding disorder.

Side effects: hypotension, fever, bruising, GI hemorrhage, nausea, vomiting, GU hemorrhage, bleeding.

Dose and Administration: Acute myocardial infarction: IV: Adult: 15mg bolus, then 0.75mg/kg over 30 minutes, followed by 0.5mg/kg over 60 minutes. Total dose should not exceed 100mg.

Storage: store at room temperature or under refrigeration; once reconstituted it must be used within 8 hours.

Fondaparinux

Injection, 2.5mg/0.5ml, 7.5mg/0.6ml injection

Indications: prophylaxis of venous thromboembolism in medical patients immobilised because of acute illness, and patients undergoing major orthopaedic surgery of the hip or leg, or abdominal surgery; treatment of deep-vein thrombosis, superficial-vein thrombosis, and pulmonary embolism; treatment of unstable angina or non-ST-segment elevation myocardial infarction; treatment of ST-segment elevation myocardial infarction.

Cautions:bleeding disorders, active gastro-intestinal ulcer disease; recent intracranial haemorrhage; brain, spinal, or ophthalmic surgery; spinal or epidural anaesthesia (risk of spinal haematoma—avoid if using treatment doses); risk of catheter thrombus during percutaneous coronary intervention; low body-weight; elderly patients; concomitant use of drugs that increase risk of bleeding,Hepatic impairment,Renal impairment; for treatment of venous thromboembolism use if eGFR 30–50 ml/minute/1.73 m².

Contra-indications:active bleeding; bacterial endocarditis, Renal impairment: treatment of acute coronary syndromes avoid if eGFR less than 20 ml/minute/1.73 m²; for treatment of venous thromboembolism avoid if eGFR less than 30 ml/minute/1.73 m², for prophylaxis of venous thromboembolism and treatment of superficial-vein thrombosis reduce dose to 1.5 mg daily if eGFR 20–50 mL/minute/1.73 m², avoid if eGFR less than 20 mL/minute/1.73 m²;Pregnancy, Breast-feeding

Side-effects:bleeding, purpura, anaemia; less commonly gastro-intestinal disturbances, oedema, hepatic impairment, chest pain, dyspnoea, thrombocytopenia, thrombocythaemia, rash, pruritus; rarely hypotension, flushing, cough, vertigo, dizziness, anxiety, drowsiness, confusion, headache, hypokalaemia, hyperbilirubinaemia, injection-site reactions; also reported atrial fibrillation, tachycardia, and pyrexia.

Dosage and Administration:Prophylaxis of venous thromboembolism after surgery, by subcutaneous injection, 2.5 mg 6 hours after surgery then 2.5 mg once daily.Prophylaxis of venous thromboembolism in medical patients, by subcutaneous injection, 2.5 mg once daily.Treatment of superficial-vein thrombosis, by subcutaneous injection, adult body-weight over 50 kg, 2.5 mg once daily for at least 30 days (maximum 45 days if high risk of thromboembolic

complications); treatment should be stopped 24 hours before surgery and restarted at least 6 hours post operatively.

Unstable angina and non-ST-segment elevation myocardial infarction, by subcutaneous injection, 2.5 mg once daily for up to 8 days (or until hospital discharge if sooner); treatment should be stopped 24 hours before coronary artery bypass graft surgery (where possible) and restarted 48 hours post operatively.

ST-segment elevation myocardial infarction, initially by intravenous injection or infusion, 2.5 mg for first day, thereafter by subcutaneous injection 2.5 mg once daily for up to 8 days (or until hospital discharge if sooner); treatment should be stopped 24 hours before coronary artery bypass graft surgery (where possible) and restarted 48 hours post operatively.

Treatment of deep-vein thrombosis and of pulmonary embolism, by subcutaneous injection, adult body-weight under 50 kg, 5 mg every 24 hours; body-weight 50–100 kg, 7.5 mg every 24 hours; body-weight over 100 kg, 10 mg every 24 hours.

Note: Child under 17 years not recommended. An oral anticoagulant (usually warfarin,) is started at the same time as fondaparinux (fondaparinux should be continued for at least 5 days and until INR ≥ 2 for at least 24 hours

Retepase

Powder for injection, 10.4u

Indications: management of acute myocardial infarction (AMI); improvement of ventricular function; reduction of the incidence of CHF and the reduction of mortality following AMI.

Caution, Drug interactions and Contraindications; see under alteplase.

Side effects: bleeding, anemia.

Dose and Administration: Adult: 10 units IV over 2 minutes, followed by a second dose 30 minutes later of 10 units IV over 2 minutes.

Storage: store at 2-25⁰C.

Rivaroxaban

Tablet, 10mg, 15mg and 20mg

Indication: prophylaxis of venous thromboembolism in adults after hip or knee replacement surgery; Rivaroxaban does not require therapeutic monitoring.

Cautions: bleeding disorders; concomitant use of drugs that increase risk of bleeding; severe hypertension; active or recent gastro-intestinal ulceration; vascular retinopathy; anaesthesia with postoperative indwelling epidural catheter (risk of paralysis—monitor neurological signs and wait at least 18 hours after rivaroxaban dose before removing catheter and do not give next dose until at least 6 hours after catheter removal); recent surgery; Hepatic impairment; Renal impairment.

Drug interaction: tazanavir, Darunavir, Fosamprenavir, Indinavir, Itraconazole, Ketoconazole, Lopinavir, Nelfinavir, Posaconazole, Rifampicin, Ritonavir, Saquinavir, Tipranavir, Voriconazole, Diclofenac, Ketorolac. Renal impairment use with caution if eGFR 15–29 mL/minute/1.73 m² or if eGFR 30–49 mL/minute/1.73 m.

Contraindications: active bleeding; Renal impairment avoid if eGFR less than 15 mL/minute/1.73 m², Pregnancy, Breast-feeding

Side-effects: nausea; haemorrhage; less commonly constipation, diarrhoea, dyspepsia, dry mouth, vomiting, hypotension, oedema, tachycardia, thrombocythaemia, syncope, dizziness,

headache, renal impairment, pain in extremities, pruritus, and rash; jaundice also reported

Dose and Administration: Prophylaxis of venous thromboembolism following knee replacement surgery, adult over 18 years, 10 mg once daily for 2 weeks starting 6–10 hours after surgery. Prophylaxis of venous thromboembolism following hip replacement surgery, adult over 18 years, 10 mg once daily for 5 weeks starting 6–10 hours after surgery

Tenecteplase

Powder for injection, 50mg

Indications: management of acute myocardial infarction (AMI)

Caution and Contraindications see under alteplase.

Side effects: hematoma, bleeding, stroke, GI hemorrhage, epistaxis, GU bleeding.

Dose and Administration: Adult: Acute myocardial infarction: IV bolus over 10 seconds, 30-50 mg according to body weight; maximum 50mg.

Storage: store at room temperature or under refrigeration 2-8⁰C. If reconstituted and not used immediately, store in refrigerator and use within 8 hours.

3.9. Diagnostic Agents

Iohexol

Injection, 140mg/ml, 180mg/ml, 200mg/ml, 240mg/ml, 300mg/ml, 3500mg

Indications: for intrathecal administration in adults including myelography (lumbar, thoracic, cervical, total columnar) and in contrast enhancement for computerized tomography (myelography, cisternography, ventriculography).

Contraindications: known hypersensitivity to iohexol. Myelography should not be performed in the presence of

3. Cardiovascular Medicines

significant local or systemic infection where bacteremia is likely. Intrathecal administration of corticosteroids with iohexol is contraindicated. Because of the possibility of overdose, immediate repeat myelography in the event of technical failure is contraindicated

4. RESPIRATORY MEDICINES

4.1. Antitussives/Expectorants/Mucolytics

Cough is an important physiological protective mechanism, but may also occur as a symptom of an underlying disorder such as asthma, gastro-oesophageal reflux disease, and postnasal drip. Treatment of the disorder often alleviates the cough, but there are times when symptomatic treatment is appropriate. The treatment chosen depends on whether the cough is productive or non-productive.

A non-productive cough such as that often seen with the common cold serves no useful purpose for the patient, and cough suppressants may provide some relief, particularly if given at night. Of the commonly used cough suppressants, pholcodine and dextromethorphan are considered to have fewer adverse effects than codeine. However, there is little evidence that these drugs are effective in severe cough. Codeine or similar opioids are not generally recommended as cough suppressants in children, and should be avoided altogether in those under 1 year of age.

A productive cough is characterized by the presence of sputum and may be associated with conditions such as chronic bronchitis, bronchiectasis, or cystic fibrosis. Cough suppressants are inappropriate, since the cough serves the purpose of clearing the airways; expectorants such as guaifenesin have been used on the grounds that increasing the volume of secretions in the respiratory tract facilitates removal by ciliary action and coughing. Mucolytics such as carbocisteine have been shown to affect sputum viscosity and structure and patients with productive cough have reported alleviation of their symptoms, but no consistent improvement has been demonstrated in lung function.

**Acetaminophen+Pseudoephedrine
Hydrochloride+Chlorpheniramine**

Tablet, 325mg +15mg +1mg

Indications: Temporary reliefs of running nose, sneezing, minor aches and pains headache, fever and nasal congestion associated with the common cold

Caution: avoid concomitant use of other paracetamol containing medicines, should be given with caution for patients with impaired kidney function or liver function and to patients with alcohol dependence, Pseudoephedrine is distributed in to breast milk and hence use by nursing mothers is not recommended, Chlorpheniramine causes drowsiness – do not drive or operate machinery while taking and avoid alcohol

Contraindications, side effects: see individual preparations

Dose and administration: *oral:Analgesic: Based on Acetaminophen component: Children:* 10-15 mg/kg/dose every 4-6 hours as needed; do not exceed 5 doses in 24 hours.**Adult:** 325-650mg every 4-6 hours as needed; do not exceed 4g/day.**Based on Chlorpheniramine component: Children:** 2-6 years: 1mg every 4-6 hours (maximum: 6mg/24hrs); 6-12 years: 2mg every 4-6 hrs (maximum: 12mg/24hrs); Children > 12 years and Adult: 4mg every 4-6 hrs (maximum: 24mg/24hrs). **Decongestant: Based on Pseudoephedrine component: Children;** 2-6 years: 15 mg every 4 hrs (max 90mg/24hrs); 6-12 years: 30 mg every 4 hrs (max 180mg/24hrs); Children > 12 years and Adult: 60mg every 4 hrs (maximum: 360mg/24hrs)

Bromhexine Hydrochloride

Elixir, 4mg/ml

Syrup, 5mg/5ml

Indications: acute and chronic bronchopulmonary diseases associated with abnormal mucous secretion and impaired mucous transport.

Cautions: history or symptoms of peptic ulceration, severe hepatic and renal impairment

Contraindications: known hypersensitivity or idiosyncratic reaction to bromhexine hydrochloride (or any of the other ingredients in the product).

Side effect: gastrointestinal effects may occur; and transient elevation in serum aminotransferase has been reported.

Dose and administration: *Oral:* **Child** (<2 years): 1mg 3 times/ day; **Child** (2 to 6 years): 4mg twice daily or 2mg 3 times/ day; **Child** (6 to 12 years):4 mg 3 times/day; **Child** (>12 years) and **Adults:** 8mg 3 times/day.

Storage: keep in a cool dry place where the temperature stays below 30°C.

Carbocisteine

Syrup, 2% (2gm/100ml), 5 % (5gm/100ml) in 125 ml

Indications: for respiratory disorders associated with productive cough.

Cautions: history of peptic ulcer disease.

Contraindications: active peptic ulceration.

Side effects: headache, GIT disturbances such as nausea, diarrhea and gastrointestinal bleeding, and skin rashes.

Dose and Administration: *Oral:* **Adult:** initially 750 mg 3 times daily, reduced to 1.5 g/day in divided doses, as soon as a response is obtained. **Child:** 6-12 years, 250 mg 3 times daily; 2-5 years, 62.5-125 mg 4 times daily.

Storage: at room temperature.

Codeine Phosphate

Tablet, 30 mg

Linctus, 15 mg/5ml

Indications: Antitussive in lower doses; treatment of mild to moderate pain.

Cautions: patients with asthma, hepatic and renal impairment, history of drug abuse and also in children, hypersensitivity reactions to other phenanthrene derivative opioid agonists.

Drug interactions: alcohol, CNS depressants, buprenorphine, monoamine oxidase (MAO) inhibitors, naltrexone, antidiarrhoeal agents.

Contraindications: children under 1 year old, productive cough, elderly, respiratory depression, head injury, acute alcoholism, acute asthma, heart failure secondary to chronic lung disease.

Side effects: constipation particularly troublesome in long term use; dizziness, nausea, vomiting; difficulty with micturation; ureteric or biliary spasm; dry mouth, headaches, sweating, facial flushing; dependence, euphoria, sedation, respiratory depression, circulatory collapse, anaphylactoid reaction.

Dose and Administration: Tablet, **Adult:** 10-20mg every 4 -6 hours. Maximum, 120mg in twentyfour hours. **Child:** (6-12 years of age), Oral, 5 to 10mg every four to six hours, not to exceed 60mg per day. *Linctus*, **Adult:** 5-10ml 3 - 4 times daily. **Child** (but not generally recommended) 5-12 years, 2.5 - 5ml 3-4 times daily.

Storage: at room temperature in a well-closed container.

Dexchlorpheniramine

Syrup, 2mg/5ml

Tablet, 2mg, 4mg, 6mg

Indication: perennial and seasonal allergic rhinitis and other allergic symptoms including urticaria

Cautions: history of bronchial asthma; glaucoma or increased intraocular pressure; a stomach ulcer; an enlarged prostate, bladder problems, or difficulty urinating; hyperthyroidism; cardiovascular disease; hypertension;

Drug interaction: monoamine oxidase inhibitor such as isocarboxazid, phenelzine, or tranylcypromine, alcohol and other sedatives.

Contraindications: pregnancy; breast feeding; Lower Respiratory Disease; Hypersensitivity to Dexchlorpheniramin or other antihistamines; Monoamine oxidase inhibitor therapy

Side effect: allergic reactions; dryness of mouth, nose, and throat; anorexia; nausea; vomiting; diarrhea; constipation; dizziness or drowsiness, tachycardia; hypotension, thickening of bronchial secretions, tightness of chest and wheezing, Hemolytic anemia, thrombocytopenia, agranulocytosis; change in vision

Dose and administration: Oral: **Adult** 2mg 3-4 times daily; **Child** (6-12 years) 1mg 3-4 times/day, **Child** (2-5 years) 0.5mg 3-4 times/day

Storage: Store at room temperature between 15 and 30 degrees. Protect from light and moisture

Dexchlorpheniramine+Guaifenesin+Pseudoephedrine

Syrup, 2mg +100mg + 20mg/5ml

Indication: Treatment of cough, nasal congestion, and associated aches, and general discomfort due to colds, flu, or allergy

Cautions and side effects: Dexchlorpheniramine, Guaifenesin and Pseudoephedrine (see Sections 4.1, 4.2, 17.1), respectively.

Dextromethorphan Hydrobromide

Tablet, 15mg

Syrups, 5mg/5ml, 7.5mg/5ml, 15mg/5ml

Drops, 15mg/ml

Indications: symptomatic relief of non-productive cough due to minor throat and bronchial irritation occurring with colds or inhaled irritants.

Cautions: as for pholcodine

Drug interactions: CNS depressants, monoamine oxidase inhibitors including furazolidine and procarbazine, amiodarone, fluoxetine, haloperidol, quinidine, thioridazine.

Contraindications: respiratory failure, acute asthma, in children up to two years of age.

Side effects: mild dizziness, mild drowsiness, nausea or vomiting, stomach pain.

Dose and Administration: *Oral:* **Adult:** 10 to 20 mg every 4 hours, or 30 mg every 6 to 8 hours, to a usual maximum of 120 mg in 24 hours. **Child** (6-12 years), 5 to 10 mg every 4 hours or 15 mg every 6 to 8 hours to a maximum of 60mg in 24 hours, and children (2 to 6 years) 2.5 to 5 mg every 4 hours, or 7.5 every 6 to 8 hours, to a maximum of 30 mg in 24 hours.

Storage: at room temperature in a well-closed container.

Guaifenesin

Tablet, 100mg, 200mg

Capsules, 200mg

Syrup, 100mg/5ml

Indications: symptomatic relief of productive cough due to colds and minor upper respiratory infections.

Cautions: persistent or chronic cough such as that occurring with smoking, asthma, chronic bronchitis, or emphysema, or for cough accompanied by excessive phlegm.

Drug interaction: heparin

Contraindications: sensitive to Guaifenesin.

Side effects: diarrhoea, drowsiness, nausea or vomiting, stomach pain.

Dose and Administration: *Oral:* **Adult:** 200-400mg every 4 hours. **Child** (6 to 12 years), 100 to 200mg every 4 hours, and children (2 to 6 years), 50 to 100mg every 4 hours.

Storage: at room temperature in a tight container

Pholcodine

Syrup, 0.06%, 0.12%

Indications: dry cough

Cautions: asthma; chronic, persistent, or productive cough, renal impairment

Contraindications: chronic bronchitis, chronic obstructive pulmonary disease, bronchiectasis, patients at risk of respiratory failure, hepatic impairment, severe renal impairment

Drug interactions: phenothiazines, benzodiazepines and TCAs.

Side effects: nausea, vomiting, constipation, sputum retention, drowsiness, dizziness, excitation, confusion, rash

Dose and Administration: *Oral:Adult:* 5-10mg 3-4 times daily.**Child:** over 5 years, 2.5-5mg 3-4 times daily; 1-5 years, 2-2.5 mg 3 times daily.

4.2. Bronchodilators /Antiasthmatics

Management of Asthma

Asthma is a chronic inflammatory disease in which the patient suffers episodes of reversible airways obstruction due to bronchial hyper responsiveness; in a few patients, inflammation may lead to irreversible obstruction. Common precipitating factors include exposures to cold weather, upper respiratory tract infections, bad smells, exercise, ingestion of drugs like aspirin and beta blockers etc.,.The course of acute asthmatic attack is often unpredictable and is potentially life threatening. Concerning the chronic form of the disease, one should always try to classify the disease based on severity before initiating treatment. Accordingly, it is classified as intermittent or persistent asthma. The later is again divided into mild, moderate and severe persistent asthma.Management of asthma involves prophylactic measures to reduce inflammation and airways resistance and to maintain airflow, as well as specific regimens for the treatment of acute attacks.

The standard drugs used for the management of asthma are the beta2 agonists and corticosteroids. Therapy is preferably given by inhalation to deliver the drug to the desired site of action. This permits smaller dosages than would be required with oral administration with a consequent reduction in side effects.

Pregnancy: Poorly controlled asthma in pregnant women can have an adverse effect on the fetus, resulting in perinatal mortality, increased prematurity and low birth - weight. For this reason using medications to obtain optimal control of asthma is justified. Administration of drugs by inhalation during pregnancy has the advantage that plasma drug concentrations are not likely to be high enough to have an effect on the fetus. Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia.

Management of Chronic Obstructive Pulmonary Disease (COPD)

COPD is a common disorder frequently associated with cigarette smoking, infections, environmental pollution, and occupational dust exposure may also have an aetiological role. The most important therapeutic intervention is encouraging those patients who smoke to stop; psychological support and adjunctive drug therapy may be required. Drug treatment is primarily symptomatic and palliative using bronchodilators, corticosteroids, and oxygen therapy. First-line drug therapy for the treatment of COPD consists of bronchodilators to alleviate bronchospasm and any reversible component of the airways obstruction.

For mild disease, bronchodilators such as beta2 agonists, ipratropium bromide or combination of both may be useful. Regular oral theophylline may be added, bearing in mind the risk of adverse events. For moderate to severe cases a trial of oral

corticosteroid therapy should be considered. The use of mucolytics or expectorants is controversial.

Selective Beta2 agonist, inhaled and systemic

Beta2 agonists relax the bronchial smooth muscle to produce bronchodilatation by selectively stimulating beta2-adrenergic receptors. Short-acting beta2 agonists such as salbutamol or terbutaline are the initial drugs of choice for acute bronchospasm; if inhaled, they can have an almost immediate bronchodilating effect. Simultaneous administration of more than one drug within this group is hazardous.

Short-acting beta2 agonists should not be used on a regular basis, but only “as required”. Patients requiring beta2 agonists more than twice a week should be commenced on inhaled steroids.

Salmeterol and formoterol are selective beta2 agonists with a prolonged duration of action. These agents are indicated for maintenance therapy in chronic persistent asthma, and COPD. Salmeterol has a delayed onset of action and is not suitable for treatment of an acute exacerbation. Various formulations and routes of administration are available.

Inhalation: Aerosol inhalers (metered dose) are highly effective and preferred to oral medication for mild to moderate attacks of bronchospasm. Bronchodilator response is rapid and is sustained for 4 hours or longer, depending on the severity of the asthma and the dose administered. Compared with oral preparations, the dose delivered is small and side effects are few.

Note:

- *Use of the inhaler should be demonstrated carefully to the patient and technique checked at subsequent visits. The importance of breathing out first, then inhaling slowly and holding the breath for 10 seconds after inhalation should be stressed. Some patients, especially the elderly, arthritic, and young children, may be unable to use metered-dose inhalers without spacers.*

4. Respiratory Medicines

- *Use of one of the various spacer devices, preferably large volume ($\geq 500\text{ml}$), will often improve delivery of aerosol, eliminating the need for precise co-ordination of activation and inhalation.*
- *The maximum dose per 24-hour period and the number of inhalations permissible at one time should be explained carefully to the patient and that if relief is not obtained with the prescribed dose, medical advice should be sought.*
- *When a patient requires a beta2 agonist more than twice a week, add inhaled corticosteroids. Inhaled corticosteroids increase response to beta2 agonist.*
- *Dry powder inhalers are useful when patients cannot use pressured aerosols correctly, as they are activated by the patient's inspiration.*

Oral: *Oral beta2 agonists should rarely be prescribed. Onset of action is slower than inhaled therapy and incidence of side-effects significantly higher, but the action is slightly more prolonged than with aerosol inhalers. The slow-release preparations may be of value in patients with nocturnal asthma.*

Intravenous: *Intravenous beta2 agonists, used in severe asthma, possess bronchodilator potency comparable to that of aminophylline and are probably safer to use if blood level measurement of the latter is not possible.*

Glucocorticoids, inhaled

Inhaled corticosteroids reduce airways inflammation and are very effective in the prophylactic management of chronic persistent asthma. They must be used regularly for maximum benefit. Beclometasone, budesonide and fluticasone are equally effective if used in equivalent doses. There appears to be a relatively flat dose response within the high-dose range. Suppression of the adrenohypophyseal axis has been reported with high doses, especially with fluticasone. Chlorofluorocarbon (CFC) propellants in aerosol metered-dose inhalers are being replaced by hydrofluoroalkane (HFA) propellants, and doses may differ.

Anticholinergics, inhaled

An antimuscarinic may be the bronchodilator of choice in the management of chronic obstructive pulmonary disease. In

patients with asthma they are usually reserved for use in life-threatening acute asthma exacerbations.

Ipratropium bromide an atropine derivative anticholinergic agent, is a potent inhibitor of vagus mediated bronchoconstriction and has significant bronchodilator capacity, exerted by blocking vagal influences on bronchomotor tone.

Xanthines

These agents have a narrow therapeutic index with significant toxicity. Theophylline, a methylxanthine derivative, is used primarily for the relief of bronchospasm. Recent evidence indicates that theophyllines have some anti-inflammatory effect. Once daily administration in lower doses, previously considered to be sub-therapeutic, may be of some benefit.

Other effects include CNS stimulation, increased gastric secretion, vasodilation and mild diuresis; increased rate and depth of respiration, an increase in diaphragmatic contractility, and positive inotropic and chronotropic effects on the heart. Aminophylline is a combination of theophylline with ethylenediamine which dissociates in the stomach to be absorbed as theophylline. (Aminophylline 1.27g is equivalent to about 1g theophylline). Aminophylline is more water soluble than theophylline and may be given parenterally. IV infusion has not been shown to be beneficial in acute asthma or exacerbations of COPD when added to corticosteroids and nebulized bronchodilators.

Compound bronchodilator preparations

Most compound bronchodilator preparations have no place in the management of patients with airways obstruction. In general, patients are best treated with single-ingredient preparation, such as a selective beta₂ adrenoceptor stimulant or ipratropium bromide, so that the dose of each drug can be adjusted. This flexibility is lost with combinations, although those in which

both components are effective may occasionally have a role when compliance is a problem.

Adrenaline (Epinephrine)

Injection, 0.1 % in 1 ml ampoule

Indications: for acute bronchial asthma, and acute anaphylactic reactions; see section 2.8. under Adrenaline.

Cautions, Drug interactions, Contraindications, Side effects; see section 2.8.under Adrenaline.

Dose and Administration: *Acute bronchial asthma: S.C or I.M:Adult:*S.C. initially, 0.2 – 0.5mg (0.2—0.5ml), repeated every 20 minutes as necessary up to 3 doses or IV (slow & cautions), 0.1 to 0.25mg. **Child:**S.C. 0.01mg (0.01ml)/ kg of body weight, up to a maximum of 0.3mg (0.3ml)/dose. The dose may be repeated every 15 minutes for 3 or 4 doses as necessary.

Note: only a 1: 10, 000 epinephrine solution should be used for intravenous administration.

Storage: at room temperature, in a light – resistant container.

Aminophylline (Theophylline and Ethylenediamine)

Tablet, 100mg, 200mg

Tablet (m/r), 100mg, 225mg, 350mg

Injection, 250mg/10ml, 10ml, in 10 and 20ml

Indications: reversible airways obstruction, acute severe asthma.

Cautions: as for theophylline, and also, IV injection must be administered *very slow* intravenous injection (over at least 20 minutes) to prevent dangerous CNS and cardiovascular side effects.

Drug interactions, Contraindications; see under theophylline

Side effects: as for theophylline; also allergy to Ethylenediamine can cause urticaria, erythema, and exfoliative dermatitis.

Dose and Administration: *Tablet, Oral: Adult*, 100-300mg, 3-4 times daily, after food. *Tablet (m/r, 225mg)*, 1 tablet twice daily initially, increased after 1 week to 2 tablets twice daily. *Tablet (m/r, 350mg)* is for smokers and other patients with decreased theophylline half-life. *Tablet (m/r, 100mg)*, children over 3 years, 6mg/kg twice daily initially, increased after 1 week to 12mg/kg twice daily; some children with chronic asthma may require 13-20mg/kg every 12 hours. *Slow I.V. injection or preferably by slow I.V. infusion.* Avoid rapid intravenous injection. It should be given cautiously, particularly in patients who have previously been taking theophylline and/or ephedrine. **Adult:** *Slow, I.V.*, 250—500mg (5mg/kg) over 20 minutes, or diluted with 10ml of water for injection. Maintenance—If required, 0.5mg/kg of body weight per hour by *slow I.V. infusion* for a period of 24 hours only. **Child:** *Slow I.V.* 5mg/kg of body weight; Maintenance-If required, 6 months-9 years-1mg/kg of body weight per hour by slow intravenous infusion. 10 to 16 years—0.8mg/kg of body weight per hour by slow intravenous infusion.

Storage: at room temperature protect from light.

Beclomethasone Dipropionate

Oral inhalation (aerosol), 50 mcg/dose, 100 mcg/dose

Indications: chronic persistent asthma.

Cautions: active or quiescent pulmonary tuberculosis; pregnancy, particular care is required when patients are transferred from systemic corticosteroid to inhaled products; diabetes, hypertension, osteoporosis, peptic ulcer, glaucoma, cataracts, hepatic impairment, withdrawal should be slowly.

Drug interactions: salmeterol

Contraindications: bronchiectasis (moderate to severe), sensitivity to the drug or any ingredient (e.g. fluorocarbons, oleic acid) in the formulation; not to be used in status

asthmaticus or for the relief of acute bronchospasm; children less than 6 years of age.

Side effects: oral candidiasis (creamy white, curd like patches inside mouth); cough without symptoms of infection; rarely skin rash and difficulty in swallowing; hoarseness.

Dose and Administration:Adult: 200 micrograms twice daily or 100 micrograms three or four times daily. Severe cases 600 – 800 micrograms daily;**Child:** 50 – 100 micrograms two to four times daily.*Note: Gargling and rinsing the mouth with water after each dose is recommended to help prevent hoarseness, throat irritation, and oral candidiasis. The use of a spacing device may also greatly decrease the incidence of these local adverse effects.*

Storage: at room temperature

Budesonide

Suspension: 0.25, 0.5mg/ml

Indications: prophylaxis of asthma

Cautions: breast feeding, systemic infection (e.g. tuberculosis), Paradoxical bronchospasm

Drug Interactions: Itraconazole, Ketoconazole, Nelfinavir, Ritonavir, Telaprevir

Contraindication: allergic to budesonide or components of the formulation

Side effects: adrenal suppression, adrenal crisis and coma in children; excessive doses should be avoided, High doses have been associated with lower respiratory tract infections, including pneumonia, in older patients with chronic obstructive pulmonary disease, Bone mineral density may be reduced following long-term inhalation of higher doses, predisposing patients to osteoporosis Anxiety, depression, sleep disturbances, and behavioral changes including hyperactivity, irritability, and aggression (particularly in children), hyperglycemia, cataracts, skin thinning and bruising .

Dose and administration:Budesonide Inhalation Suspension is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age. Dosing recommendations based on previous therapy are as follows:Bronchodilators alone: 0.25 mg twice daily; Inhaled corticosteroids: 0.25 mg twice daily up to 0.5 mg twice daily; Oral corticosteroids: 0.5 mg twice daily.In all patients, it is desirable to downward-titrate to the lowest effective dose once asthma stability is achieved.

Budesonide + Formoterol Fumarate

Aerosol, 80mcg + 4.5mcg, 160mcg + 4.5mcg

Cautions, Drug interactions, Contraindications and Side effects; see under Salmeterol and Fluticasone.

Dose and Administration:Adult: 1-2 inhalations twice daily; may be temporarily increased to a maximum of 4 inhalations twice daily. When control has been achieved, titrate to lowest dose at which effective control is maintained. **Child:** over 12 years, as for Adults.

Ephedrine sulphate

Injection, 50mg/ml

Indications: treatment of bronchial asthma, nasal congestion, acute bronchospasm, idiopathic orthostatic hypotension, anesthesia-induced hypotension

Cautions:blood volum depletion should be corrected before ephedrine therapy is instituted; use caution in patients with unstable vasomotor symptoms diabetes, hyperthyroidism, prostatic hyperplasia, a history of seizures or those on other symptomimetic agents; also use caution in the elderly and those patients with cardiovascular disorders, such as coronary artery disease, arrhythmias, and hypertension. Ephdrine may cause hypertantion resulting in intracania.Alpha-adrenergic blocking

agents may reduce the vasopressor response to ephedrine by causing vasodilation. Beta-adrenergic blocking drugs may block the cardiac and bronchodilating effects of ephedrine.

Drug interactions: α -blockers: Atropine sulfate, β -blockers, Cardiac glycosides, Ergotamine, ergometrine, methylergometrine, oxytocin, Guanethidine, Hydrocarbon inhalation anaesthetics, such as cyclopropane, halothane, Methyldopa, MAO Inhibitors, Reserpine, Sympathomimetic Agents, Tricyclic antidepressants, Clonidine, Urinary Alkalinizers, such as acetazolamide, dichlorphenamide, sodium bicarbonate and sodium citrate, Theophylline:

Contraindications: closed angle glaucoma, patients with pheochromocytoma, patients with asymmetric septal hypertrophy (idiopathic hypertrophic subaortic stenosis), patients undergoing therapy MAO inhibitors, or within 14 days of ceasing such therapy, since MAO inhibitors may prolong and intensify the cardiac and pressor effects of ephedrine, patients undergoing general anaesthesia with cyclopropane or halothane or other halogenated hydrocarbons, patients with tachyarrhythmias or ventricular fibrillation, patients with hypersensitivity to ephedrine and in patients with psychoneurosis.

Dose and Administration: Adults: I.M, SC: 25-50mg, parenteral adult dose should not exceed 150 mg in 24 hours. I.V: 5-25 mg/dose slow I.V. push repeated after 5-10 minutes as needed, then every 3-4 hour not to exceed 150 mg/24 hours. **Child:** I.M: slow I.V push: 0.2-0.3mg/kg/dose every 4-6 hours.

Storage: protect from light

Ephedrine + Theophylline

Tablet, 11mg + 120mg

Elixir, 6mg + 30mg in each 5ml

Syrup, 2.24% + 0.30%

Indications: symptomatic relief of chronic bronchial asthma; asthmatic bronchitis; and other bronchospastic disorders; prophylactically use to stop or decrease asthmatic attacks.

Drug interactions, Contraindications, Side effects: See Ephedrine and Theophylline

Dose and Administration: **Child (> 25kg):** ½ to 1 regular release tablet 3 to 4 times/day or at first sign of an asthmatic attack. **Adult:** 1 to 2 regular release tablets 3-4 times/day or at first sign of an asthmatic attack.

Storage: at room temperature

Fluticasone furoate

Nasal spray, 27.5mcg

Indication: treatment of symptoms of seasonal and perennial allergic rhinitis in adults and children ≥ 2 years.

Cautions: epistaxis, nasal ulceration, *Candida albicans* infection, nasal septal perforation, impaired wound healing. Avoid use in patients with recent nasal ulcers, nasal surgery, or nasal trauma. Development of glaucoma or posterior subcapsular cataracts. Monitor patients closely with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts, immunosuppression.

Drug interactions: ritonavir, potent CYP 3A4 inhibitors, such as ketoconazole.

Contraindications: Hypersensitivity to the medicines and any component of the formulation.

Side-effect: headache, epistaxis, pharyngolaryngeal pain, nasal ulceration, back pain, pyrexia, and cough.

Dose and Administration: For intranasal use only.

Usual starting dosages: **Adults** and adolescents ≥ 12 years: is 110 mcg once daily administered as 2 sprays (27.5 14 mcg/spray) in each nostril. **Children** 2-11 years: is 55 mcg once daily administered as 1 spray (27.5 mcg/spray) in each nostril.

Salmeterol + Fluticasone

Powder for oral inhalation, 50mcg + 100mcg, 50mcg + 250mcg, 50mcg + 500mcg

Indications: maintenance treatment of asthma in adults and children ≥ 4 years; not for use for relief of acute bronchospasm; maintenance treatment of COPD associated with chronic bronchitis.

Cautions: see under beclomethasone and salbutamole.

Drug interactions: diuretics (loop, thiazide); CYP3A4 inhibitors (e.g. azole antifungals, ciprofloxacin); MAO inhibitors, TCAs (wait at least 2 weeks after discontinuing these agents); beta-adrenergic blockers (e.g. propranolol), beta2 agonists.

Contraindications: hypersensitivity to salmeterol or fluticasone; status asthmaticus; acute episodes of asthma.

Side effects: headache, hyperglycaemia, hypokalaemia, pharyngitis, upper respiratory tract infection, diarrhea, GI pain/discomfort, oral candidiasis, nausea/vomiting, musculoskeletal pain, bronchitis, cough, dysphonia, sinusitis, upper respiratory tract inflammation, viral respiratory tract infection.

Dose and Administration: *Oral inhalation: COPD: Adult:* 50/250 mcg twice daily, 12 hours apart. *Asthma: Adult and Child ≥ 12 :* One inhalation twice daily, morning and evening, 12 hours apart. *Child 4-11 years:* 50/250 mcg twice daily, 12 hours apart.

Note: Do not use to transfer patients from systemic corticosteroid therapy. This drug is available in 3 strengths; initial dose prescribed should be based upon previous asthma therapy. Dose should be increased after 2 weeks if adequate response is not achieved. Patients should be titrated to lowest effective dose once stable. (Because each strength contains salmeterol 50mcg/inhalation, dose adjustments should be made by changing inhaler strength. No more than 1 inhalation of any strength should be taken more than twice a day). Maximum dose: 50/500 mcg, one inhalation twice daily.

4. Respiratory Medicines

Patients not currently on inhaled corticosteroids: 50/100 mcg. Patients currently using inhaled beclomethasone dipropionate: \leq 420 mcg/day: 50/100 mcg. 462-840 mcg/day: 50/250 mcg

Storage: store at room temperature.

Formoterol fumarate

Inhalational powder, 12mcg/dose

Indications: maintenance treatment of asthma and prevention of bronchospasm in patients \geq 5years of age with reversible obstructive airway disease, including patients with symptoms of nocturnal asthma, who require regular treatment with inhaled, short-acting beta2 agonists; maintenance treatment of bronchoconstriction in patients with COPD; prevention of exercise-induced bronchospasm in patients \geq 5 years of age.

Cautions: do not use as a component of chronic therapy without an anti-inflammatory agent; do not exceed recommended dose; cardiovascular disease, convulsive disorders, diabetes, glaucoma, hyperthyroidism or hyperkalemia. Safety and efficacy have not been established in children $<$ 5 years of age.

Drug interactions: adrenergic agonists, antidepressants (tricyclic), beta-blockers, corticosteroids, diuretics, MAO inhibitors, theophylline derivatives.

Contraindications: hypersensitivity reactions.

Side effects: children are more likely to have infection, inflammation, abdominal pain, nausea and dyspepsia. Serum glucose increased, serum potassium decreased, chest pain, tremor, dizziness, insomnia, dysphonia, rash, bronchitis, infection, dyspnea, tonsillitis.

Dose and Administration:*Relief of bronchoconstriction:* **Child \geq 12 years and Adult:** 6mcg or 12mcg as a single dose (maximum dose: 72 mcg in any 24-hour period). The prolonged use of high dosage (48 mcg/day for \geq 3 consecutive days) may

be a sign of suboptimal control, and should prompt the re-evaluation of therapy.

Storage: prior to dispensing, store in refrigerator at 2 to 8°C; after dispensing store at room temperature.

Ipratropium Bromide

Aerosol Solution, 20mcg/metered

Inhalation; 400mcg/metered inhalation

Indications: relief of bronchospasm in reversible air ways obstruction, especially COPD and in elderly patients, it has also been used in cystic fibrosis.

Cautions: prostatic hypertrophy; pregnancy; acute angle closure glaucoma.

Drug interactions: anticholinergics.

Side effects: dry mouth occasionally reported, rarely urinary retention, constipation, tachycardia, palpitations and arrhythmias, hypersensitivity reactions, including urticaria, angioedema, anaphylaxis.

Dose and Administration:*Chronic asthma or chronic obstructive pulmonary disease:***Aerosol inhalation:** **Adult:** 20-40 micrograms, in early treatment up to 80 micrograms at a time, 3-4 times daily; **Child:** up to 6 years, 20 micrograms 3 times daily; 6 to 12 years, 20-40 micrograms 3 times daily.**Inhalers:****Adult:** 40 micrograms 3 times daily; if necessary, a second dose may be inhaled 5 minutes after the first.

Storage: at room temperature protect from freezing. Protect from light.

Isoprenaline Sulphate

Tablet (Sublingual), 5mg, 10mg

Injection, 2.5mg/2ml

Indications: symptomatic treatment of bronchial asthma and reversible bronchospasm which may occur association with

chronic bronchitis, pulmonary emphysema, bronchiectasis and other chronic obstructive pulmonary diseases.

Cautions, Cotraindications, Side effects - see under Adrenaline, sec. 2.8

Drug interactions: see under Adrenaline and also beta1 agonists such as Adrenaline: -dryness or irritation of mouth or throat, nervousness, or restlessness, pinkish to red coloration of saliva, insomnia, anxiety, tension, fear, or excitement, chest discomfort or pain, dizziness or light headedness, continuing fast heartbeat, continuing or severe headache.

Dose and Administration: *Sublingual*, **Adult:** 10-20mg, not to exceed 60mg; **Child:** 5-10mg, not to exceed 30mg.

Storage: at room temperature in a well closed, light resistant container.

Montelukast

Oral granules (sparkles): 4mg

Tablets, Chewable: 4mg, 5mg

Tablets, film coated: 10mg

Indications: prophylaxis and chronic treatment of asthma; relief of symptoms of seasonal allergic rhinitis and perennial allergic rhinitis.

Caution: pregnancy and lactation

Drug interactions: CYP2C8/9 inducers may decrease effects of montelukast (e.g. carbamazepine, Phenobarbital, phenytoin, rifampin). CYP3A4 inducers may decrease effects of montelukast (e.g carbamazepine, nevirapine, Phenobarbital, phenytoin)

Contraindications: hypersensitivity to Montelukast or any component of the formulation.

Side effects: cough, nasal congestion, flu like symptoms, dizziness, fever, fatigue, rash, abdominal pain, dental pain, dyspepsia

Dose and Administration:**Children 6 to 23 months:** *perennial allergic rhinitis:* 4 mg (*oral granules*) once daily.**12 to 23 months:** *Asthma:* 4 mg (*oral granules*) once daily, taken in the evening. **2 to 5 years:** *Asthma, seasonal or perennial allergic rhinitis:* 4mg (*chewable tablet or oral granules*) once daily, taken in the evening.**6 to 14 years:** *Asthma, seasonal or perennial allergic rhinitis:* chew one 5mg chewable tablet per day, taken in the evening. **Adults and children ≥ 15 years:** *Asthma, seasonal or perennial allergic rhinitis:* tablet: 10 mg/day, taken in the evening.
Storage: store at 20⁰c to 25⁰c.

Salbutamol (Albuterol)

Tablet, 2mg, 4mg, 4mg (s/r)

Syrup, 2mg/5ml

Oral inhalation (aerosol), 0.1mg per dose

Nebulizer Solution, 2.5mg/2.5ml

Indications: asthma and other conditions associated with reversible airways obstruction.

Cautions: hyperthyroidism, myocardial insufficiency, arrhythmias, susceptibility to QT-interval prolongation, hypertension, elderly. *Note: it is important that asthma be well controlled throughout pregnancy. Inhaled administration is particularly advantageous as therapeutic action can be achieved at lower plasma levels with very little risk to the fetus.*

Drug interactions: corticosteroids, cardiacglycosides, diuretics, xanthines and antidepressants.

Contraidications: eclampsia and severe pre-eclampsia, intra-uterine infection, intra-uterine fetal death, antepartum haemorrhage (which requires immediate delivery), placenta praevia, and cord compression; threatened miscarriage.

Side effects: fine tremor, nervousness, headache, dizziness, cardiac stimulation with tachycardia & palpitations (infrequent

with aerosol inhalation) are usually dose-related. High doses may cause nausea & vomiting, and prolonged use has led to reversible hypertrichosis. Hypersensitivity reactions are rare.

Dose and Administration:*Tablets: Oral: Adult:* 2 to 6mg (base) - three or four times a day initially, the dosage being increased and tolerated up to a maximum of 8mg four times a day. **Child** (6-12 years): 2mg (base) - three or four times a day initially, the dosage being increased and tolerated up to a maximum of 24mg per day in divided doses.*Syrup: Oral: Adult:* 2mg to 6mg (base)- three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 8mg four times a day.**Child** (2 to 6years): 0.1mg (base) per kg of body weight three times a day initially, the dosage being increased as needed and tolerated up to 0.2mg per kg of body weight, not to exceed 4mg three times a day.**Child** (6 to 14 years): 2mg (base)- three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 24mg per day in divided doses.*Inhalation (aerosol): Oral inhalation: Adult:* 0.18 to 0.2mg (1 to 2 inhalations/puffs) every four to six hours as required

Note: Shake well before use.

Nebulizer solution: 2ml of 0.5% solution (10mg) given over 3 minutes up to 4 times daily or continuous inhalation of 50-100mcg/ml (1 in 100 or 1 in 50 dilution)

Note: nebulizer: may be used in sever and unresponsive asthma.

Storage: Aerosol - store at room temperature away from heat and direct sunlight. Syrup, Tablet - store between 2 and 30⁰c, in a well-closed container, protect from light and from freezing.

Salbutamol + Bromhexine + Guaifenesine + Menthol

*Syrup, 2mg + 4mg + 100mg + 1mg,
2mg+4mg+100mg+1mg/10ml, 1mg+2mg+50mg+0.5mg/5ml*

Indications: for symptomatic management of all productive – including asthmatic – coughs.

Cautions: cardiovascular disorders like ischemic heart disease, hypertension and cardiac arrhythmias; hyperthyroidism, diabetes, those who are unusually responsive to sympathomimetics or who have convulsive disorders. Pregnancy and lactation. Peptic ulceration, severe hepatic and renal dysfunction. Menthol containing products should be avoided in those with hiatal hernia, gallstones and in near-term pregnant females.

Drug interactions: sympathomimetics, beta blockers, MAOIs, nonpotassium-sparing diuretics, digoxin tricyclic antidepressants to cause untoward reactions.

Contraindications: hypersensitivity reaction.

Side effects: nausea, vomiting, skin rashes, headache, and dizziness may rarely occur.

Storage: store below 25°C in a dry place, protected from light.

Sodium Cromoglycate

Capsules with inhaler, 20 mg

Indications: Indicated as a prophylaxis and in the management of bronchial asthma

It is also indicated to prevent bronchospasm induced by exercise or by exposure to allergens, cold dry air, environmental pollutants, or other known precipitating factors when exposure is either episodic or continuous.

Cautions: nursing women, pediatric and geriatric patients. Caution should also be used when decreasing the dosage of cromolyn or discontinuing the drug in patients with asthma.

Contraindications: sensitivity to cromolyn, coronary artery disease or history of cardiac arrhythmias.

Side effects: wheezing, nasal congestion, cough, hoarseness, irritation of the throat and trachea, bronchospasm, nausea, headache, dizziness, unpleasant taste, joint pain and swelling.

Dose and Administration: Adult and Child 2 years and older: *Asthma, bronchial (prophylaxis): Oral inhalation:* 20 mg (1 capsule) four times a day at regular intervals, the dosage being adjusted as needed and tolerated. *Bronchospasm (prophylaxis): Oral inhalation:* 20 mg (1 capsule) as a single dose just prior to exposure to the precipitating factor; or, if used chronically, 20 mg (1 capsule) four times a day at regular intervals, the dosage being adjusted as needed and tolerated. **Child up to 2 years of age:** *The capsule for inhalation should not be used.*

Storage: at room temperature in tight, light-resistant containers.

Theophylline

Tablet (anhydrous theophylline), 100mg, 200mg, 200mg (s/r)

Elixir, 33mg in each 15 ml (anhydrous theophylline)

Indications: treatment of acute, severe and chronic persistent asthma and other conditions associated with reversible bronchospasm; COPD.

Cautions: peptic ulcer, hyperthyroidism, hypertension, cardiac arrhythmias or other cardiovascular disease, or epilepsy; heart failure, hepatic dysfunction or chronic alcoholism, acute febrile illness, and to neonates and the elderly (since in all of these circumstances theophylline clearance may be decreased)

Drug interactions: other xanthine medications, allopurinol, antiarrhythmics, cimetidine, disulfiram, fluvoxamine, interferon-alfa, macrolide antibacterials and quinolones, oral contraceptives, phenytoin, alcohol, ritonavir, rifampicin, sulfinpyrazone, smoking, sympathomimetic agents, corticosteroids, diuretics, halothane or ketamine, lithium, beta blockers.

Contraindications: hypersensitivity to theophylline or xanthine derivatives; coronary artery disease (when, in the physician's judgment, myocardial stimulation might prove harmful).

Side effects: tachycardia, palpitations, nausea, gastro-intestinal disturbances, headache, insomnia, arrhythmias.

Dose and Administration: Adult: as anhydrous theophylline, *Oral:* general range 6-18mg/kg/day.

Chronic bronchospasm: sustained-release formulations; initially the usual daily dose is 12mg/kg or 400mg (whichever is less) divided into 2-3 doses 8-12 hourly; dose may be increased by 2-3mg/kg/day at 3-day intervals. Addition as a once-daily slow-release formulation at night may ameliorate night dipping. The general therapeutic range is 10-20mcg/ml (55-110mcmol/l), although benefit may be seen at sub-therapeutic doses.

Child: *Oral:* 1-9 years, 20mg/kg/day; 9-12 years, 16mg/kg/day. The total daily dose is divided into 2-3 doses for 8-12 hourly administration of sustained release preparations, or into 4 doses for 6 hourly administrations of short-acting preparations. Because of a general higher metabolic rate of theophylline in children, the sustained-release agents often have to be given 8 hourly. Both the final maintenance dose and the dose interval should be guided by serum levels obtained after steady state has been achieved. *Note: patients should not be transferred from one modified release theophylline or aminophylline preparation to another without clinical assessment and the measurement of serum-theophylline concentrations because of bioavailability.*

Storage: store in a well-closed container at room temperature.

Theophylline and Guaifenesin

Tablet 150mg + 90mg

Capsule, 150mg + 90mg; 300mg + 180mg

Elixir, 150mg + 90mg/15ml

4. Respiratory Medicines

Indications: for relief and/or prevention of symptoms of bronchial asthma and reversible bronchospasm associated with chronic bronchitis and pulmonary emphysema.

Cautions, Drug interactions and Contraindications; see notes under theophylline and guaifenesin

Side effects: gastroesophageal reflux: see notes under theophylline & guaifenesin.

Dose and Administration: Adult: Oral: 16mg/kg/day or 400mg per day, in divided doses, every 6-8 hours.

Note: complete prescribing information for this medication should be consulted for additional detail.

Storage: Guaifenesin preparations should be stored in tight containers at room temperature.

5. CENTRAL NERVOUS SYSTEM MEDICINES

5.1. Analgesics / Antipyretics

Pain is not only associated with physical suffering or hurting but has an emotional or mental component, hence it is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Pain can be classified as acute or chronic. Acute pain is usually of short duration and the cause often identifiable (disease trauma). Chronic pain persists after healing is expected to be complete, or is caused by a chronic disease. Pain may be modified by psychological factors and attention to these is essential in pain management. Drug treatment aims to modify the peripheral and central mechanisms involved in the development of pain.

Non-opioid analgesics are particularly suitable for pain in musculoskeletal conditions whereas the opioid analgesics are more suitable for moderate to severe visceral pain. Those non-opioid analgesics which also have anti-inflammatory actions include salicylates and NSAIDS (Nonsteroidal anti-inflammatory drugs), they can reduce both pain and inflammation of chronic inflammatory disorders such as rheumatoid arthritis, but they do not alter or modify the disease process itself.

Fever (pyrexia) is defined as an increase in body temperature due to an elevated thermoregulatory set-point temperature. Common causes of fever include infections, inflammatory disorders, neoplastic disease, and some drug treatment. Methods for reducing body temperature in fever include the use

of antipyretic drugs and/or physical means. Antipyretic agents used include paracetamol, salicylates and some other NSAIDs.

Non - opioid analgesics

Paracetamol, aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs) are the first choice for treating mild or moderate pain and are used in moderate or severe pain to potentiate the effects of opioids. They are suitable for use in acute or chronic pain.

Acetylsalicylic acid (Aspirin) is indicated for headache, transient musculoskeletal pain, dysmenorrhoea and pyrexia. In inflammatory conditions, most physicians prefer anti-inflammatory treatment with another NSAID which may be better tolerated and more convenient for patient. Acetylsalicylic acid is also used for its anti-platelet properties.

Adverse effects with analgesic doses are generally mild but include a high incidence of gastro-intestinal irritation with slight blood loss (Minimized by taking the dose after food, or enteric coated preparations), bronchospasm and skin reactions in hypersensitive patients, and increased bleeding time. Anti-inflammatory doses are associated with a much higher incidence of adverse reactions, and they also cause mild chronic salicylism which is characterized by tinnitus and deafness. Its use is not advisable in the latter stage of pregnancy, or in children because of an association with Reye syndrome (encephalopathy and liver damage).

Paracetamol is similar in analgesic and antipyretic efficacy to acetylsalicylic acid. Unlike acetyl salicylic acid and other NSAIDs, paracetamol has little anti-inflammatory activity which limits its usefulness for long-term treatment of pain associated with inflammation; however it is useful in the management of osteoarthritis, a condition with only a small

inflammatory component. Since paracetamol does not have aspirin's hypersensitivity hematological or gastro-intestinal adverse effects, it is particularly useful in patients in whom salicylates or other NSAIDs are contraindicated, such as asthmatics and those with a history of peptic ulcer, or for children under the age of 12 years in whom salicylates are contraindicated because of the risk of Reye syndrome. However large doses of paracetamol can produce severe or sometimes fatal hepatotoxicity; patients with cachexia or those with existing liver disease may be more susceptible.

Non-steroidal anti-inflammatory drugs (NSAIDs): Many of the effects of non-steroidal anti-inflammatory drugs (NSAIDs) appear to be due to their inhibitory action on cyclo-oxygenases which are involved in the biosynthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation, and fever and NSAIDs therefore find their main use as analgesics, anti-inflammatory agents, and antipyretics. Administered as a single dose or in short-term intermittent therapy they provide adequate analgesia to relieve mild to moderate pain. However, it may take several days to two weeks of use before their anti-inflammatory effects become evident.

The combined analgesic and anti-inflammatory effects of NSAIDs make them particularly useful for the symptomatic relief of painful and/or inflammatory conditions including musculoskeletal and joint disorders.

Differences in anti-inflammatory activity between different NSAIDs are small, but there is considerable variation in individual patient tolerance and response. The main differences between NSAIDs are in the incidence and type of side effects. Before treatment is started the prescriber should weigh efficacy against possible side effects.

Side effects:The commonest side-effects occurring during therapy with NSAIDs are generally gastrointestinal disturbances; these are usually mild and reversible but in some patients peptic ulcer and severe gastro-intestinal bleeding have been reported; CNS related side effects include headache, dizziness, nervousness, tinnitus, depression, drowsiness, and insomnia; hypersensitivity reactions may occur occasionally and include fever, asthma, and rashes. Hematological adverse effects of NSAIDs include anaemias, thrombocytopenia, neutropenia, eosinophilia, and agranulocytosis. Fluid retention may occur (rarely precipitating congestive heart failure in elderly patients). Renal failure may be provoked by NSAIDs especially in patients with pre-existing renal impairment. Rarely, papillary necrosis or interstitial fibrosis associated with NSAIDs may lead to renal failure. Hepatic damage alveolitis, pulmonary eosinophilia, pancreatitis, eye changes, Stevens – Johnson syndrome and toxic epidermal necrolysis are other rare side effects. Induction of or exacerbation of colitis has been reported. Aseptic meningitis has been reported rarely with NSAIDs. Patients with connective tissue disorders such as systemic lupus erythematosus may be especially susceptible.

Cautions and contraindications:NSAIDs should be used with caution in the elderly (risk of serious side effects and fatalities), in allergic disorders (they are contraindicated in patients with a history of hypersensitivity to aspirin or any other NSAID. Which include those in whom attacks of asthmas, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID), during breast-feeding and pregnancy and in coagulation. In patients with renal, cardiac, or hepatic impairment caution is required since the use of NSAIDs may result in deterioration of renal function; the dose should be kept as low as possible and renal function should be monitored.

NSAIDs should not be given to patients with active peptic ulceration. While it is preferable to avoid them in patients with current or previous gastro-intestinal ulceration or bleeding, and to withdraw them if gastro-intestinal lesions develop, nevertheless patients with serious rheumatic diseases (e.g. rheumatoid arthritis) are usually dependent on NSAIDs for effective relief of pain and stiffness.

In general caution should be taken in patient with renal impairment; hepatic impairment; cardiac disease; elderly; pregnancy and breastfeeding; coagulation defects; allergic disorders.

Aceclofenac

Tablet, 100mg

Indications: pain and inflammation in rheumatoidarthritis, osteoarthritis and ankylosingspondylitis

Cautions: acute prophyrias

Contraindications: hyper sensitivity to diclofenac; aspirin; other NSAIDs or any components of the formulation pregnancy [3rd trimester]

Dose and Administration: Adult, *oral*100 mg twice daily (reduce to 100mg daily initially in hepatic impairment); child not recommended

Storage: store at room temperature.

Acetylsalicylic acid (Aspirin)

Tablet, 75mg, 81mg, 100mg (soluble); 300mg, 324mg (microfined); 500 mg (enteric coated)

Indications: relief of mild to moderate pain, pyrexia; prophylaxis of platelet aggregation; treatment of rheumatic fever, and acute and chronic inflammatory disorders.

Cautions: caution in patients with gastritis, peptic ulcer, elderly, lactation (high dose)

Drug interactions: antidiabetic agents, including insulin; agents inhibiting platelet aggregation (e.g. penicillins, dipyridamole and valproic acid); thrombolytic agents and heparin; agents causing gastric irritation; methotrexate, probenecid; zidovudine.

Contraindications: history of severe sensitivity reaction to acetylsalicylic acid, bleeding ulcers or other hemorrhagic states, nasal polyps associated with asthma, febrile and dehydrated children (especially with viral infections).

Side effects: gastrointestinal irritation causing abdominal pain, nausea, vomiting and occult or overt mucosal bleeding. Chronic administration of high doses may cause gastric erosion and acute haemorrhage, potentiated by alcohol. Pseudo-allergic reactions such as bronchospasm, rhinitis, urticaria, angioedema and anaphylaxis like shock may occur, most frequently in asthmatics, or in patients with nasal polyps or severe atopy. True hypersensitivity reactions may also occur. Tinnitus and decreased hearing, impaired renal function, decreased prothrombin time and hepatotoxicity are more likely when serum levels are > 200mcg/ml, but may be caused by low doses, especially in the elderly.

Dose and Administration: *Oral: Adult: Analgesic and antipyretic:* 325-650mg every 4-6 hours up to 4g/day. *Anti-inflammatory:* initial: 2.4-3.6g/day in divided doses; usual maintenance: 3.6-5.4 g/day. **Child:** *Analgesic and antipyretic:* 10-15mg/kg/dose every 4-6 hours, up to a total of 4g/day. Orally, preferably with or after food with a full glass of water. Child should not take more than 5 doses/day or for longer than 10 days at a time, and adult should not take for longer than 10 days at time.

Note: Aspirin tablets or dispersible aspirin tablets are adequate for most purposes as they act rapidly. Enteric-coated tablets are beneficial in minimizing gastric irritation effect of aspirin, but have a slow onset of action and are therefore unsuitable for single-dose analgesic use (though their prolonged action may be useful for night pain). Acetylsalicylic acid preparations should not be used if a strong vinegar-like odor is present.

Storage: at room temperature, in a tight container. Protect from heat.

Celecoxib

Capsule, 100mg, 200mg

Indications: relief of the signs and symptoms of osteoarthritis, ankylosing spondylitis, and rheumatoid arthritis; management of acute pain; treatment of primary dysmenorrhea.

Cautions: consider BP before and after treatment and during treatment, patients with thrombotic events (e.g myocardial infarction and stroke), hypertension, cardiac failure, edema, patients with a prior history of peptic ulcer or gastrointestinal bleeding especially in elderly or debilitated patients; patients with impaired renal function, heart failure, liver dysfunction, elderly; considerable dehydration; late pregnancy; breast feeding; Safety and effectiveness in pediatric patients below the age of 18 years have not been evaluated.

Drug interactions: ACE-inhibitors, Fluconazole, Lithium, Warfarin, Glyburide, ketoconazole, methotrexate, phenytoin, and tolbutamide.

Contraindications: known hypersensitivity to Sulfonamides; allergic reactions to sulfonamides and aspirin or other NSAIDs; asthma, urticarial, ischemic heart diseases, cerebrovascular diseases, peripheral arterial diseases, and moderate to severe heart failure.

Side effects: Celecoxib is generally well tolerated. It has lower incidence of stomach side effects irritation, ulcers, and even bleeding than other anti-inflammatory drugs.

Dose and administration:Adult: Oral: Acute pain or primary dysmenorrheal: Intial dose: 400mg, followed by an additional 200mg if needed on day 1; maintainance dose: 200mg twice daily as needed

Ankylosing spondylitis: 200mg/day as a single dose or in divided doses twice daily; if no effect after 6 weeks, may increase to 400mg/day. If no response following 6 weeks of treatment with 400mg/day, consider discontinuation and alternative treatment.Osteoarthritis: 200mg/day as a single dose or in divided dose twice daily.Rheumatoid arthritis: 100-200mg twice daily

Storage: store at room temperature between 15 and 30 degrees

Diclofenac Sodium

Capsule (S/R), 75 mg

Injection, 25mg/ml in 3ml ampoule, 75mg/ml

Tablet (e/c), 25mg, 50mg, 75mg(s/r), 100mg(s/r)

Suppository, 12.5mg, 25mg, 50mg, 100mg

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; acute gout; post operative pain.

Cautions: should be used with caution in the elderly (risk of serious side effects and fatalities) during pregnancy and breast-feeding and in coagulation defects. Long-term use of some NSAIDs is associated with reduced female fertility, which is reversible on stopping treatment. In patients with renal, cardiac, or hepatic impairment caution is required since NSAIDs may impair renal function; the dose should be kept as low as possible and renal function should be monitored.

Drug interactions: Alendronate, lithium, methotrexate, increased risk of methotrexate toxicity), rifampin, timolol, warfarin, coumarin or indandione derivative anticoagulants, heparin, or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasia causing medications and bone marrow depressants, radiation therapy, colchicine, probenecid

Contraindications: It's contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID—which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID. All NSAIDs are contra-indicated in severe heart failure.

Side effects: Gastro-intestinal discomfort, nausea, diarrhoea, and occasionally bleeding and ulceration occur, hypersensitivity reactions, headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances such as tinnitus, photosensitivity, and haematuria, blood disorders, fluid retention, increased blood pressure, hepatic damage, alveolitis, pulmonary eosinophilia, pancreatitis, eye changes, Stevens-Johnson syndrome and toxic epidermal necrolysis are other rare side effects.

Dose and Administration: *Oral:* 75–150 mg daily in 2–3 divided doses. *Rectal:* suppositories, 75–150 mg daily in divided doses. Children 1–12 years, juvenile arthritis, orally or rectal, 1–3 mg/kg (max. 150 mg) daily in divided doses (25 mg e/c tablets, 12.5 mg and 25 mg suppositories only). Children 6–12 years, postoperative pain, rectally, 1–2 mg/kg (max. 150 mg) daily in divided doses (12.5 mg and 25 mg suppositories only) for max. 4 days.

Storage: store at room temperature in a well-closed, light resistant container. Protect from freezing.

Diclofenac sodium + misoprostol

Tablet, 75mg+200

Indications: the diclofenac component is indicated for the treatment of osteoarthritis and rheumatoid arthritis, the misoprostol component is indicated for the prophylaxis of NSAID-induced gastric and duodenal ulceration.

Caution: renal impairment

Contraindications: pregnancy

Dose and Administration: oral:Adult: osteoarthritis: 1 tablet 2-3 times/ day. Rheumatoid arthritis: 1 tablet 3to 4 times/day. If not tolerated by patients, the dose may be changed to one tablet twice daily.

Storage: store at room temperature

Ibuprofen

Capsule, 300 mg

Soft gelatin capsule, 400mg

Tablet, 200 mg, 400 mg (enteric coated, optional)

Syrup, 100mg/5ml

Suspension, 100mg/5ml

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; mild to moderate pain including dysmenorrhoea, postoperative analgesia; migraine; fever and pain in children.

Cautions: see notes above

Drug interactions: coumarin or indandione derivative anticoagulants, heparin, or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasia causing medications and

bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes above

Side effects: see notes above

Dose and Administration:Adult: *Antirheumatic: Oral:* 1.2 to 3.2gms a day in three or four divided doses. After a satisfactory response has been obtained, the dosage should be reduced to the lowest maintenance dose that provides continuing control of symptoms. *Note: Higher doses are generally required in rheumatoid arthritis than in osteoarthritis.* Analgesia/pain/fever/dysmenorrhea: 200-400 mg/dose every 4-6 hours (maximum daily dose: 1.2g, unless directed by physician). OTC labeling (analgesic, antipyretic): 200mg every 4-6 hours as needed (maximum: 1200 mg/24 hours). Child: Antirheumatics: (1-12 years of age): *Oral:* initially 30 to 40mg per kg of body weight a day in three or four divided doses then reduced to the lowest dose needed to control disease activity.

Storage: store at room temperature in a well-closed, light resistant container. Protect from freezing.

Ketoprofen

Topical gel, 25mg

Indications: Symptomatic relief of pain in such conditions as soft tissue injuries, including sport injuries, sprains, strains, musculo-tendonitis, swelling, backache and rheumatic pain musculoskeletal disorders, and after orthopaedic surgery.

Cautions: Elderly, connective-tissue, for topical use only; The appearance of cutaneous eruption following application of the gel requires interruption of treatment. Hands should be washed thoroughly before use and immediately after each application of product (unless they are being treated). It is recommended to protect treated areas by wearing clothing during all the

application of the product and two weeks following its discontinuation to avoid the risk of photosensitization. Not for use with occlusive dressing. Topical application of large amounts may result in systemic effects including hypersensitivity and asthma, cardiac impairment, uncontrolled hypertension, heart failure, ischaemic heart disease, peripheral artery disease, cerebrovascular disease, Crohn's disease or ulcerative colitis, hepatic impairment, renal impairment.

Drug interaction: Methotrexate, Probenecid, ACE Inhibitors, Adrenergic Neurone Blockers, Aliskiren, Alpha-blockers, Angiotensin-II Receptor Antagonists, Antidepressants, SSRI, Aspirin, Baclofen, Beta-blockers, Calcium-channel Blockers, Cardiac Glycosides, Ciclosporin, Clonidine, Clopidogrel, Corticosteroids, Coumarins, Dabigatran Etexilate, Diazoxide, Diuretics, Diuretics, Potassium-sparing and Aldosterone Antagonists, Erlotinib, Heparins, Hydralazine, Iloprost, Ketorolac, Lithium, Methotrexate, Methyldopa, Mifamurtide, Minoxidil, Moxonidine, Nitrates, NSAIDs, Penicillamine, Pentoxifylline, Phenindione, Potassium Canrenoate, Prasugrel, Quinolones, Ritonavir, Sodium Nitroprusside, Sulfonylureas, Tacrolimus, Venlafaxine, Zidovudine.

Contraindications: Known hypersensitivity reactions, such as symptoms of asthma, allergic rhinitis to ketoprofen, fenofibrate, tiaprofenic acid, acetylsalicylic acid, or to other NSAIDs (including when taken by mouth), Children under 15 years.

Side effects: Local skin reactions such as erythematous, pruritis and burning sensations.

Dose and Administration: For cutaneous use: Penetration of the gel by gentle and prolonged massage on the painful or inflamed surface for up to seven days. Two to four daily applications of approximately 2 to 4g gel, representing

approximately 5 to 10cm. The usual maximum dose is 15g per day.

Storage: at room temperature, avoid freezing.

Mefenamic Acid

Tablet, 500mg,

Dispersible tablet, 100mg

Indications: pain and inflammation in rheumatoid arthritis and osteoarthritis; postoperative pain; mild to moderate pain; dysmenorrhoea and menorrhagia

Cautions: elderly, connective-tissue disorders, cardiac impairment, uncontrolled hypertension, heart failure, ischaemic heart disease, peripheral artery disease, cerebrovascular disease, Crohn's disease or ulcerative colitis, Hepatic impairment, Renal impairment, epilepsy, acute porphyria, fluid retention

Drug interactions: Anticoagulants (e.g warfarin and heparin), other antiplatelet medicines (e.g clopidogrel, aspirin), CYP2C8/9 substrates (e.g amiodarone, fluoxetine, glimepiride), NSAIDs, lithium, cyclosporine, ACE-inhibitors, angiotension antagonists, diuretics, hydralazine, cholestyramine and colestipol.

Contraindication: allergic disorders, (they are contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID—which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID), coagulation defects, severe heart failure, active gastro-intestinal ulceration or bleeding or perforation, Pregnancy, Breast-feeding, severe liver disease, renal disease, perioperative pain in the setting of coronary artery bypass surgery

Side-effects: Gastro-intestinal disturbances including discomfort, nausea, diarrhoea, and occasionally bleeding and

ulceration occur (see also NSAIDs and Gastro-intestinal Events, Systemic as well as local effects of NSAIDs contribute to gastro-intestinal damage, hypersensitivity reactions (particularly rashes, angioedema, and bronchospasm, headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances such as tinnitus, photosensitivity, and haematuria, Blood disorders, Fluid retention, blood pressure may be raised; suppositories may cause rectal irritation; of worsening of asthma, Hepatic damage, alveolitis, pulmonary eosinophilia, pancreatitis, visual disturbances, Stevens-Johnson syndrome, and toxic epidermal necrolysis

Dose and Administration: **Adult over 18 years**, 500 mg 3 times daily. **Child 12–18 years**, *acute pain including dysmenorrhoea, menorrhagia*, 500 mg 3 times daily

Naproxen + Esomeprazole

Tablet, 500mg+20mg

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; dysmenorrhoea; acute gout

Cautions: elderly, connective-tissue disorders, cardiac impairment, uncontrolled hypertension, heart failure, ischaemic heart disease, peripheral artery disease, cerebrovascular disease, Crohn's disease or ulcerative colitis, Hepatic impairment, renal impairment

Drug interaction: Methotrexate, Probenecid, ACE Inhibitors, Adrenergic Neurone Blockers, Aliskiren, Alpha-blockers, Angiotensin-II Receptor Antagonists, Antidepressants, SSRI, Aspirin, Baclofen, Beta-blockers, Calcium-channel Blockers, Cardiac Glycosides, Ciclosporin, Clonidine, Clopidogrel, Corticosteroids, Coumarins, Dabigatran Etxilate, Diazoxide, Diuretics, Diuretics, Potassium-sparing and Aldosterone

Antagonists, Erlotinib, Heparins, Hydralazine, Iloprost, Ketorolac, Lithium, Methotrexate, Methyldopa, Mifamurtide, Minoxidil, Moxonidine, Nitrates, NSAIDs, Penicillamine, Pentoxifylline, Phenindione, Potassium Canrenoate, Prasugrel, Quinolones, Ritonavir, Sodium Nitroprusside, Sulfonylureas, Tacrolimus, Venlafaxine, Zidovudine

Contraindication: pregnancy(third trimester), breast feeding, allergic disorders, attacks of asthma, angioedema, urticaria or rhinitis, coagulation defects, severe heart failure, active gastro-intestinal ulceration or bleeding or perforation, Pregnancy, Breast-feeding, severe liver disease, Renal impairment avoid if eGFR less than 30 mL/minute/1.73 m²

Side effects: Gastro-intestinal disturbances including discomfort, nausea, diarrhoea, and occasionally bleeding and ulceration occur (see also NSAIDs and Gastro-intestinal Events, Systemic as well as local effects of NSAIDs contribute to gastro-intestinal damage; taking oral formulations with milk or food, or using enteric-coated formulations, or changing the route of administration may only partially reduce symptoms such as dyspepsia, hypersensitivity reactions (particularly rashes, angioedema, and bronchospasm, headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances such as tinnitus, photosensitivity, and haematuria, Blood disorders, Fluid retention, blood pressure may be raised; suppositories may cause rectal irritation; of worsening of asthma, Hepatic damage, alveolitis, pulmonary eosinophilia, pancreatitis, visual disturbances, Stevens-Johnson syndrome, and toxic epidermal necrolysis

Dose and Administration: Adult:*Rheumatic disease*, 0.5 to 1g daily in 1–2 divided doses; *Acute musculoskeletal disorders and dysmenorrhoea*: 500 mg initially, then 250 mg every 6–8 hours as required; maximum dose after first day 1.25 g daily. *Acute*

gout: 750 mg initially, then 250 mg every 8 hours until attack has passed; *child under 16 years not recommended*

Children: *Pain and inflammation in musculoskeletal disorders, dysmenorrhea-oral: Child 1 month–18 years* - 5 mg/kg twice daily (maximum 1 g daily). *Juvenile idiopathic arthritis-oral: Child 2–18 years* 5–7.5 mg/kg twice daily (max. 1 g daily)

Paracetamol

Tablet, 100mg, 500mg

Suppository, 125mg, 250mg

Syrup, 120mg/5ml, 250mg/5ml

Drops, 100mg/ml

Injection, 1g in 100ml

Indications: mild to moderate pain or pyrexia.

Cautions: caution in alcoholics, and in patients with hepatic diseases, and severe renal function impairment, anaemia and other disorders of the haemopoietic system.

Drug interactions: avoid simultaneous use of single toxic doses or long-term high doses of paracetamol with alcohol, or phenobarbitone; oral anticoagulants.

Contraindications: severe hepatic or renal disease.

Side effects: rare in therapeutic doses. Allergic reactions such as skin rashes, neutropenia and thrombocytopenia may occur rarely.

Dose and Administration: Mild to moderate pain, pyrexia, *Oral:*

Adult: 0.5 to 1g every 4-6 hours, maximum 4g daily. **Child:** 3 months-1 year 60-125mg, 1-5 years 120 - 250mg, 6-12 years 250 - 500mg these doses may be repeated every 4 - 6 hours if necessary (maximum 4 doses in 24 hours). **Rectum: Adult:** 0.5 - 1g, every 4-6 hours, maximum 4g daily. **Child:** 1 - 5 years 125 - 250mg, 6 - 12 years 250 - 500mg; doses inserted every 4 - 6 hours if necessary, maximum 4 doses in 24 hours. **Post-immunization pyrexia: Oral:** infant 2-3 months, 60mg followed

by a second dose if necessary 4-6 hours later; warn parents to seek medical advice if pyrexia persists after second dose. **Injection: Adult and Adolescents > 50 kg:** 1g per administration (100ml vial), up to 4 times a day. Maximum daily dose not exceed 4g. **Child** weighing more than 33 kg (approximately 11 years old), adolescents and adults weighing less than 50 kg: 15 mg/kg per administration, i.e. 1.5 ml solution per kg up to 4 times a day. The minimum interval between each administration must be 4 hours. The maximum daily dose must not exceed 60 mg/kg (without exceeding 3 g). **Children** weighing more than 10 kg (approximately 1 year old) and less than 33 kg: 15 mg/kg per administration, i.e. 1.5 ml solution per kg up to 4 times a day. The minimum interval between each administration must be 4 hours. The maximum daily dose must not exceed 60mg/kg (not exceeding 2 g).

Storage: at room temperature

Paracetamol + Pseudoephedrine Hydrochloride + Chlorpheniramine

Tablet, 325mg + 15mg + 1mg

Syrup, 160mg+15mg+1mg/5ml

Indications, Caution, Contraindications, side effects and Dose and administration: see section 3 (respiratory medicines).

Opioid analgesics

The opioid analgesics may be usually classified as low-efficacy opioids (e.g. codeine) and high-efficacy opioids (e.g. morphine, methadone and pethidine). Codeine may effectively relieve mild to moderate pain not responding to aspirin or paracetamol. It has useful antitussive activity at doses lower than those required for analgesia, and is also effective in controlling diarrhoea. Because of their different mechanisms of

action, codeine has additive analgesic effects with paracetamol, aspirin or other non-steroidal anti-inflammatory agents, and such combinations can be used beneficially. Combination with other opioids should be used with caution. It is much less potent than morphine and much less liable, in normal doses, to produce adverse effects including dependency. It is effective for mild to moderate pain but is too constipating for long-term use.

Morphine and Pethidine are opioid analgesics which are effective in relieving moderate to severe pain, particularly of visceral origin; there is a large variation in patient response. Weaker opioids such as codeine are suitable for mild to moderate pain. Pethidine produces prompt but short-acting analgesia, it is less constipating than morphine, but even in high doses it is less effective.

Morphine remains one of the most valuable opioid analgesics. Its euphoriant action can be a useful property for providing a sense of well-being in patients with severe pain. It is used to relieve severe acute pain, or chronic pain, e.g. in terminally ill patients. It is also used for pre-operative sedation, as a supplement to anaesthesia and in acute pulmonary oedema secondary to left ventricular failure, and is the choice to relieve pain in acute ischaemic myocardial conditions.

A neurotoxic metabolite, norpethidine, accumulates during repeated administration and can cause central nervous system excitation, including myoclonus and seizures. These adverse effects together with the short duration of analgesic action make pethidine unsuitable for severe, continuing pain. It is used for analgesia in labor; however other opioid analgesics such as morphine are often preferred.

Pethidine is preferred to morphine in certain clinical situation, e.g. during labour, in biliary, bowel or ureteric colic. It is less bronchospasmogenic than morphine.

Methadone as an antitussive linctus, it may be used to control non-productive cough in special cases, e.g. lung cancer. It may be used in the management of opioid dependence and withdrawal; prolonged therapy may be required, with carefully adjusted, individualized doses.

Other agent such as tramadol is an atypical opioid structurally akin to tilidine, but apart from its morphine-receptor agonist action, it inhibits neuronal reuptake of serotonin and noradrenaline. It does not appear to release histamine.

Pentazocine has both agonist and antagonist properties and precipitates withdrawal symptoms, including pain in patients dependent on other opioids. By injection it is more potent than dihydrocodeine or codeine, but hallucinations and thought disturbances may occur. It is not recommended and, in particular, should be avoided after myocardial infarction as it may increase pulmonary and aortic blood pressure as well as cardiac work.*Note:*

- *Opioid analgesics have neither antipyretic nor anti-inflammatory activity.*
- *The risk of dependency with the weaker opioids is lower than with the high-efficacy opioids, but a considerable potential may exist in patients with a history of drug abuse or patients who are “dependence-prone”.*
- *Tolerance to the analgesic efficacy of opioids may develop with repeated and prolonged administration, and dependence and abuse are further problems. However, in the management of chronic pain in terminal illness the dependence-producing potential is of less importance, and doses should be titrated up wards until adequate analgesia is provided. Their tendency to cause respiratory depression should also be noted.*
- *The low-efficacy opioids also have a tendency to suppress respiration, and in overdose they are marked respiratory depressants. Toxicity is aggravated by alcohol or other CNS depressants.*
- *The opioids all have, in varying degrees, the potential to cause constipation, urinary retention, nausea, vomiting and cough suppression; combinations of opioids should be avoided.*

G. Medicines Used In Anaesthesia

- *Opioids should be used with caution in hypotensive states, in impaired hepatic function, when decreased respiratory reserve is present, and in combination with certain drugs such as MAO inhibitors.*
- *Morphine should be used with caution in asthmatic patients.*
- *At higher doses, all opioids may cause muscle rigidity.*
- *Prolonged administration of opioids and addiction during pregnancy may cause dependence and withdrawal in the neonate.*

Codeine Phosphate

Tablet, 30mg

Injection, 30mg/ml in 1ml ampoule

Indications: mild to moderate pain, also used in the symptomatic relief of non-productive cough (section 3.1)

Cautions: renal and hepatic impairment, dependence; and also see section 3.1

Drug interactions: see section 3.1, under codeine phosphate

Contraindications: respiratory depression, obstructive airways disease, acute asthma attack; where risk of paralytic illness.

Side effects: see section 3.1, under codeine phosphate

Dose and Administration: Mild to moderate pain:

Oral: **Adult:** 30 - 60 mg every 4 hours when necessary to a maximum of 240mg, daily. *Injection: I.M:* 30-60mg every 4 hours when necessary. **Children:** *oral:* 1-12 years, 3mg/kg daily in divided doses.

Storage: at room temperature

Fentanyl

Injection, 50mcg/ml

Indications: relief of pain,

Cautions, Drug interactions, Contraindications, Side effects and Storage, see above

Dose and Administration: Acute pain management: **Adult:** Severe: I.M, I.V: 50-100 mcg/dose every 1-2hours as needed;

patients with prior opiate exposure may tolerate higher initial doses. Patient-controlled analgesia (PCA): I.V.: Usual concentration: 10mcg/ml. Demand dose: Usual: 10mcg; range: 10-50mcg. Lockout interval: 5-8 minutes. Mechanically-ventilate patients (based on 70 kg patient): Slow I.V.: 0.35-1.5mcg/kg every 30-60 minutes as needed; infusion: 0.7-10mcg/kg/hour

Methadone hydrochloride

Injection, 10 mg/ml, 20mg/ml in 1 ml ampoule

Tablet, 5 mg

Indications: for relief of severe pain, cough suppressant, opioid dependence.

Cautions: as for morphine. Methadone has a long half-life and accumulation may occur with repeated doses, especially in elderly or debilitated patients; caution in hepatic and renal impairment.

Drug interactions: as for morphine, and also fluconazole, zidovudine.

Contraindications: as for morphine, see notes above.

Side effects: as for morphine. Methadone has a more prolonged effect than morphine and readily accumulates with repeated doses. It may have a relatively greater respiratory depressant effect than morphine and, although reported to be less sedating, repeated doses of methadone may result in marked sedation. It causes pain at injection sites; subcutaneous injection causes local tissue irritation and induration.

Dose and Administration: **Adult:** Analgesia: Oral: 2.5-10mg every 3-4 hours as needed. IV: initial: 2.5-10mg every 8-12 hours in opioid-naive patients also be administered by SC or IM injection.

Storage: store at room temperature.

Morphine Sulphate

Tablets, 5mg, 10 mg, 15mg, 20mg, 30mg

Oral solution, 5mg/5ml, 20mg/5ml, 50mg/5ml

10 mg/5ml, 100 mg/5ml

Suppository, 10mg, 15mg, 20mg, 30mg

Granules for oral suspension, 30mg, 60mg, 100mg, 200mg per sachet

Capsule (modified release), 20mg, 50mg, 100mg, 200mg

Injection (as hydrochloride), 10 mg/ml, 20mg/ml in 1ml ampoule

Indications: analgesic, antidiarrhoeal, anaesthesia adjunct and antitussive; see also notes above.

Cautions: renal and hepatic impairment; elderly and debilitated, dependence; hypothyroidism; convulsive disorders; decreased respiratory reserve and acute asthma; hypotension, prostatic hypertrophy; pregnancy and breastfeeding, adrenocortical insufficiency, obstructive bowel disorders, myasthenia gravis, withdraw gradually, not drive or operate machinery; see also notes above.

Drug interactions: CNS depressants; e.g alcohol, anaesthetic agents; antidiarrheals; anticholinergics, antihypertensives; cimetidine; metoclopramide; MAO inhibitors.

Contraindications: acute respiratory depression, acute alcoholism, where risk of paralytic ileus; raised intracranial pressure or head injury; avoid injection in pheochromocytoma; during labour, diarrhea caused by poisons, antibiotic-associated pseudomembranous enterocolitis, acute abdominal conditions and biliary colic; see also notes above.

Side effects: nausea, vomiting, constipation, drowsiness, also dry mouth, anorexia, spasm of urinary and biliary tract, bradycardia, tachycardia, palpitations, euphoria, decreased libido, rash, urticaria, pruritus, sweating, headache, facial

flushing, vertigo, postural hypotension, hypothermia, hallucinations, confusion, tolerance & dependence, miosis, larger doses produce respiratory depression and hypotension.

Dose and Administration: **Adult:** *IM or SC:* 5 -15mg (usually 10 mg initially, based on an adult weighing 70 Kg); repeated 3-4 hourly as required. *IV:* 2.5 mg increments every 5 - 10 minutes, up to a maximum of 15 mg. *Oral:* 5 - 20 mg 4 hourly. When changing to a controlled release formulation, give the current total 24 - hour requirement in 2 divided doses. Controlled release tablets: Initially 10 - 20 mg twice daily, increased according to individual requirements.

Child: *IM or SC:* over one month old, 0.1-0.2 mg/kg.

Neonates: *IM or SC:* 0.1mg/kg. *Note: Facilities must be available to provide ventilatory support if necessary.*

Storage: store at room temperature.

Pentazocine

Tablet, 50mg

Injection, 30mg/ml in 1ml ampoule

Indications: moderate to severe pain.

Cautions: as for morphine; pentazocine has weak opioid antagonist actions and may precipitate withdrawal symptoms if given to patients who are physically dependent on opioids.

Drug interactions: see under pethidine Hydrochloride.

Contraindications: see under Pethidine Hydrochloride and notes above; patients dependent on opioids; arterial or pulmonary hypertension, heart failure.

Side effects: as for morphine; also hallucinations, nightmares, thought disturbances, hypertension, tachycardia, agranulocytosis, toxic epidermal necrosis.

Dose and Administration: *Oral: Adult:* Pentazocine hydrochloride 50mg every 3 - 4 hours preferably after food

(range 25 - 100mg); maximum 600mg daily; **Child** 6 - 12 years 25 mg every 3-4 hours.*SC, IM, or IV injections:* **Adult:** moderate pain, 30mg; severe pain 45 - 60 mg every 3 - 4 hours when necessary; **Child** over 1 year, *by S.C or IM injection*, up to 1mg/kg, *by IV injection* up to, 500 micrograms/kg.

Storage: at room temperature in a tight, light resistant container. Protect from freezing (Injection).

Pethidine Hydrochloride

Tablet, 50mg

Injection, 50mg/ml in 1 and 2ml ampoules

Indications: analgesia in moderate to severe pain including labour, anaesthesia adjunct; see also introduction notes.

Cautions: as for morphine above, also atrial fibrillation or other cardiac diseases where tachycardia might pose a problem.

Drug interactions: as for morphine, also MAO inhibitors, and cimetidine

Contraindications: as for morphine above, also renal failure or severe hepatic disease.

Side effects: as for morphine above; the effect on smooth muscle may be relatively less intense than with morphine and constipation occurs less frequently. Local reactions often follow injection of pethidine; general hypersensitivity reactions occur rarely. Pethidine given intravenously may increase the heart rate.

Dose and Administration: **Adult:***Oral:* 50 - 150mg every 4 hours.*IM* (preferred), *SC:* 50 -150mg (usually 100mg) every three to four hour as needed; **Child:** *Oral or IM:* 0.5-2.0mg/kg/dose, repeated 8 hourly if required. Maximum 6mg/kg/day.

Storage: store at room temperature protect from light and from freezing.

Phenazopyridine

Tablet, 100 mg

Indications: symptomatic relief of urinary burning, itching in association with urinary tract infection.

Cautions: G6PD deficiency or discontinue if the skin or sclerae become discolored.

Contraindications: allergic reaction to phenazopyridine; hepatitis, impaired renal function.

Side effects: anemia, aseptic meningitis, dermatitis, allergic, hepatotoxicity, methemoglobinemia, renal function impairment or failure, dizziness, headache, indigestion, pruritus, stomach cramps or pain.

Dose and Administration:*Oral: Adult:* 100-200 mg 3 times /day, after meals for up to 2 days when it is used concomitantly with an antibacterial agent.

Child: 12 mg/kg/day in 3 divided doses administered after meals for 2 days.

Storage: store at room temperature in a tight container.

Tramadol

Tablet/Capsule, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 300 mg

Oral drops, 100 mg/ml (40 drops)

Nasal spray, 20 mg/0.1ml

Injection, 50 mg/ml

Indications: moderate to severe pain.

Cautions: hepatic or renal impairment, and when risk of seizures exists.

Drug interactions: carbamazepine, CNS depressants, anaesthetics, alcohol, MAO inhibitors.

Contraindications: increased intracranial pressure or head injury, respiratory depression.

Side effects: as for morphine, but less potential for abuse, respiratory depression, or constipation.

Dose and Administration: Adult:*Oral:* 50 - 100 mg 4 - 6 hourly, maximum 400 mg/day.

Sustained release formulation, initially 100 mg twice daily, increased to 150 mg or 200 mg twice daily.*Drops:* initially 50 mg (20 drops or 0.5 ml), repeated in 30-60 minutes if analgesia is not achieved; maximum 400 mg/day (160 drops).*IV:* over 2 - 3 minutes or by infusions, IM or SC, 50-100 mg 4 - 6 hourly; maximum 400 mg/day.**Elderly**>75 years: *Oral:* 50-100 mg every 4-6 hours (not exceed 300 mg/day)

Storage: store at room temperature.

5.2. Antimigraine Headache Medicines

Migraine is characterized by recurrent attacks of headache which may take up to 72 hours to resolve. Treatment of migraine attacks may be successfully carried out with non-opioid analgesics such as aspirin, other NSAIDs, or paracetamol (preferably in a soluble or dispersible form) taken at the earliest signs of an attack concomitant anti-emetic treatment may be required. Attacks which do not respond to non-opioid analgesics may be treated with ergot preparations such as Ergotamine Tartrate. But the value of ergotamine for migraine is limited by difficulties in absorption and by its side effects, particularly nausea, vomiting, abdominal pain, and muscular cramps; it is best avoided. The recommended doses of ergotamine preparations should not be exceeded and treatment should not be repeated at intervals of less than 4 days.

To avoid habituation the frequency of administration of ergotamine should be limited to no more than twice a month. It should never be prescribed prophylactically but in the

management of cluster headache a low dose is occasionally given for 1 to 2 weeks.

An alternative to ergot compounds for the acute treatment of migraine is the selective serotonin agonist sumatriptan succinate, this drug act by constricting dilated cranial blood vessels and inhibiting release of sensory neuropeptides from the perivascular trigeminal afferents, thereby blocking the consequences of trigeminovascular activation. Sumatriptan is relatively safe and well tolerated but should be avoided in patients with known, or at risk of, cardiovascular disease.

Paracetamol+Acetylsalicylic acid+Caffeine

Tablet, 250mg+250mg+65mg, 400mg+250mg+65mg

Indications: relief of mild to moderate pain; mild to moderate pain associated with migraine headache.

Dose and Administration: *Oral:* **Adult:**Based on acetaminophen component:Mild to moderate pain: 325-650mg every 4-6 hours as needed; do not exceed 4 g/day

Mild to moderate pain associated with migraine headache: 500mg/dose (in combination with 500mg aspirin and 130mg caffeine) every 6 hours while symptoms persist; do not use for longer than 48 hours

Based on aspirin component:Mild to moderate pain: 325-650mg every 4-6 hours as needed; do not exceed 4 g/day.Mild to moderate pain associated with migraine headache: 500mg/dose (in combination with 500mg acetaminophen and 130mg caffeine) every 6 hours; do not use for longer than 48 hours.

Ergotamine Tartrate

Tablet, 1mg, 2mg (sublingual)

Injection 0.25 mg/ml in 1ml ampoule

Indications: as single agent or in combination with caffeine to prevent or abort migraine, cluster headache (histamine cephalagia), and other vascular headaches. Not recommended for migraine prophylaxis because of the possibility of adverse effects.

Cautions: risk of peripheral vasospasm (stop medication immediately if numbness or tingling in extremities or anginal pain develops, may aggravate MI, or aggravate intermittent claudication), elderly, daily rebound headaches indicative of ergotamine dependence; discontinuation after regular normal dosage may result in withdrawal headache; See also notes above.

Drug interactions: beta blockers, macrolide antibiotics, sumatriptan containing preparation, sympathomimetic agents such as adrenaline; vasoconstrictor - containing local anesthetic, systemic vasoconstrictors, ciprofloxacin, diclofenac, doxycycline, quinidine, verapamil, MAO inhibitors.

Contraindications: hypersensitivity to ergotamine, pregnancy and breastfeeding, children, peripheral vascular disorders, coronary artery disease, obliterative vascular disease and Raynaud Syndrome, severe hypertension, sepsis, severe renal or hepatic dysfunction; hyperthyroidism, prolonged use of excessive dosage

Side effects: nausea, vomiting, vertigo, abdominal pain, diarrhea, muscle cramps, increased headache; pericardial pain, myocardial ischaemia; rarely myocardial infarction; repeated high dosage may cause ergotism with gangrene and confusion; pleural and peritoneal fibrosis may occur with excessive use.

Dose and Administration: *Treatment of acute migraine attack:* **Sublingual: Adult:** 2mg under tongue at the start of the attack, repeated at intervals of at least thirty minutes, if necessary, up to a total of 6mg per day.

Oral: Adult: 1- 2 mg at first sign of attack, maximum 4mg in 24 hours; do not repeat at intervals of less than 4 days maximum 8mg in any one week; not to be used more than twice in any 1 month.

*Note: **Ergotamine Tartrate was formerly given by subcutaneous or IM injection but dihydroergotamine mesylate is generally used if parenteral administration is necessary.*

Storage: at room temperature in a well closed, light resistant container.

Ergotamine Tartrate + Caffeine¹

Tablet, 1mg + 100mg

Suppository, 2mg + 100mg

Indications: as for ergotamine.

Cautions: as for ergotamine; and also, breast-feeding women.

Drug interactions: as for ergotamine, also CNS stimulant, MAO inhibitors.

Contraindications: as for ergotamine, also anxiety disorders, insomnia, peptic ulceration, and severe cardiac disease.

Side effects: as for ergotamine above, also insomnia.

Dose and Administration: **Oral: Adult:** 1 - 2 tablets at onset; maximum 4 tablets in 24 hours; not to be repeated at intervals of less than 4 days; maximum 8 tablets in one week; child not recommended. **Rectal:** 1 suppository at onset; maximum 2 in 24 hours; not to be repeated at intervals of less than 4 days; maximum 4 suppositories in one week.

¹And any other combination ratio proven to be therapeutically effective can be used

Ergotamine Tartrate + Cyclizine Hydrochloride + Caffeine Hydrate²

Tablet, 2 mg + 50mg + 100mg

Indication: as for ergotamine and caffeine above.

Cautions: as for ergotamine and caffeine, also pediatrics, geriatrics.

Drug interactions: as for ergotamine and caffeine, also drugs with anticholinergic effect.

Contraindications: as for ergotamine and caffeine, also patients which may adversely affected by anticholinergic effects.

Side effects: as for ergotamine and caffeine, also cyclizine has antihistaminic, anticholinergic, and CNS depressant effects.

Dose and Administration:*Oral:Adult:* 1 tablet at onset, followed after 30 minutes by ½ - 1 tablet, repeated every 30 minutes if necessary; maximum 4 tablets per attack and 6 tablets in one week, child not recommended.

Propranolol

Tablets, 10 mg, 20 mg, 40mg, 60mg, 80mg

Indications, cautions, Drug interactions, contraindications, side effects and storage; see section 3.2 under propranolol

Dose and Administration: Initial dose: 80 mg/day orally in divided doses. Maintenance dose: 160 to 240 mg/day. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within 4 to 6 weeks after reaching the maximum dose, propranolol therapy should be discontinued.

Sumatriptan

Tablets, 50 mg, 100 mg

Injection, 12 mg/ml

²And any other combination ratio proven to be therapeutically effective can be used

Nasal spray, 20 mg/0.1ml

Indications: treatment of acute migraine attacks with or without aura, cluster headache.

Cautions: patients with a history of seizure disorder, impaired hepatic or renal function, nursing mothers, pregnancy; safety and effectiveness in children have not been established.

Drug interactions: ergotamine, MAO inhibitors, selective serotonin re-uptake inhibitors, lithium.

Contraindications: hypersensitivity to the drug, IV use, coronary artery disease (CAD); risk factor for CAD such as hypertension, hypercholesterolemia, obesity, diabetes, smoking, and strong family history.

Side effects: chest pain, heaviness or tightness, transient increase in blood pressure, bronchospasm, flushing, tingling, dizziness, dysphagia, muscle cramps and weakness; transient pain at injection site, nausea and vomiting; vertigo.

Dose and Administration:Adult: Oral: initially 50 mg; depending on response, this may be increased to 100 mg. If symptoms recur after an initial beneficial response, the dose may be repeated after 2 - 4 hours; maximum 300 mg in 24 hours. SC: 6 mg. If symptoms recur after an initial beneficial response, 6 mg may be repeated after at least 1 hour; maximum 12 mg/24 hours.

Nasal spray; Intranasal: 20 mg administered in one nostril. If symptoms recur, the dose may be repeated after a minimum of 2 hours; Maximum 40 mg/24 hours.

Storage: store at 2-30 °C; protect from light.

5.3. Anxiolytics Sedatives, Hypnotics and Antipsychotics

5.3.1. Anxiolytics

Benzodiazepine therapy

The benzodiazepines are primarily indicated for the treatment of anxiety states and as hypnotics. Other indications include: Peri-operative- as premedication; Management of alcohol withdrawal (delirium treatments)- attenuating the acute withdrawal symptoms; Treatment of seizure disorders; Muscle relaxant.

All benzodiazepines act by facilitating the action of gamma-aminobutyric acid (GABA) which is the major inhibitory neurotransmitter in the CNS. Benzodiazepine receptors have been identified in the brain, located in close proximity to GABA receptors. Activation of the benzodiazepine receptors promotes the activity of the GABA receptors.

The benzodiazepines may be divided into four groups on the basis of the elimination half-lives of the parent compound and the active metabolites (if any): Ultra short-acting (half life < 6 hours); Midazolam; Short-acting (half life 6-12 hours); oxazepam, temazepam; Intermediate-acting (half life 12-24 hours); Alprazolam, bromazepam; Long-acting (half life > 24 hours); chlordiazepoxide, diazepam, medazepam, flurazepam. Duration of action of a drug is dependent on many factors other than elimination half-life. This system of classification may thus not always accurately predict the duration of clinical effect.

Alprazolam

Tablet, 0.25mg, 0.5mg, 1mg

Indication: treatment of anxiety, panic disorder with or without agoraphobia; anxiety associated with depression.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam and also notes above.

Dose and Administration: *Oral:Adult:* 0.25 - 0.5mg 3 times daily (elderly or debilitated 0.25 mg 2-3 times daily), increased if necessary to a total of 3mg daily.

Storage: store at room temperature in a tight, light resistant container.

Bromazepam

Tablet, 1.5mg, 3mg, 6mg

Indications: anxiety (short - term use, not more than two weeks)

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Oral:Adult:* 6 to 18mg daily in divided doses; elderly (or debilitated) half adult dose; maximum (in exceptional circumstances in hospitalized patients) 60mg daily in divided doses.

Storage: store at room temperature in a well-closed container.

Chlordiazepoxide

Tablet, 5mg, 10mg, 25mg

Indications: anxiety (short - term use); adjunct in acute alcohol withdrawal.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Anxiety: Oral:Adult:* 10mg 3 times daily increased if necessary to 60 - 100mg daily in divided doses; elderly (or debilitated) half adult dose.

Note:the doses stated above refer equally to chlordiazepoxide and to its hydrochloride.

Storage: store at room temperature in a tight, light resistant container.

Diazepam

Tablet, 2mg, 5mg, 10mg

Suppository, 5mg, 10mg

Syrup, 2mg/5ml

Injection, 5mg/ml in 2ml ampoule

Indications: short-term treatment of anxiety or insomnia; adjunct in acute alcohol withdrawal; status epilepticus; febrile convulsions; muscle spasm; peri-operative use.

Cautions: elderly, in patients with impaired liver or kidney function, muscle weakness; elderly or debilitated patients; respiratory disease, history of alcohol abuse, marked personality disorder; pregnancy; breastfeeding; avoid prolonged use and abrupt withdrawal; porphyria.

Note:- drowsiness may affect performance of skilled tasks (e.g. driving); effects of alcohol enhanced.

Drug interactions: alcohol, antidepressants, antihistamines, antipsychotics, sedative, general anaesthetics, other hypnotics or sedatives, and opioid analgesics (sedation or respiratory and cardiovascular depression may be enhanced); flvoxamine, ketoconazole, nefazodone (concurrent use may inhibit the hepatic metabolism of benzodiazepines that are metabolized by oxidation); plastic infusion tubing (diazepam may adhere to plastic infusion tubing), zidovudine, aminophylline.

Contraindications: preexisting CNS depression or coma, acute pulmonary insufficiency, or sleep apnoea, severe hepatic impairment; myasthenia gravis; respiratory depression; diazepam should not be used for the treatment of chronic psychosis or for phobic or obsessional states. Avoid injections containing benzyle alcohol in neonates.

Side effects: drowsiness and light headedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention, blood

disorders and jaundice, skin reactions raised liver enzymes, on IV injection, pain, thrombophlebitis and rarely apnea.

Dose and Administration: Oral: **Adult:** *Anxiety:* 2mg 3 times daily increased if necessary to 15 - 30 mg daily in divided doses; elderly (or debilitated) half adult dose.

Insomnia associated with anxiety: 5- 15 mg at bedtime.

Child: night terrors and somnambulism: 1 - 5 mg at bedtime. IM or slow IV injection (into a large vein, at a rate of not more than 5mg/minute): for severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal, 10mg, repeated if necessary after not less than 4 hours. *Note: Only use intramuscular route when oral and intravenous routes not possible.*

Rectum as suppositories: anxiety when oral route not appropriate, 10 to 30mg (higher dose divided), dosage form not appropriate for less than 10mg.

Storage: at room temperature in light resistant container protect from freezing.

Flurazepam

Capsule, 15 mg, 30 mg

Indications: short-term treatment of insomnia.

Cautions: elderly, pregnancy and children < 15 years.

Drug interactions:azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, protease inhibitor, quinidine, verapamil, cimetidine, clozapine, CNS depressants, digoxin, disulfiram, metoprolol.

Contraindications: narrow-angle glaucoma, pregnancy.

Side effects: chest pain, constipation, drowsiness, memory impairment, hangover effect, euphoria, hallucinations, rash, vomiting, diarrhea, nausea, blurred vision, tinnitus, and apnea.

Dose and Administration: Oral: **Adult:** 15-30 mg at bedtime. **Elderly:** 15mg at bedtime; avoid use if possible

Storage: store in light-resistant containers and at room temperature.

Medazepam

Capsule, 5mg, 10mg

Medazepam is a long acting benzodiazepine with properties similar to those of diazepam.

Indications: used for short-term treatment of anxiety disorders.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Oral:Adult:*10-30mg daily in divided doses; in severe conditions up to 60mg daily has been given.

Storage: store at room temperature.

Midazolam Hydrochloride

Injection, 1mg/ml, 2 mg/ml in 5ml ampoule, 5 mg/ml in 2ml ampoule

Syrup, 2mg/ml

Tablet, 10 mg

Indications: preoperative sedation and provides conscious sedation prior to diagnostic or radiographic procedures; intravenous anesthesia (induction and maintenance).

Cautions, Drug interactions, Contraindications and Side effects; see under diazepam.

Dose and Administration: *Adult:Preoperative sedation: IM:* 0.07 to 0.08 mg/kg 30-60 minutes prior to surgery/procedure; usual dose: 5mg.*IV:* 0.02-0.04mg/kg; repeat every 5 minutes as needed to desired effect or up to 0.1-0.2mg/kg.*Conscious sedation: IV:* initial; 0.5-2mg slow IV over at least 2 minutes; slowly titrate to effect by repeating doses every 2-3 minutes if needed; usual total dose: 2.5-5mg; use decreased doses in

elderly. *Anesthesia: IV: Induction:* Unpremedicated patients: 0.3-0.35mg/kg (up to 0.6mg/kg in resistant cases). Premedicated patients: 0.15-0.3 mg/kg. *Maintenance:* 0.05 to 0.3mg/kg as needed or continuous infusion 0.25 to 1.5mcg/kg/minute. *Conscious sedation for procedures or preoperative sedation: Oral:* 0.25-0.5 mg/kg as a single dose procedure, up to a maximum of 20 mg; administer 30-45 minutes prior to procedure. **Child** < 6 years or less- cooperative patients may require as much as 1 mg/kg as a single dose; 0.25 mg/kg may suffice for child 6-16 years of age.

Storage: store at room temperature.

Oxazepam

Tablet, 10 mg

Indications: short-term management and relief of anxiety.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

The elderly are more sensitive to CNS effects, use the smallest effective dose.

Dose and Administration: Oral **Adult:** Anxiety: 10 - 15 mg 2 - 4 times daily. *Insomnia:* 5 - 30 mg 1 - 2 hours before bedtime. *Psychotic patients and alcoholics:* 30 mg 3 to 4 times daily may be required.

Note: if used as hypnotic, it should be administered at least 1 to 2 hours before bed time as absorption is slower than with diazepam.

Storage: store at room temperature

Temazepam

Capsules, 10mg, 15mg, 20mg, 30mg

Indications: short-term treatment of insomnia.

Cautions: elderly or debilitated patients; respiratory disease, renal and hepatic impairment.

Drug interactions: narcotic analgesics, barbiturates, phenothiazins, MAO inhibitors, cimetidine, ciprofloxacin, clozapine, and oral contraceptive.

Contraindications: narrow-angle glaucoma, pregnancy.

Side effects: confusion, dizziness, drowsiness, anxiety, headache, hangover, euphoria, rash, decreased libido, diarrhea, blurred vision, diaphoresis.

Dose and Administration:Adult: 15-30mg at bedtime.

Elderly or debilitated patients: 15mg

Storage: store at room temperature.

Zolpidem

Tablet, 10mg

It is an imidazopyridine, chemically distinct from the benzodiazepines, but exhibiting selective high affinity for a benzodiazepine receptor subtype. Its sedative action predominates over its muscle relaxant and anticonvulsant activity (in contrast to the benzodiazepines), and its indication is for the treatment of insomnia.

Dose and Administration: Oral: **Adult:** 10mg at bedtime. Hepatic impairment and the elderly: 5 mg.

5.3.2. Hypnotics

These agents act by depressing the central nervous system. Although widely prescribed, both physical and psychological dependence, as well as tolerance, occur. They have no analgesic effects, and in the presence of pain, adequate analgesia is desirable. Anterograde amnesia has been described even with single doses of hypnotics.

Chloral Hydrate

Capsule, 500 mg

Suppository, 60 mg

Syrup, 250 mg/5ml, 500 mg/5ml, 1 g/ml

Indications: short term sedative and hypnotic (< 2 weeks), sedative / hypnotic for diagnostic procedures; sedative prior to EEG evaluations.

Cautions: respiratory disease, pregnancy and breast-feeding, neonates.

Drug interactions: CNS depressants, warfarin, IV furosemide, benzodiazepine.

Contraindications: hepatic or renal impairment; cardiac disease, gastritis or ulcers.

Side effects: gastric irritation with nausea and vomiting, ataxia, headache, malaise, nightmares and delirium; eosinophilia, reduction in white cell count; dependence with prolonged use.

Dose and Administration:Adult: Oral, Rectal: Sedation, anxiety: 250 mg 3 times / day. Hypnotic: 500 - 1000 mg at bed time or 30 minutes prior to procedure, not to exceed 2 g/24 hours. **Child:** Sedation or anxiety: Oral, Rectal: 5 - 15 mg/kg/dose every 8 hours (maximum: 500 mg/dose). Prior to EEG: Oral, Rectal: 20 - 25 mg/kg/dose, 30-60 minutes prior to EEG; may repeat in 30 minutes to maximum of 100 mg/kg or 2 g total. Hypnotic: Oral, Rectal: 20 - 40 mg/kg/dose up to a maximum of 50 mg/kg/24 hours or 1 g/dose or 2 g/24 hours. Conscious sedation: Oral: 50 - 75 mg/kg/dose 30 - 60 minutes prior to procedure; may repeat 30 minutes after initial dose if needed, to a total maximum dose of 120 mg/kg or 1 g total.

Storage: store in light resistant, airtight container and at room temperature.

Pentobarbitone (pentobarbital)

Capsule, 50mg, 100mg

Suppository (Sodium), 30mg, 60mg

Injection (sodium), 50mg/ml in 50ml

Indications: sedative/hypnotic; preanesthetic; high-dose barbiturate coma for treatment of increased intracranial pressure or status epilepticus unresponsive to other therapy.

Cautions: elderly, debilitated, renally impaired, hepatic dysfunction, or paediatric patients. Patients with depression or suicidal tendencies.

Drug interactions: other CNS depressants, ethanol, narcotic analgesics, antidepressants, or benzodiazepines, chloramphenicol, MAO inhibitors, valproic acid, griseofulvin, clarithromycin, cyclosporine, erythromycin, nevirapine, protease inhibitors, rifampin, oral contraceptives, oral anticoagulants.

Contraindications: hypersensitivity to barbiturates; hepatic impairment; dyspnea or airway obstruction; porphyria; pregnancy.

Side effects: bradycardia, hypotension, drowsiness, CNS excitation or depression, lethargy, headache, insomnia, anxiety, dizziness, rash, nausea, vomiting, constipation, thrombocytopenia.

Dose and Administration:Adult: Hypnotic: *IM:* 150-200mg. *IV:* initial: 100mg, may repeat every 1-3 minutes up to 200-500 mg total dose.Preoperative sedation: *IM:* 150-200mg. **Child:** Hypnotic: *IM:* 2-6 mg/kg; maximum 100mg/dose. Preoperative sedation: ≥ 6 months: *IM:* 2-6mg/kg; maximum: 100mg/dose.*IV:* 1-3mg/kg to a maximum of 100mg until asleep.

Storage: at room temperature in air tight container.

Phenobarbitone (Phenobarbital)

Tablet 10mg, 15mg, 30mg, 60mg, and 100mg

Elixir, 20mg/ 5ml

Injection (Sodium), 25mg/ml in 1ml ampoule, 100mg/ml in 1ml ampoule, 4%

Indications: sedative-hypnotic.

Cautions: pediatric, elderly, and debilitated patients.

Drug interactions: alcohol, CNS depressants, adrenocorticoids, glucocorticoids and mineralocorticoids; or chloramphenicol; corticotropin; coumarin or indandione - derivative anticoagulants, carbamazepine, estrogen-containing contraceptives; valproic sodium or valproic acid; vitamin D; xanthines such as aminophylline, caffeine, oxtriphylline, theophylline, rifampin; monoamine oxidase inhibitors including furazolidone, paralyline and procarbazine; doxycycline.

Contraindications: pregnancy and breastfeeding, and in patients with acute intermittent or variegated or history of porphyria, insomnia caused by pain, drug abuse or dependence (history of), hepatic coma or hepatic function impairment, acute or chronic pain; respiratory disease involving dyspnea or obstruction, particularly status asthmaticus; sensitivity to barbiturates.

Side effects: Common: drowsiness (especially with initiation of therapy). Uncommon: ataxia and nystagmus (usually dose-related), dizziness and psychomotor impairment. Rare: skin reactions, including Stevens-Johnson syndrome, photosensitivity; folic acid deficiency and megaloblastic anaemia. Prolonged use may lead to dependence, with a withdrawal syndrome on termination of treatment; also rickets and osteomalacia due to vitamin D deficiency, hypoproteinaemia and hepatitis.

Dose and Administration: Hypnotic: **Adult:** *Oral:* 100 to 320mg (base) at bedtime; *IM or IV:* 100 to 325mg.

Child: dosage must be individualized by physician.

Sedative: Oral:**Adult:** daytime- 30-120mg (base) in two or three divided doses a day;**Child:** *daytime*, 2mg (base)/kg of body weight three times a day; Preoperative, 1 to 3mg (base) per kg of body weight. *IM or IV:* **Adult:** daytime, 30 to 120mg a day in two or three divided doses, preoperative (*IM*), 130-200mg sixty to ninety minutes before surgery. **Child:** preoperative, 1 to 3mg per kg of body weight, sixty-ninety minutes prior to surgery.

Storage: at room temperature in a tight container protect from freezing.

Promethazine

Tablet, 25mg

Indications: night sedation and insomnia or it is indicated as sedative hypnotic.

Cautions: epilepsy, prostatic hypertrophy, urinary retention, glaucoma, hepatic disease, jaundice, also during pregnancy and breast-feeding, in children and elderly. It causes drowsiness. Patients should be advised to avoid car driving, machine operating or doing activities requiring alertness.

Drug interactions: alcohol, CNS depressants, anticholinergics, antithyroid, epinephrine, extrapyramidal reaction causing medication, levodopa, metrizamide, monoamine oxidase inhibitors including furazolidone and procarbazine.

Contraindication: hypersensitivity to promethazine; coma; treatment of lower respiratory tract symptoms, including asthma; children < 2 years of age.

Side effects: drowsiness, headache, psychomotor impairment, urinary retention, dry mouth, blurred vision, gastrointestinal disturbances, rashes, photosensitivity reactions, palpitation, and arrhythmias, hypersensitivity reaction (including bronchospasm, angioedema, and anaphylaxes), convulsions, sweating, myalgia, paraesthesia, blood disorders, tremor, liver dysfunction, sleep

disturbance, depression, hypotension, and hair loss, extra pyramidal effects.

Dose and Administration: **Adult:***Oral:* 25mg at bed time, increased to 50mg if necessary. **Child** (2-5 years): 15 to 20mg; 5-10 years: 20 to 25mg at bed time.

Storage: at room temperature in a tight, light-resistant container.

5.3.3. Antipsychotics

Antipsychotics may be used in a wide variety of psychotic disorders including schizophrenia, Delirium and dementia, the manic phase of bipolar disorder (manic depressive illness), psychotic depression, and other acute psychotic illnesses.

Buspirone

Tablet, 5mg, 10mg

Indications: management of generalized anxiety disorder (GAD)

Cautions: hepatic or renal impairment; does not prevent or treat withdrawal from benzodiazepines.

Drug interactions: MAOinhibitors, trazodone, warfarin, grapefruit juice, erythromycin, clarithromycin, diclofenac, doxycycline, itraconazole, nefazodone, rifampin and verapamil.

Contraindications: Hypersensitivity to buspirone

Side effects: Commonly dizziness, nausea, headache, nervousness, lightheadedness, and excitement; less frequently unsteady gait, diarrhea, weakness, hostility, skin rash, and tremors.

Dose and Administration: Oral: Child and Adolescents: Initial: 5mg daily; increase in increments of 5mg/day at weekly intervals as needed, to a maximum dose of 60mg/day divided into 2-3 doses. Adult: 15mg/day (7.5mg twice daily); may increase in increments of 5mg/day every 2-4 days to a maximum dose of 60mg/day; target dose for most people is 30mg/day (15mg twice daily). **Elderly:** Initial 5mg twice daily,

increase by 5mg/day every 2-3 days as needed up to 20-30 mg/day; maximum daily dose: 60mg/day.

Storage: store at room temperature

Chlorpromazine Hydrochloride

Tablet, 25 mg, 50mg, 100mg

Oral Drop, 25mg/ml in 10ml bottle, 40mg/ml in 10ml and 30ml bottles

Syrup, 25mg/5ml

Injection, 25mg/ml in 1 and 2ml ampoules, 50mg/ml in 2ml ampoule

Indications: symptomatic management of psychotic disorders in patients with and for the management of excessive anxiety, tension, and agitation.

Cautions: cardiovascular and cerebrovascular disease, respiratory disease, parkinsonism, epilepsy, acute infection, pregnancy, breast-feeding, renal and hepatic impairment, history of jaundice, leucopenia, hypothyroidism, myasthenia gravis, prostatic hypertrophy, closed-angle glaucoma. Caution also in elderly particularly in very hot or cold weather.

Note: Avoid abrupt withdrawal. Avoid direct contact with chlorpromazine for it causes contact sensitization. Advice patients not to drive cars or operate machineries or do activities requiring alertness

Drug interactions: alcohol, CNS depressants, tricyclic antidepressants such as amitriptyline, antithyroid agents, epinephrine, extra pyramidal reaction causing medication, hypotension producing medication, levodopa, lithium, metrizamide, amphetamines, anticonvulsants including barbiturates.

Contraindications: severe cardiovascular disease, severe CNS depression, and comatose states.

Side effects: akathisia (restlessness or need to keep moving), blurred vision associated with anticholinergic effects; deposition of opaque material in lens, cornea and retina (blurred vision), dystonic extrapyramidal effects (muscle spasms of the face, neck, and back; tic-like or twitching movements; twisting movements of the body; inability to move eyes; weakness of arms and legs), parkinsonian extrapyramidal effects (difficulty in speaking or swallowing; loss of balance control; mask like face; shuffling walk; stiffness of arms or legs; trembling and shaking of hands and fingers); hypotension (fainting), pigmentary retinopathy (blurred vision, defective colour vision, difficulty seeing at night); tardive dyskinesia (lip smacking or packering; putting of cheeks, rapid or worm-like movements of tongue; uncontrolled chewing movements; uncontrolled movements of arms and legs); ammenorrhea and gallatorrhea (female), gynecomastia and impotence (in male), hypothermia (decrease body temperature below Normal); dry mouth; tachycardia, urinary retention; increased appetite and weight gain, cholestatic jaundice, corneal opacity.

Dose and Administration:Adult: *Psychotic disorder:*

Oral: initially 25 to 200 mg (base) two or four times a day, the dosage being increased by 20 to 50mg a day over 3 or 4 days as needed or tolerated. Maximum 1000mg/day.*IM:* (severe) 25 to 50mg (base), the dosage being repeated in one hour if needed and every three to twelve hours thereafter as needed and tolerated. The dosage may be gradually increased over several days as needed and tolerated.**Child** (6 years and older): *Oral:* 0.5mg per kg of body weight every four to six hours, the dosage being adjusted as needed and tolerated.*IM:* 0.55 mg per kg of body weight one or two hours before surgery.

Storage: At room temperature. Protect from light and freezing

Clozapine

Tablet, 25 mg, 50 mg, 100 mg

Indications: schizophrenia, in patients unresponsive to or intolerant of, conventional antipsychotic medicine.

Cautions: it causes severe agranulocytosis and neutropenia, so it should be prescribed strictly where there is central monitoring unit. Initially complete blood count should be monitored weekly for 18 weeks, if it is stable, then every 2 weeks. If Leukocyte count is less than 3,000/mm³ or absolute neutropenia less than 1500/mm³ medication should be discontinued. Prostatic enlargement, narrow-angle glaucoma, history of seizures.

Drug interactions: benzodiazepines, risperidone, amiodarone, ciprofloxacin, ketoconazole, norfloxacin, lidocaine, dextrometorphan, lidocaine, amphetamines, codein, tramadol, and phenobarbital.

Contraindications: history of drug-induced agranulocytosis, bone marrow disorders, severe liver, renal or cardiac disease, toxic or alcoholic psychoses, uncontrolled epilepsy.

Side effects: drowsiness, sedation, fatigue, orthostatic hypotension, dizziness, headache, dry mouth, blurred vision, hypersalivation (common), weight gain, nausea, vomiting, constipation, urinary incontinence and retention, increase in hepatic enzymes. Risk of agranulocytosis and neutropenia is far greater than with other neuroleptics. Fatal myocarditis and cardiomyopathy.

Dose and Administration: *Oral: Adult:* Initially 12.5 to 25 mg daily gradually increased in 25 to 50 mg increments to achieve therapeutic doses in 2 to 3 weeks. Usual range 200 to 450 mg/day in divided doses; up to 600 mg/day may be required. Maximum 900 mg/day.

Storage: store in tight containers at a temperature not exceeding 30°C.

Fluphenazine decanoate

Depot injection, 25 mg/ml in 1ml and 2ml ampoules and in 10ml vial.

Indications: psychotic disorders, particularly chronic schizophrenia who are non compliant patient

Cautions: cardiovascular and cerebrovascular disorders, respiratory disease, epilepsy, acute infections, pregnancy, breastfeeding, renal and hepatic impairment, history of jaundice, leukopenia, hypertrophy, angle-closure glaucoma, elderly.

Drug interactions: anticholinergics, antiepileptics, antihypertensives, antiparkinsonian agents, CNS depressants, metabolic enzyme inducers, antacids.

Contraindications: children, confusional states, impaired consciousness due to CNS depression, parkinsonism, intolerance to antipsychotics, depression, bone-marrow depression, and phaeochromocytoma.

Side effects: extrapyramidal side effects, especially in the elderly; anticholinergic effects, hypotension and sedation; photosensitivity, effects on the heart, jaundice and blood dyscrasias. Increased risk of extrapyramidal reactions with depot injections. Pain may occur at the injection site, and occasionally erythema, swelling and nodules.

Dose and Administration: Adult: Deep IM: initially 12.5 mg; subsequent doses determined by individual response. Usual range 6.25 - 25 mg every 2 - 4 weeks. Higher doses (up to 50 mg per 2 weeks) are rarely required. **Elderly:** Doses at the lower end of the range should be used.

Storage: store at room temperature.

Fluphenazine Hydrochloride

Tablet, 1mg

Indications: schizophrenia, mania, severe anxiety, and other psychoses.

Cautions: pregnancy, breast-feeding, cardiovascular and cerebrovascular disease, parkinsonism, epilepsy, acute infections, history of jaundice, leucopenia, liver and kidney disease, hypothyroidism, myasthenia gravis, prostatic hypertrophy, closed angle glaucoma and elderly patients particularly in very hot or very cold weather

Drug interactions: alcohol, CNS depression producing medications, tricyclic anti-depressants, anti-thyroid agents, epinephrine, extrapyramidal reaction causing medications, hypotension-producing medications, levodopa, lithium, metrizamide, fluoxetine, fluvoxamine, paroxetine, maprotiline, astemizole, terfenadine, sotalol.

Contraindications: severe CNS depression, comatose states, active alcoholism, blood dyscrasias, hepatic function impairment, Reye's syndrome, bone marrow disorders, history of cardiac arrhythmias, congenital long QT syndrome, marked cerebral atherosclerosis.

Side effects: extrapyramidal symptoms, akathisia, tardive dyskinesia, blurred vision, hypothermia, drowsiness, apathy, pallor, night mares, insomnia, depression and more rarely agitation, EEG changes, convulsions; anti muscarinic and cardiovascular symptoms.

Dose and Administration: Adult: Initial: *Oral:* 2.5 to 10 mg a day in divided doses every six to eight hours, the dosage being gradually increased as needed and tolerated. Maintenance: *Oral:* 1 to 5 mg a day as a single dose or in divided doses. Usual adult prescribing limits: - up to 20 mg a day.

Note: Emaciated or debilitated patients usually require a lower initial dosage (1 to 2.5 mg daily), the dosage being gradually increased as needed and tolerated.

Child: *Oral:* 250 to 750 mcg (0.25 to 0.75 mg) one to four times a day. **Elderly:** *Oral:* 1 to 2.5 mg a day, the dosage being gradually increased as needed and tolerated.

Storage: in a tight, light-resistant container at room temperature.

Haloperidol

Tablet, 1mg, 2mg, 5mg

Oral liquid, 2ml/ml

Injection, 5mg/ml in 1ml ampoule

Indications: schizophrenia and other psychotic disorders, mania, psychomotor agitation and violent behaviour; adjunct in severe anxiety.

Cautions: cardiovascular and cerebrovascular disorders, respiratory disease, parkinsonism, epilepsy, acute infections, pregnancy, breastfeeding, renal and hepatic impairment (avoid if severe), history of jaundice, leucopenia (blood counts if unexplained fever or infection); hypothyroidism, myasthenia gravis, prostatic hypertrophy, angle-closure glaucoma; elderly (particularly in very hot or very cold weather); children and adolescents; avoid abrupt withdrawal; patients should remain supine and the blood pressure monitored for 30 minutes after intramuscular injection; see also interactions.

Drug interactions: amitriptyline, carbamazepine, clomipramine, ether (anaesthetic), ethosuximide, halothane, ketamine, nitrous oxide, phenobarbital, phenytoin, procainamide, quinidine, rifampicin, ritonavir, thiopental, valproic acid.

Contraindications: impaired consciousness due to CNS depression; bone-marrow depression; pheochromocytoma; porphyria, basal ganglia disease.

Side effects: see notes above and under chlorpromazine; but less sedating and fewer antimuscarinic or hypotensive

symptoms; pigmentation and photosensitivity reactions rare; extrapyramidal symptoms, particularly dystonic reactions and akathisia especially in thyrotoxic patients; rarely weight loss, hypoglycaemia, inappropriate antidiuretic hormone secretion.

Dose and Administrations:*Oral: Adult:* initially 1.5 to 3mg, 2 to 3 times daily or 3 to 5mg 2 to 3 times daily in severely affected or resistant patients (up to 30mg daily in resistant schizophrenia);

Elderly (or debilitated) initially half adult dose;

Child initially 25 to 50 micrograms/kg daily in 2 divided dose (maximum 10mg daily).

Acute psychotic conditions: deep IM injection: Adult: two 10mg, subsequent doses every 4 to 8 hours according to response (up to every hour if necessary) to total maximum of 18 mg; *Child not recommended.*

Storage: at room temperature in light resistant container. Protect from freezing.

Haloperidol Decanoate

Injection (Depot Oily), 50mg/ml, 100mg/ml in 1ml

Indications: maintenance in schizophrenia and other psychoses.

Cautinos, Contraindications, and Side effects see under haloperidol.

Dose and Administration: Adult: deep I.M injection: initially 50mg every 4 weeks, if necessary increasing by 50 mg increments to 300 mg every 4 weeks; higher doses may be needed in some patients. **Elderly:** initially 12.5 to 25 mg every 4 weeks. **Adult: Psychosis: Oral:** 0.5 to 5mg, 2 to 3 times/day; usual maximum: 30 mg/day

IM (as decanoate): initial; 10 to 20 times the daily oral dose administered at 4 week intervals.

Olanzapine

Tablet, 5mg

Indications: schizophrenia.

Cautions: hepatic impairment, diabetes mellitus; porphyria.

Contraindications: narrow-angle glaucoma.

Side effects: somnolence, agitation, dizziness, asthenia, weight gain, constipation, dry mouth, rhinitis, headache, fever, myalgia and musculoskeletal pains, neck rigidity, orthostatic hypotension, tachycardia, peripheral oedema, raised hepatic enzymes, hypertriglyceridaemia.

Dose and Administration: *Oral: Adult:* initially 5-10 mg once daily. Usual therapeutic dose, 10 mg.

Storage: store at room temperature and protect from light and moisture.

Pimozide

Tablet, 2mg, 4mg, 10mg

Indications: suppression of severe motor and phonic tics in patients with Tourette's disorder who have failed to respond satisfactorily to standard treatment.

Caution: neuroleptic malignant syndrome; renal or hepatic impairment.

Drug interactions: barbiturates, alcohol, analgesics.

Contraindications: treatment of simple tics, patient with severe toxic CNS depression, hypersensitivity to the drug.

Side effects: amenorrhea, dysmenorrhea, vomiting, anorexia, rash and urticaria.

Dose and Administration: Tourette's disorder: *Oral:*

Adult and Child >12 years: initial: 1 to 2mg/day in divided doses, then increase dosage as needed every other day; range is usually 7 to 16 mg/day, maximum dose: 10mg/day or

0.2mg/kg/day are not generally recommended. **Child ≤ 12 years:** initial: 0.05mg/kg preferably once at bed time; may be increased every third day; usual range: 2 to 4 mg/day; do not exceed 10mg/day (0.2mg/kg/day).

Storage: store at room temperature.

Risperidone

Tablets, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg

Oral solution, 1 mg/ml

Indications: for acute and chronic schizophrenic psychoses with positive and/or negative symptoms, or when affective symptoms are prominent. It is also used for the management of behavioural symptoms (aggression, wandering, and agitation) and psychosis associated with dementia.

Cautions: Parkinson's disease, cardiovascular disease, and hepatic or renal impairment.

Drug interactions: chlorpromazine, fluoxetine, miconazole, quinidine, quinine, ritonavir, clozapine, metoclopramide, levodopa, carbamazepine.

Contraindications: hypersensitivity to risperidone.

Side effects: are similar to those of chlorpromazine; it has a lower tendency to induce extrapyramidal symptoms than the classic neuroleptics, although extrapyramidal phenomena, tardive dyskinesia and the neuroleptic malignant syndrome have all been reported. Orthostatic hypotension has been observed, particularly with high initial doses. It can induce a dose dependent increase in plasma prolactin concentration. Weight gain may be notable.

Dose and Administration: *Oral: Adult:* 2 mg/day on the 1st day, 4 mg/day on the 2nd day, 6 mg/day on the 3rd day; then individualised if necessary. Usual range 4 to 8 mg/day. **Elderly** (or in renal or hepatic impairment): initially 1 mg/day, increased

by 1 mg/day up to 2 to 4 mg/day. *Note: Doses > 10 mg/day do not appear to produce increased efficacy, and may cause increased side effects.*

Storage: protect from light.

Thioridazine Hydrochloride

Tablet, 10mg, 25mg, 100mg

Indications: under specialist supervision, second line treatment of schizophrenia in adults (see notes above).

Cautions: see under chlorpromazine; ECG screening and electrolyte measurement before treatment, after each dose increase and at 6 month intervals; also monitor for visual defects on prolonged use; avoid in porphyria.

Drug interactions: antiepileptics (except carbamazepine), barbiturates, antihypertensives and B-blockers, anticoagulants; anaesthetics, analgesics, anti-arrhythmics, antibacterials, antidepressants, antifungals, antihistamines, antimalarials, other antipsychotics, antivirals, diuretics, lithium, pentamidine isetionate, sibutramine

Contraindications: in patients with: Clinically significant cardiac disorders (e.g. cardiac failure, angina, cardiomyopathy or left ventricular dysfunction; QTc interval prolongation (see cautions & Drug interactions); a history of ventricular arrhythmias or Torsades de pointes; Bradycardia or 2nd or 3rd degree heart block; A family history of QTc interval prolongation; Uncorrected hypokalaemia or hypomagnesaemia

Side effects: see under chlorpromazine; less sedating than chlorpromazine, and extrapyramidal symptoms and hypothermia rarely occur; more likely to induce hypotension and increased risk of cardiotoxicity and prolongation of QT interval, pigmentary retinopathy (with reduced visual acuity, brownish colouring of vision, and impaired night vision) occurs rarely

with high doses; sexual dysfunction, particularly retrograde ejaculation may occur.

Dose and Administration: *Oral: Adult:* 50 to 300 mg daily (initially in divided doses): Maximum 600 mg daily (in hospital patients only); child not recommended.

Storage: at room temperature in a tight, light resistant container.

Trifluoperazine hydrochloride

Tablets, 1 mg, 5 mg

Capsules, 2 mg, 10 mg

Syrup, 1 mg/5 ml

Injection, 1 mg/ml; 2 mg/ml

Indications: treatment of schizophrenia and for management of psychotic disorders.

Cautions: cardiovascular disease, seizures, hepatic dysfunction, narrow-angle glaucoma, or bone marrow suppression, myasthenia gravis or parkinson's disease.

Drug interactions: aminoglutethimide, carbamazepine, nevirapine, phenobarbital, phenytoin, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, isoniazid and protease inhibitors.

Contraindications: severe CNS depression; bone marrow suppression; blood dyscrasias, coma.

Side effects: hypotension, cardiac arrest, extrapyramidal symptoms, dizziness, headache, constipation, stomach pain, vomiting, hepatotoxicity, dizziness, and headache.

Dose and Administration: **Adult:** *Oral:* initially 5 mg twice daily or 10 mg daily in modified - release form, increased by 5 mg after 1 week, then at intervals of 3 days, according to the response. *I.M:* 1 to 2 mg every 4-6 hours as needed up to 10 mg/24 hours maximum; for elderly 1 mg every 4 to 6 hours; increase at 1 mg increments; do not exceed 6 mg/day. **Child** up

to 12 years: *Oral*: initially up to 5 mg daily in divided doses, adjusted according to response, age, and body weight. *I.M*: 1 mg twice daily. *Short term adjunctive management of severe anxiety*: *Oral*: **Adult**: 2 - 4 mg daily in divided doses or 2 - 4 mg daily in modified-release form, increased if necessary to 6 mg daily; **Child** 3 - 5 years, up to 1 mg daily, 6 - 12 years, up to 4 mg daily.

Storage: store at room temperature.

5.4. Antidepressants

The major classes of Antidepressants include the tricyclic and related antidepressants, the Selective Serotonin Re-uptake Inhibitors (SSRIs), and the Mono-Amine Oxides Inhibitors (MAOIs); and a range of other compounds not usually categorized in to groups.

This section covers Tricyclic Antidepressants (TCAs), SSRIs and Serotonin noradrenaline re-uptake inhibitors (SNRIs) and Norepinephrine-dopamine reuptake inhibitor (NDRI).

TCAs are most effective for treating moderate to severe endogenous depression associated with psychomotor and physiological changes such as loss of appetite and sleep disturbances; improvement in sleep is usually the first benefit of therapy. Since there may be an interval of 2 weeks before the antidepressant action takes place electroconvulsive treatment may be required in severe depression when delay is hazardous or intolerable. Some tricyclic antidepressants are also effective in the management of panic disorder.

TCAs are also important in some forms of neuralgia; and in nocturnal enuresis in children. Tricyclic and related antidepressant drugs can be roughly divided in to those with additional sedative properties and those, which are less so.

Amitriptyline: it is tertiary amine tricyclic antidepressants. Agitated and anxious patients tend to respond best to this drug because of its additional sedative property. Though amitriptyline can be sedating, it is not recommended for use purely as a sedative - hypnotic, as other agents have greater efficacy with fewer adverse effects.

Amitriptyline and imipramine are well established and relatively safe and effective, but nevertheless have more marked antimuscarinic and cardiac side effects than other TCAs.

SSRIs which include fluoxetine, fluvoxamine, sertraline, escitalopram and others have minimal anticholinergic effects and are less cardiotoxic than the TCAs. Recent evidence suggests that there is an increased risk of suicidality in depressed children and adolescents given antidepressant medications, and SSRIs in particular. This increased risk has not been identified with SSRI treatment for anxiety disorders. Serotonin and noradrenaline re-uptake inhibitors (SNRIs), e.g. duloxetine, have tolerability profiles comparable to those of SSRIs. Duloxetine weakly inhibits dopamine re-uptake with no significant affinity for histaminergic, dopaminergic, cholinergic or adrenergic receptors.

NDRI, e.g., Bupropion, for the treatment of depression, it is often used in conjunction with an SSRI. It is one of the few antidepressants that do not have sexual side effects, and it is sometimes used to counteract the loss of libido and other sexual side effects caused by SSRIs. Bupropion has many uses besides treatment of depression, used in a smoking cessation (see section 4.7).

5.4.1. Tricyclic Antidepressants

Amitriptyline

Tablet, 10mg, 25mg, 50mg

Indications: depressive illness, particularly where sedation is required; nocturnal enuresis in children.

Cautions: cardiac disease (Particularly with arrhythmias), history of epilepsy, pregnancy and breastfeeding, elderly, hepatic impairment (avoid if severe), thyroid disease, phaeochromocytoma, history of mania, psychoses (may aggravate psychotic symptoms) angle closure glaucoma, history of urinary retention, concurrent electro-convulsive therapy; if possible avoid abrupt withdrawal; anaesthesia (increased risk of arrhythmias and hypotension); porphyria

Drug interactions: alcohol, other CNS depressants, antithyroid agents, phenothiazine, cimetidine, clonidine, guanadrel, guanethidine, extrapyramidal reaction causing medications, metrizamide, MAO inhibitors and sympathomimetics.

Contraindications: recent myocardial infarction, arrhythmias (particularly heart block), not indicated in manic phase, severe liver disease.

Side effects: dry mouth, sedation, blurred vision (disturbance of accommodation, increased intraocular pressure), constipation, nausea, difficulty with micturation; cardiovascular. Side effects such as ECG changes, arrhythmias, postural hypotension, tachycardia, syncope, particularly with high doses; sweating, tremor, rashes and hypersensitivity reactions (including urticaria, photosensitivity), behavioural disturbances (particularly children), hypomania or mania, confusion (particularly elderly), interference with sexual function, blood sugar changes; increased appetite and weight gain (occasionally weight loss), endocrine side effects such as testicular enlargement, gynaecomastia, galactorrhoea; also convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leucopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia (may

be due to inappropriate antidiuretic hormone secretion), abnormal liver function tests (jaundice);

Dose and Administration: *Oral Adult:* Depression: initially 50-75 mg (elderly and adolescents 30 - 75 mg) daily in divided doses or as a single dose at bedtime increased gradually as necessary to 150 - 200 mg;

Child: under 16 years not recommended for depression; *Nocturnal enuresis:* Child 7 to 10 years, 10 to 20 mg, 11 to 16 years, 25 to 50mg at night; maximum period of treatment (including gradual withdrawal) 3 months full physical examination before further course.

Storage: at room temperature in a well closed container.

Amitriptyline + Chlordiazepoxide

Capsule, 12.5mg + 5mg; 25mg + 10mg

Indications: treatment of moderate to severe anxiety and/or agitation and depression.

Dose and Administration: *Oral:* 3-4 tablets in divided doses; this may be increased to 6 tablets/day as required; some patients respond to smaller doses and can be maintained on 2 tablets.

Clomipramine Hydrochloride

Capsules, 10mg, 25mg, 50mg

Indications: phobic and obsessional states, panic attacks.

Cautions: cardiac disease, history of epilepsy, pregnancy, breastfeeding, elderly, hepatic impairment, thyroid disease, phaeochromocytoma, history of mania, psychoses, angle-closure glaucoma, history of urinary retention, concurrent electroconvulsive therapy, avoid abrupt withdrawal, anaesthesia.

Drug interactions: alcohol, artemether + Lumefantrine, carbamazepin, chlorpromazine, epinephrine, ethosuximide,

fluphenazine, haloperidol, phenobarbital, phenytoin, procainamide, quinidine, ritonavir, valproic acid.

Contraindications: recent myocardial infarction, arrhythmias (especially heart block); manic phase in bipolar disorders, severe liver disease; children, porphyria.

Side effects: sedation, dry mouth, blurred vision, constipation, nausea, difficulty in micturition; cardiovascular adverse effects particularly with high dosage including ECG changes, arrhythmias, postural hypotension, tachycardia, syncope, sweating, tremor, rash and hypersensitivity reactions, behavioral disturbances, hypomania or mania, confusion, interference with sexual function, blood sugar changes, increased appetite and weight gain, endocrine adverse effects, convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leukopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia, abnormal liver function test.

Dose and Administration: *Oral:Adult:* initially 50 to 75mg/day, increased gradually to 150 mg/day if necessary. May be given as a single dose at night or in 2 to 3 divided doses.**Elderly:** initially 10mg/day, increasing carefully to 30 - 50mg/day.

Obsessive-Compulsive disorder: Dosage may have to be increased beyond those generally used, e.g. to more than 200mg/day; maximum 250mg/day.

Child: initially 10/mg/day, increased gradually to 20mg for 5-7 years old, and to 20 to 50 mg for 8 - 14 year olds. Alternatively, 18 - 23kg, 0.5 to 0.9 mg/kg/day; 25 - 48 kg, 0.8 to 1.1mg/kg/day

Storage: store at room temperature.

Imipramine

Tablet, 10mg, 25mg

Indications: management of depressive illness. Nocturnal enuresis (adjunctive therapy) in children over 6 years of age, after exclusion of organic pathology; adjuvant to pain relief in chronic pain syndromes, also drug management of panic disorders.

Cautions: hyperthyroidism (or on thyroxin therapy), arrhythmias, epilepsy, prostatic enlargement, closed-angle glaucoma or impaired liver function.

Drug interactions: antihistamines, antipsychotics and anticholinergic type antiparkinsonian agents, cimetidine, fluoxetine, paroxetine and steroids, hepatic enzyme-inducing agents, MAO inhibitors.

Contraindications: early post myocardial infarction period and heart block.

Side effects: dry mouth, blurred vision, constipation, and difficulty with micturition. Blood pressure changes, syncope, tachycardia, arrhythmias, precipitation of epileptic seizures, sedation, excessive sweating, muscle tremors, restlessness, weakness, interference with sexual function and confusional states, especially in the elderly, extrapyramidal symptoms, allergic skin reactions and, rarely, cholestatic jaundice and blood disorders, including agranulocytosis. Occasionally produce agitation and insomnia.

Dose and Administration: *Oral: Adult: Depression:* initial: 25mg 3-4 times/day, increase dose gradually, total dose may be given at bedtime; maximum: 300mg/day. **Elderly:** initially 10-25mg at bedtime; increasing up to 100mg/day as required and if tolerated.

Child: *Nocturnal enuresis:* 6 - 7 years, 10 - 25mg; 8 - 11 years, 25 - 50mg; > 11 years, 25 - 75mg; given as a single dose after the evening meal.

Storage: store at room temperature.

Nortriptyline

Tablet, 10mg, 25mg

Indications: Depressive illness; nocturnal enuresis in children; neuropathic pain

Cautions: bipolar disorder; schizophrenia; pregnancy; a history of seizures, bladder problems, or glaucoma; hyperthyroidism; diabetes.

Drug interactions: Anticholinergic medications (e.g., atropine, benztropine, pinaverium), carbamazepine, certain antiarrhythmic medications (e.g., propafenone, flecainide, encainide), cimetidine, fluoxetine, guanethidine, other antidepressants especially MAO inhibitors (e.g., phenelzine, tranylcypromine), phenothiazines (e.g., perphenazine, chlorpromazine), quinidine, reserpine, sympathomimetic medications (e.g., epinephrine)

Contra-indications: Hepatic impairment, Pregnancy; use only if potential benefit outweighs risk, Breast-feeding

Side-effects: abdominal pain, stomatitis, diarrhoea, hypertension, oedema, flushing, restlessness, fatigue, and mydriasis.

Dose and Administration: Adults: *Depression:* 25 mg 3 or 4 times daily; dosage should begin at a low level and be increased as required (max. 150 mg daily); Adolescent and elderly 30 to 50 mg daily in divided doses; **child not recommended for depression.**

Nocturnal enuresis: **child** 7 years 10 mg, 8 to 11 years 10 to 20 mg, over 11 years 25 to 35 mg, 30 minutes before bedtime; max period of treatment (including gradual withdrawal) 3 months full physical examination and ECG before further course. *Neuropathic pain [unlicensed]:* initially 10 mg daily at night, gradually increased if necessary to 75 mg daily; higher doses under specialist supervision

5.4.2. Selective Serotonin Re-uptake Inhibitors (SSRIs)

Escitalopram

Tablet, 5mg, 10mg, 20mg

Indications: treatment of major depressive disorder; generalized anxiety disorder (GAD).

Cautions: previous seizure disorder, monitor worsening of depression or suicidality.

Drug interactions: non selective MAO inhibitors (phenelzine), fluconazole, fluvoxamine, gemfibrozil, isoniazid, omeprazole, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, protease inhibitors, quinidine and verapamil. Combined use of sumatriptan; NSAIDs, aspirin. Carbamazepine, phenytoin, rifampin, nevirapine, phenoarbutal, phenytoin and rifamycins

Contraindications: hypersensitivity reaction, concomitant use or within 2 weeks of MAO inhibitors.

Side effects: headache, somnolence, insomnia, nausea, chest pain, hypertension, palpitation, dizziness, fatigue, dreaming abnormal, concentration impaired, fever, irritability, lethargy, lightheadedness, migraine, vertigo, yawning, rash, hot flashes, libido decreased, anorgasmia, menstrual cramps, menstrual disorder, diarrhea, xerostomia, appetite decreased, constipation, indigestion, abdominal pain, abdominal cramps, appetite increased, flatulence, heartburn, toothache, vomiting, weight gain/loss, impotence, urinary tract infection, blurred vision, sinusitis, cough.

Dose and Administration: *Depression, GAD: Oral: Adult:* initial: 10mg/day; dose may be increased to 20mg/day after at least 1 week. **Elderly:** 10mg/day; bioavailability and half-life are increased by 50% in the elderly

Storage: store at room temperature.

Fluoxetine

Capsule, 20mg

Indications: depressive disorders, bulimia nervosa; obsessive-compulsive disorder (OCD).

Cautions: hepatic or renal impairment, epilepsy and diabetes.

Drug interactions: flecainide, metoprolol, nifedipine, diclofenac, omeprazole, clozapine, fluphenazine, haloperidol, risperidone, antidepressants, terfenadine, carbamazepine and phenytoin; CNS depressants, diazepam and alprazolam; highly protein-bound drugs; lithium, MAO inhibitors; moclobemide, serotonergic agents.

Side effects: headache and gastrointestinal disturbances, CNS effects; mania or hypomania may be precipitated in some patients. Seizure threshold may be lowered, predisposing to epilepsy. Skin rashes have been reported and may be a warning of a serious systemic reaction, possibly related to vasculitis. Decreased libido and sexual dysfunction, weight loss, asthenia, hypoglycemia, hyponatraemia, and elevated transaminase levels. Altered platelet function and abnormal bleeding.

Dose and Administration: *Oral: Adult: Depression:* 20mg/day. May be increased by 20mg/day, if required; maximum 60 mg/day. The elderly: use the lowest effective dose. *Bulimia nervosa:* increase up to 60mg/day. *OCD:* 20-60mg/day; maximum 80 mg/day. **Child:** *Depression:* 8-18 years: 10-20 mg/day; lowerweight children can be started at 10mg/day, may increase to 20 mg/day after 1 week if needed. *OCD:* 7-18 years: initial: 10mg/day; in adolescents and higher-weight children, dose may be increased to 20mg/day after 2 weeks. Range: 10-60 mg/day.

Storage: store at controlled room temperature.

Fluvoxamine maleate

Tablets, 40 mg, 100 mg

Indications: Major depressive disorders, especially where sedation is undesirable; panic disorder; obsessive-compulsive disorder, social phobia.

Cautions: mania, epilepsy, cardiac disease, hepatic or renal impairment.

Drug interactions: MAO inhibitors, cimetidine, lithium, phenytoin, serotonergic agents, sumatriptan, TCAs, phenothiazine neuroleptics, antiarrhythmics class Ic (e.g. propafenone), warfarin.

Contraindications: hypersensitivity to fluvoxamine.

Side effects: nausea, somnolence, sweating, tremor, dry mouth, asthenia, insomnia, constipation, dizziness, sexual dysfunction, dyspepsia, vomiting, diarrhea, anxiety, decreased appetite and headache. Extrapyramidal effects have been reported, also skin rashes, bruising and elevations of hepatic enzymes, with isolated reports of serious liver function abnormalities. Hyponatraemia has been reported, especially in the elderly.

Dose and Administration: *Oral: Adult: Depression:* initially 100mg daily as a single dose in the evening, increased if necessary; usual range 100 - 200 mg/day; maximum 300mg/day. Doses above 150mg/day should be given in 2-3 divided doses. *OCD:* initially 50mg daily for 3- 4 days, increased gradually; usual range 100-200mg/day; maximum 300mg/day. If no improvement within 10 weeks, treatment should be reconsidered. *Child: OCD:* 8-17 years: initial: 25mg at bedtime; adjust in 25 mg increments at 4-7 day intervals, as tolerated, to maximum therapeutic benefit: Range: 50-200mg/day. Maximum: 8-12 years: 200mg/day, adolescents: 300mg/day; lower doses may be effective in female versus male patients.

Storage: store at room temperature.

Paroxetine

Tablet, 20mg

Indications: Major depression, obsessive-compulsive disorder, panic disorder; social anxiety disorder; post-traumatic stress disorder; generalised anxiety disorder

Cautions: Also achlorhydria or high gastric pH (reduced absorption of oral suspension)

Contraindications: Hepatic impairment, Renal impairment, Pregnancy and Breast-feeding

Side effects: also yawning; abnormal dreams; raised cholesterol; less commonly arrhythmias, confusion, urinary incontinence; rarely panic attacks and paradoxical increased anxiety during initial treatment of panic disorder (reduce dose), depersonalisation, and neuroleptic malignant syndrome-like event; rarely restless legs syndrome; very rarely peripheral oedema, acute glaucoma, hepatic disorders (e.g. hepatitis), and priapism; also reported tinnitus, extrapyramidal reactions (including orofacial dystonias) and withdrawal reactions

Dose and Administration: *Major depression, social anxiety disorder, post-traumatic stress disorder, generalised anxiety disorder:* **Adult** over 18 years: usually 20 mg each morning, higher doses on specialist advice only; maximum 50 mg daily (**elderly** 40 mg daily); **child** under 18 years not recommended.

Obsessive-compulsive disorder: **Adult** over 18 years: initially 20 mg each morning increased gradually in steps of 10 mg to usual dose of 40 mg daily, higher doses on specialist advice only; max. 60 mg daily (**elderly** 40 mg daily).

Panic disorder: **Adult** over 18 years: initially 10 mg each morning increased gradually in steps of 10 mg to usual dose of 40 mg daily, higher doses on specialist advice only; maximum 60 mg daily (elderly 40 mg daily).

Sertraline hydrochloride

Tablets, 50mg, 100mg

Indications, Cautions, Drug interactions and Side effects; see under fluvoxamine.

Dose and Administration: *Oral:Adult:Depression:* initially 50mg daily, usual range 50 - 100 mg/day. May be increased, if necessary, by 50mg over several weeks up to a maximum of 200 mg/day.*OCD:* the minimum effective dose is 50mg/day. Increase, if necessary, in 50mg increments over several weeks up to a maximum of 200mg/day.*Panic disorder:* initially 25mg daily, increased to 50mg/day after 1 week, and thereafter, if necessary, in 50mg increments up to a maximum of 200mg/day.**Child:** *OCD:* 6-12 years: initial: 25mg once daily; 13-17 years: initial: 50mg once daily.

Storage: store at controlled room temperature.

5.4.3. Serotonin and noradrenaline re-uptake inhibitors (SNRIs)

Duloxetine

Tablet, 30mg, 40mg, 60mg

Indications: treatment of major depressive disorder.

Cautions: renal impairment or with concomitant CNS depressants.

Drug interactions: MAO inhibitors, TCAs, buspirone, SSRIs, tramadol, amiodarone, chlorpromazine, ciprofloxacin, delavirdine, fluvoxamine, fluoxetine, ketoconazole, miconazole, norfloxacin, ofloxacin, aminoglutethimide, carbamazepine, phenobarbital, and rifampicin.

Contraindications: hypersensitivity to the drug, concomitant use or within 2 weeks of MAO inhibitors; uncontrolled narrow angle glaucoma.

Side effects: insomnia, somnolence, dizziness, headache, nausea, xerostomia, constipation, appetite decreased.

Dose and Administration: *Oral:* **Adult:** initial: 40-60 mg/day; dose may be divided (i.e., 20 or 30 mg twice daily) or given as a single dose of 60mg; maximum dose: 60 mg/day. **Elderly:** treatment or major depressive disorder; initial dose; 20mg 1-2 times/day; increase to 40-60mg/day as a single daily dose or in divided dose.

Storage: store at room temperature.

5.4.4. Norepinephrine-dopamine reuptake inhibitor

Bupropion

Tablet, 75mg, 100mg

Indications: treatment of depression; adjunct in smoking cessation.

Caution: elderly; predisposition to seizures (prescribe only if benefit clearly outweighs risk) including concomitant use of drugs that lower seizure threshold, alcohol abuse, history of head trauma, and diabetes; measure blood pressure before and during treatment.

Drug interactions: prochlorperazine, chlorpromazine, and other antipsychotic medications of the phenothiazine class. Additionally, persons who are withdrawing from benzodiazepines [for example, diazepam, alprazolam] are at increased risk for seizures. Carbamazepine, MAO inhibitors, warfarin

Contraindications: Acute alcohol or benzodiazepine withdrawal; severe hepatic cirrhosis; CNS tumour; history of seizures, eating disorders, or bipolar disorder

Side effects: dry mouth, gastro-intestinal disturbances, taste disturbance; agitation, anxiety, dizziness, depression, headache,

impaired concentration, insomnia (reduced by avoiding dose at bedtime), tremor; fever; pruritus, rash, sweating; less commonly chest pain, flushing, hypertension, tachycardia, anorexia, asthenia, confusion, tinnitus, and visual disturbances; rarely hepatitis, jaundice, palpitation, postural hypotension, vasodilatation, abnormal dreams, ataxia, dystonia, depersonalisation, hallucinations, hostility, incoordination, irritability, impaired memory, paraesthesia, seizures, twitching, blood-glucose changes, urinary frequency, urinary retention, exacerbation of psoriasis, and Stevens-Johnson syndrome; very rarely aggression, delusions, paranoid ideation, and restlessness; also reported suicidal ideation

Dose and Administration: Adult: over 18 years, start 1–2 weeks before target stop date, initially 150 mg daily for 6 days then 150 mg twice daily (max. single dose 150 mg, max. daily dose 300 mg; minimum 8 hours between doses); period of treatment 7–9 weeks; discontinue if abstinence not achieved at 7 weeks; consider max. 150 mg daily in patients with risk factors for seizures; Elderly max. 150 mg daily

Storage: at room temperature, 15–25 C.

5.5. Mood Stabilizers

Lithium is regarded as a mood stabilizer, with antimanic and antidepressant effects. Primary use is as a prophylactic agent in bipolar affective disorders, where it has been shown to reduce chiefly the manic, but also the depressive relapses. It is also useful in treating the acute manic stage, but is rarely recommended for depressive illnesses of the unipolar type.

Lithium carbonate

Tablet, 300 mg, 400 mg

Indications: treatment and prophylaxis of mania, prophylaxis of bipolar disorder and recurrent depression.

Cautions: measure serum-lithium concentration about 4 days after starting treatment, then weekly until stabilized, then at least every 3 months, monitor thyroid function and renal function, maintain adequate fluid and sodium intake, reduction of dose or discontinuation may be necessary, in diarrhoea, vomiting and intercurrent infection, pregnancy, breastfeeding, elderly, diuretic treatment, myasthenia gravis, surgery, if possible, avoid abrupt withdrawal.

Drug interactions: combination of lithium with other drugs, including over-the-counter medicines, should be carefully monitored, ACE inhibitors, antithyroid agents of iodides, neuroleptics, non-steroidal anti-inflammatory agents, thiazide and loop diuretics, xanthines.

Contraindications: cardiac disease, renal impairment or urinary retention, CNS disorders, e.g. epilepsy.

Side effects: gastrointestinal disturbances, fine tremor, polyuria, polydipsia, weight gain and oedema; signs of intoxication include blurred vision, muscle weakness, increasing gastrointestinal disturbances, increased CNS disturbances and require withdrawal of treatment, with severe overdose, hyperreflexia and hyperextension of the limbs, convulsions, toxic psychoses, syncope, oliguria, circulatory failure, coma, occasionally death, goitre, raised antidiuretic hormone concentration, hypothyroidism, hypokalaemia, ECG changes, exacerbation of psoriasis and kidney changes may occur.

Dose and Administration: *Oral: Adult:* initially 20 mg/kg/day in divided doses, adjusting the dose, if necessary, to achieve a plasma concentration of 0.4 - 0.8 millimol/L. Sustained - release preparations are given once or twice daily.

Storage: store in a well-closed container at room temperature.

5.6. Anticonvulsants

Treatment should always be started with a single drug, but the choice of an anticonvulsant can only be made on an individual basis and will depend on the efficacy of the drug and the patient's tolerance of treatment. If a drug fails to control the seizures after it has been used in full therapeutic dosage for an adequate period, or if it is not tolerated, it should be gradually substituted with another with the first drug being withdrawn only when the new regimen is mainly established. If monotherapy is ineffective, two drugs should be given in combination and several regimens may need to be tried before the most appropriate is found.

Carbamazepine is used as a first-line drug in the treatment of partial seizures with or without secondary generalization and tonic-clonic seizures; it is also effective in other forms of epilepsy. It may exacerbate absence and myoclonic seizures, and may cause deterioration of juvenile myoclonic epilepsy if used to treat tonic-clonic seizures occurring within the syndrome. Carbamazepine is often preferred in children because it lacks the dysmorphic adverse effects associated with phenytoin. However, carbamazepine does possess some unique pharmacokinetic characteristics, particularly in children and manipulation of dosage forms and schedules to accommodate individual needs may be necessary. Carbamazepine elimination is more rapid in children and accumulation of the active metabolite is often higher than in adults.

Phenytoin is used as a first-line drug in the treatment of partial and tonic-clonic seizures; it may also be used in other forms of epilepsy, with the exception of absence and myoclonic seizures. The non-linear pharmacokinetics of phenytoin make it difficult to use, particularly at higher doses, because small increases in doses may produce large rises in plasma concentrations.

Phenytoin may be unsuitable in adolescents and women because of potential coarsening of the facial features, acne, or hirsutism. Gingival hyperplasia and tenderness can also be a problem. The potential effects of phenytoin on cognition may make it less suitable in young children.

Valproic acid or valproate is used as a first-line drug in the treatment of absence, tonic-clonic, and myoclonic seizures. It may also be used for partial seizures and is effective in some epileptic syndromes.

Phenobarbitone is used in all forms of epilepsy with the exception of absence seizures. It has been widely used in children and neonates in particular, perhaps because of convenient of administration and linear pharmacokinetics, but there is concern about its effects on cognition.

The use of benzodiazepines for the long-term treatment of epilepsy is limited by problems of tolerance, sedation, and the development of dependence; withdrawal seizures are also a problem. *Diazepam* is not used in the prophylaxis of epileptic seizures but is of value in the treatment of febrile convulsions

Withdrawal: Treatment is normally continued for a minimum of two years after the last seizure. Withdrawal should be extended over a period of several months since abrupt withdrawal can lead to complications such as status epilepticus. Abrupt discontinuation is therefore never warranted. Many adult patients relapse once treatment is withdrawn and it may be justified to continue treatment indefinitely, particularly when the patient's livelihood or lifestyle can be endangered by recurrence of a seizure.

Pregnancy and Breastfeeding: There is an increased risk of birth defects with the use of anticonvulsants, particularly carbamazepine, valproate and phenytoin. However, if there is good seizure control, there is probably no advantage in changing

pregnant patients' antiepileptic drugs. In view of the risks of neural tube and other defects, patients who may become pregnant should be informed of the risks and referred for advice, and pregnant patients should be offered counseling and antenatal screening. To counteract the risk of neural tube defects, adequate foliate supplements are advised for women before and during pregnancy. In view of the risk of neonatal bleeding associated with carbamazepine, phenobarbital and phenytoin, prophylactic phytomenadione (vitamin k1) is recommended for the neonatal and the mother before delivery. Antiepileptic drugs can be continued during breastfeeding.

Acetazolamide

Tablet, 125 mg, 250 mg

Indications: treatment of centrencephalic epilepsies.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.6. under acetazolamide.

Dose and Administration: *Oral: Adult:* 8-30mg/kg/day in 1-4 divided doses.

Child: 8-30 mg/kg/day in 1-4 divided doses, not to exceed 1g/day.

Carbamazepine

Tablet, 100mg, 200mg

Syrup, 100mg/5ml

Indications: partial and secondary generalized tonic-clonic seizures, some primary generalized seizures; trigeminal neuralgia, prophylaxis of bipolar disorder unresponsive to lithium.

Cautions: hepatic or renal impairment; cardiac disease (see also contraindications). Skin reactions, history of hematological reactions to other drugs; glaucoma; pregnancy (see notes above),

breastfeeding (see notes above); avoid abrupt withdrawal (see notes above); see also interactions

Drug interactions: acetazolamide, amitriptyline, chloroquine, chlorpromazine, ciclosporin, cimetidine, clomipramine, clonazepam, oral contraceptives, dexamethasone, erythromycin, ethosuximide, fludrocortisone, fluphenazine, haloperidol, hydrocortisone, isoniazide, levonorgestrel, medroxyprogesterone, mefloquine, norethisterone, phenobarbital, phenytoin, prednisolone, valproic acid, verapamil, warfarin.

Contraindications: atrioventricular conduction abnormalities; history of bone marrow depression; porphyria.

Side effects: dizziness, drowsiness, headache, ataxia, blurred vision, diplopia (may be associated with high plasma levels); gastrointestinal intolerance including nausea and vomiting, anorexia, abdominal pain, dry mouth, diarrhea or constipation; commonly, mild transient generalized erythematous rash (withdraw if worsens or is accompanied by other symptoms); leukopenia and other blood disorders (including thrombocytopenia, agranulocytosis and aplastic anemia); cholestatic jaundice, hepatitis, acute renal failure, Stevens Johnson syndrome (erythema multiform), toxic epidermal necrolysis, alopecia, thromboembolism, arthralgia, fever, proteinuria, lymphnode enlargement, arrhythmias, heart block and heart failure, dyskinesias, parasthesia, depression, impotence, male infertility, gynaecomastia, galactorrhoea, aggression, activation of psychosis, photosensitivity, pulmonary hypersensitivity, hyponatraemia, oedema, disturbances of bone metabolism with osteomalacia also reported; confusion and agitation in elderly.

Dose and Administration: Adult: *Oral: Epilepsy:* initially, 100 - 200 mg twice daily, with increments of 100-200mg/day at

weekly intervals according to seizure control and adverse symptoms. Maintenance range (i.e. minimum effective dosage) is generally 600-1200 mg/day in divided doses, but up to 1.6g/day may occasionally be necessary. **Elderly:** start with 100mg twice daily and increase as required. *Trigemial neuralgia and pain syndromes:* initially 100mg twice daily, increased by 100mg every 12 hours until pain is relieved (maximum 1.2g/day). Once pain is controlled, the dose may be decreased over a period of a few weeks to a maintenance dose, usually 400-800 mg/day.

Prophylaxis of bipolar disorder unresponsive to lithium: initially 400mg daily in divided doses increased until symptoms controlled; usual range 400 - 600mg daily; max. 1.6 g daily. *Mood stabilizer:* Dosage as for epilepsy (usually 400-600mg/day). Response usually takes 7-10 days to become evident. **Child:** *Epilepsy:* 12-15 years, as for adults but maximum 1g/day. 6-12 years, initially 100mg twice daily, increasing by 100mg/day at weekly intervals until optimal response and plasma levels are obtained. Usual maintenance, 400-800 mg/day (maximum 1g/day). Under 6 years, initially 10-20mg/kg/day in 2-3 divided doses, increasing by up to 100mg/day at weekly intervals as needed. Usual maintenance 200-350 mg/day, maximum 400 mg/day; under 1 year, 100-200 mg/day.

Storage: at room temperature in a tight, light-resistant container. Protect from freezing (syrup).

Clonazepam

Injection, 1 mg/ml in 1ml ampoule

Tablet, 0.5 mg, 1mg, 2 mg

Indications: management of myoclonic and atonic/ akinetic seizures in children, and as an adjuvant agent in the management of other forms of epilepsy. It is used as an

alternative to diazepam in the emergency treatment of status epilepticus.

Cautions: respiratory disease; hepatic impairment, renal impairment; elderly and debilitated; pregnancy; breastfeeding; avoid sudden withdrawal, porphyria.

Drug interactions: acetazolamide, alcohol, carbamazepine, phenobarbital, phenytoin, ritonavir.

Contraindication: hypersensitivity to clonazepam.

Side effects: frequently - fatigue, drowsiness, ataxia and clumsiness, especially early in treatment. Paradoxical hyperkinesia, excitability, aggressiveness and other behavioral problems may occur, particularly in children with pre-existing brain damage or in patients with a history of aggressiveness. Other effects include headache and muscle weakness.

Dose and Administration: Adult: Oral: start with small doses and increase gradually to an optimum dose according to individual response. Initially 1mg at night for 4 nights, increased over 2 - 4 weeks to usual maintenance of 4 - 8 mg/day. *Status epilepticus: IV:* 1mg injected slowly, over 30 seconds; may be repeated as required. **Child: Oral:** initially 0.05mg/kg/day in 3 divided doses, increased slowly if needed to a maximum of 0.3 mg/kg/day. Usual maintenance: < 1 year, 0.5 - 1mg/day; 1 - 5 years, 1 - 3mg/day; 5 - 12 years, 3 - 6mg/day, in 3 divided doses. *Status epilepticus: IV:* 0.5mg by slow injection.

Storage: store tablets at room temperature.

Diazepam

Suppository, 5mg, 10mg

Injection, 5mg/ml in 2ml ampoule

Indications: It is indicated as adjunct in static epilepticus and severe recurrent convulsive seizures.

Cautions, Drug interactions, Contraindications, and Side effects; see notes on diazepam under 4.2.

Dose and Administration:**Adult:***anticonvulsants:IV:* 5-10mg initially, the dosage being repeated, if necessary, at 10-15 minutes interval up to a maximum dose of 30mg.**Child:***Anticonvulsant: status epilepticus and severe recurrent convulsive seizures.*Infants over 30 days of age and children up to 5 years of age:*IV (slow):* 0.2 to 0.5 mg every 2-5 minutes up to a maximum of 5mg. If necessary, therapy should be continued.**Child 5 and older:** *IV (slow):* 1mg every two to five minutes up to a maximum of 5mg. If necessary, therapy may be repeated in two or four hours. **Elderly:***Anticonvulsant:IM or IV,* initially, 2 to 5 mg per dose, the dosage being increased gradually as needed and tolerated.

Storage: store at room temperature. Protect from light and freezing.

Diphenylhydantoin (Phenytoin)

Tablet, 50 mg, 100mg

Capsule, 50 mg, 100 mg

Suspension, 30 mg/ 5 ml

Powder for injection (sodium), 250 mg in vial

Injection, 50mg/ml in 5ml vial (Sodium salt)

Indications: generalized tonic-clonic seizures; partial seizures; status epilepticus.

Cautions: renal and hepatic function impairment (reduce dose), porphyria, blood dyscrasias, and during pregnancy, breast feeding; avoid sudden withdrawal; blood counts should be determined prior to and during therapy with these drugs. Caution for sensitive to hydantoin anticonvulsants.

Drug interactions:alcohol, CNS depressant, chloramphenicol, antituberculosis agents, amiodarone, corticosteroids, cimetidine,

calcium, diazoxide (oral), antacids (aluminium-magnesium – containing and calcium carbonate – containing), anticoagulants (coumarin – or indandione – derivative), disulfiram, contraceptives, fluconazole, itraconazole, ketoconazole, miconazole, estrogen, progestins, felbamate, fluoxetine, lidocaine, phenacemide, methadone, sucralfate, valproic acid, theophylline.

Contraindications: cardiac function impairment, such as Adams- Stokes syndrome, second and third degree AV block, sino-atrial block, and sinus bradycardia (parenteral Phenytoin administration may affect ventricular automaticity and result in ventricular arrhythmias).

Side effects: nausea, vomiting, mental confusion, dizziness, headache, tremor, transient nervousness, insomnia occur commonly; rarely dyskinesias, peripheral neuropathy; ataxia, slurred speech, nystagmus and blurred vision are signs of overdose; rashes (discontinue, if mild re-introduce cautiously but discontinue immediately if recurrence), coarse facies, acne and hirsutes, fever and hepatitis, lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, poly arteritis nodosa lymphadenopathy; gingival hypertrophy and tenderness ; rarely haematological effects, including megaloblastic anaemia, leucopenia, thrombocytopenia, agranulocytosis and aplastic anaemia; plasma calcium may be lowered (rickets and osteomalacia).

Dose and Administration: *Generalized tonic-clonic seizures, partial seizures:* **Oral: Adult:** initially 3-4 mg/kg daily (as a single dose or in 2 divided doses), increased gradually at intervals of 2 weeks as necessary (with plasma- phenytoin concentration monitoring); usual dose 200 – 500 mg daily. **Child:** initially 5 mg/kg daily in 2 divided doses; usual dose range 4-8 mg/kg daily (maximum 300 mg).

Note. Plasma concentration for optimum response 10-20 mg/litre (40-80 micromol/litre). *Patient advice:* Preferably taken with or after food. *Status epilepticus:* Slow IV injection or by IV infusion (with blood pressure and ECG monitoring),

Adult: 15 mg/kg at rate of not more than 50 mg/minute, as a loading dose; maintenance doses of about 100mg by *mouth* or by slow IV injection should be given thereafter at intervals of 6-8 hours, monitored by measurement of plasma concentrations; rates and dose reduced according to weight. **Child:** 15 mg/kg as loading dose at rate of 1 mg/kg/minute (not exceeding 50 mg/minute). **Neonate:** 15-20 mg/kg as a loading dose at rate of 1-3 mg/kg/minute.

Storage: store in a well-closed container at room temperature, protect from freezing.

Ethosuximide

Capsule, 250 mg,

Syrup, 250 mg/5ml

Indications: Management of absence (petitmal) epilepsy.

Cautions: hepatic or renal impairment; blood counts and hepatic and renal function tests recommended; pregnancy; breastfeeding; avoid sudden withdrawal; porphyria. *Note: patients or their carers should be told how to recognize signs of blood disorder, and advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising or bleeding develop. May impair ability to perform skilled tasks, for example operating machinery, driving.*

Drug interactions: other antiepileptics, CNS depressants.

Contraindications: hypersensitivity to the drug.

Side effects: frequently- gastrointestinal disturbances, causing anorexia, diarrhoea, epigastric pain, nausea and vomiting. Less frequently - adverse CNS effects including drowsiness, headache, dizziness, euphoria, ataxia and depression. Rarely -

haematopoietic disorders (leucopenia, agranulocytosis, pancytopenia, aplastic anaemia), psychotic states. Skin reactions, including Stevens - Johnson syndrome, may occur.

Dose and Administration: *Oral: Adult:* initially 500mg daily, increased according to need by 250mg every 4 - 7 days to a maximum of 1.5g/day, in divided doses.

Child: 3 - 6 years, initially 250mg daily; > 6 years, 500mg daily; adjust according to plasma levels and clinical response.

Doses exceeding 1.5g/day (in divided doses), should be used only under strict supervision.

Note: Daily doses of 1 g and above should be taken as 2 or more divided doses. Plasma concentration for optimum response 40-100mg/litre (300-700 micromol/litre)

Storage: store at room temperature.

Lamotrigine

Tablet, 25mg, 50mg, 100mg, 200mg

Indications: Monotherapy and adjunctive treatment of focal seizures and generalised seizures including tonic-clonic seizures; seizures associated with Lennox-Gastaut syndrome; monotherapy of typical absence seizures in children; prevention of depressive episodes associated with bipolar disorder

Cautions: Closely monitor and consider withdrawal if rash, fever, or other signs of hypersensitivity syndrome develop; avoid abrupt withdrawal (taper off over 2 weeks or longer) unless serious skin reaction occurs; myoclonic seizures (may be exacerbated); Parkinson's disease (may be exacerbated). Blood disorders (Be alert for symptoms and signs suggestive of bone-marrow failure such as anaemia, bruising, or infection. Aplastic anaemia, bone-marrow depression and pancytopenia have been associated rarely with lamotrigine).

Drug interactions: Antidepressant, Antiepileptics, Antimalarials, Barbiturates, Oral contraceptives and Paracetamol.

Contraindications: impaired renal or hepatic function.

Side-effects: nausea, vomiting, diarrhoea, dry mouth, aggression, agitation, headache, drowsiness, dizziness, tremor, insomnia, ataxia, back pain, arthralgia, nystagmus, diplopia, blurred vision, rash ; rarely conjunctivitis; very rarely hepatic failure, aseptic meningitis, movement disorders, unsteadiness, increase in seizure frequency, exacerbation of Parkinson's disease, confusion, hallucination, blood disorders (including anaemia, leucopenia, thrombocytopenia, pancytopenia—see Blood Disorders, above), hypersensitivity syndrome (possibly including rash, fever, facial oedema, lymphadenopathy, hepatic dysfunction, disseminated intravascular coagulation, and multi-organ dysfunction). Serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis have developed especially in children; most rashes occur in the first 8 weeks. Rash is sometimes associated with hypersensitivity syndrome and is more common in patients with history of allergy or rash from other antiepileptic drugs. Consider withdrawal if rash or signs of hypersensitivity syndrome develop. Factors associated with increased risk of serious skin reactions include concomitant use of valproate, initial lamotrigine dosing higher than recommended and more rapid dose escalation than recommended.

Dose and Administration: Monotherapy, initially 25mg daily for 14 days, increased to 50mg daily for further 14 days, and then increased by max. Of 50-100mg every 7-14 days; usual maintenance as monotherapy, 100-200mg daily in 1-2 divided doses (up to 500mg daily has been required). Adjunctive therapy with valproate, initially 25mg every other day for 14

days then 25mg daily for further 14 days, thereafter increased by max. Of 25-50mg every 7-14 days; usual maintenance, 100-200 mg daily in 1-2 divided doses. Adjunctive therapy (with enzyme inducing drug) without valproate, initially 50mg daily for 14 days then 50mg twice daily for further 14 days, thereafter increased by maximum of 100mg every 7-14 days; usual maintenance 200-400mg daily in 2 divided doses (up to 700mg daily has been required).

Child: under 12 years, monotherapy, not recommended.

Child: 2-12 years, adjunctive therapy with valproate, initially 150 microgram/kg daily for 14 days (those weighing 17-33kg may receive 5mg on alternate days for first 14 days) then 300 micrograms/kg daily for further 14 days, thereafter increased by 300 microgram/kg every 7-14 days; usual maintenance 1-5mg/kg daily in 1-2 divided doses. **Child:** 2-12 years adjunctive therapy (with enzyme including drugs) without valproate, initially 600 microgram/kg daily in 2 divided doses for 14 days then 1.2mg/kg daily in 2 divided doses for further 14 days, thereafter increased by 1.2mg/kg every 7-14 days; usual maintenance 5-15 mg/kg daily in 2 divided doses.

Lorazepam

Tablet (Sublingual), 1mg, 2mg

Injection, 1mg, 4mg

Indications: conscious sedation for procedures; premedication; short-term use in anxiety or insomnia; status epilepticus, peri-operative febrile convulsions; convulsions due to poisoning.

Cautions: see under Diazepam; short acting; when given parenterally, facilities for managing respiratory depression with mechanical ventilation must be available

Drug interactions: see under Diazepam

Contraindications: Hypersensitivity to lorazepam or any component of the formulation (cross-sensitivity with other benzodiazepines may exist); acute narrow-angle glaucoma; sleep apnea (parenteral); intra-arterial injection of parenteral formulation; severe respiratory insufficiency (except during mechanical ventilation); pregnancy

Side effects: see under Diazepam

Dose and Administration: Adult: By mouth, anxiety, 1–4 mg daily in divided doses.

Adult: *Insomnia associated with anxiety*, 1–2 mg at bedtime.

Adult: By intramuscular or slow intravenous injection (into a large vein), acute panic attacks, 25–30 micrograms/kg (usual range 1.5–2.5 mg), repeated every 6 hours if necessary. *Child under 12 years: not recommended.*

Magnesium Sulfate

Injection, 50% in 20 ml

Indications: prevention of recurrent seizures in eclampsia, as seizure prophylaxis in severe pre-eclampsia

Cautions: hepatic impairment, renal failure.

Drug interactions: alcuronium, nifedipine, suxamethonium, vacuronium.

Contraindications: heart block, serious renal impairment, myocardial damage, hepatitis, Addison's disease.

Side effects: hypermagnesaemia, nausea, vomiting, thirst, flushing of skin, hypotension, arrhythmias, respiratory depression, drowsiness, confusion, loss of tendon reflexes, muscle weakness.

Dose and Administration: Adult: *IV injection*, initially 4g over 5 - 10 minutes followed by *IV infusion* at a rate of 1g every hour for at least 24 hours after the last seizure, recurrence of seizures may require additional *IV bolus* of 2g.

Storage: store at room temperature.

Paraldehyde

Injection, in 2ml, 5ml and 10ml ampoules

Indications: used to control status epilepticus resistant to conventional treatment.

Cautions: bronchopulmonary disease or hepatic impairment. Plastic syringes should be avoided.

Drug interactions: CNS depressants (alcohol, barbiturates, and other sedatives).

Contraindications: hypersensitivity to the drug.

Side effects: tissue necrosis, sterile abscesses, and nerve damage.

Dose and Administration: *IM: Adult* IM 5-10 ml. IV 5 ml diluted with at least 100 ml of 0.9% of NaCl at a rate not exceeding 1ml/min. Rectal 10-20 ml. **Pediatric:** IM 0.15ml/kg of body weight or 6ml/m² of body surface area. IV 0.1-0.15 ml/kg of body weight diluted with 0.9% of NaCl administered slowly.

Storage: store in small well-filled airtight containers. Protect from light.

Phenobarbitone (Phenobarbital)

Tablets 15mg, 30mg, 60mg, 100mg

Elixir, 20mg/5ml

Injection (sodium), 25mg/ml in 1ml ampoule, 100mg/ml in 2ml ampoule; 4%

Indications: for the control of seizures (epilepsy). Long acting barbiturate is indicated as long-term anticonvulsant therapy for the treatment of generalized tonic-clonic and simple partial (cortical focal) seizures.

Cautions: liver or renal diseases, acute or chronic pain, in weak patients, in children and the elderly, during pregnancy, labour, delivery, and breast-feeding. It has a sedative effect, and driving and operating machines should be avoided. Also treatment should not be stopped abruptly as rebound seizures may occur.

Drug interactions: central nervous system (CNS) depressants (e.g. alcohol), paracetamol, isoniazid, chloramphenicol, and oral contraceptives containing estrogens.

Contraindications: respiratory depression.

Side effects: drowsiness or sedation, respiratory depression, and a hangover effect may occur more frequently. Unusual excitement may occur in children, the elderly, and in patients with severe pain. It should be discontinued if severe skin reactions with fever occur.

Continued use may result in psychic or physical dependence. With excessive doses in coordination of muscular motion and continuous rolling movement of eyeball may also occur.

Dose and Administration: *Oral:* Several weeks (2 to 3) of therapy may be required to achieve maximum antiepileptic effect. **Adult:** *Oral:* 50 – 100 mg every 12 hours daily. **Child:** *Oral:* 15 – 50 mg every 12 hours daily. Or 1 –2 mg/kg of body weight every 8 hours daily

Anticonvulsant: **Adult:** *Oral:* 60-250 mg per day as a single dose - or in divided dose; *IV* -100-320 mg, repeated if necessary up to a total dose of 600 mg during a 24 hour period. **Child:** *Oral:* 1 to 6 mg per kg of body weight per day as a single dose or in divided doses.

Status epilepticus: *IV (slow):* 10 to 20 mg per kg of body weight, repeated, if necessary.

Storage: at room temperature, in a well-closed container.

Primidone

Tablet, 250 mg

Indications: management of grandmal, psychomotor, and focal seizures.

Cautions: renal and hepatic impairment, pulmonary insufficiency.

Drug interactions: narcotic analgesics, antidepressants, chloramphenicol, MAO inhibitors, valproic acid, phenobarbitol.

Contraindications: pregnancy, porphyria.

Side effects: drowsiness, vertigo, ataxia, fatigue, hyperirritability, rash, nausea, vomiting, anorexia, impotence, agranulocytopenia, anemia, diplopia, nystagmus.

Dose and Administration: *Oral: Adult:* initial: 125-250mg/day at bed time; increase by 125-250mg/day every 3-7 days; usual dose: 750-1500mg/day in divided doses 3-4 times/day with maximum dosage of 2g/day.

Child: initial: 50-125mg/day given at bed time; increase by 50-125mg/day increments every 3-7 days; usual dose: 10-25mg/kg/day in divided doses 3-4 times/day.

Storage: store at room temperature.

Sodium Valproate

Tablet, 200mg, 500mg

Syrup, 200mg/5ml

Indications: for all forms of epilepsy

Cautions: patients under 3 years of age, especially those with congenital metabolic disorders, organic brain disease, or mental retardation may be at particular risk of hepatotoxicity (liver function test should be carried out in those at risk). The drug should be discontinued if signs of liver dysfunction occur; bruising, or bleeding (withdraw or reduce the dose); systemic lupus erythematosus, care in withdrawing the therapy; renal

impairment, breastfeeding, pregnancy, false - positive urine tests for ketenes, interactions restrictions on driving in patients with epilepsy

Drug interactions: amitriptyline, carbamazepine, chloroquine, chlorpromazine, cimetidine, clomipramine, ethosuximide, fluphenazine, haloperidol, mefloquine, phenobarbital, phenytoin.

Contraindications: pre-existing liver disease or a family history of severe hepatic dysfunction, pancreatitis; porphyria.

Side effects: gastrointestinal disturbances, particularly an initiation of therapy (use of entericoated formulations, administration with meals, and commencement of therapy with low dose may minimize symptoms); increased appetite and weight gain, tremor, drowsiness, ataxia, confusion, headache, reversible prolongation of bleeding time and thrombocytopenia; liver dysfunction (necessitates valproate withdrawal), elevation of liver enzyme values, hyperammonaemia, pancreatitis, leucopenia and bone marrow depression.

Dose and Administration:*Oral:Adult:*initially, 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg/day at 3 days intervals to a maximum of 2.5g daily in divided doses, usual maintenance 1 - 2gdaily (20 - 30 mg/kg daily).

Child up to 20kg, initially 20mg/kg daily in divided doses, may be increased provided plasma concentrations monitored (above 40mg/kg daily also monitor clinical chemistry and haematological parameters); over 20kg, initially 400mg daily in divided doses increased until control (usually in range of 20 - 30 mg/kg daily); maximum 35mg/kg daily.

Storage: at room temperature in a tight container. Protect from freezing.

Topiramate

Tablet, 25mg, 50mg, 100mg

Indications: in adults and paediatric patients, adjunctive therapy for partial onset seizures and adjunctive therapy of primary generalized tonic-clonic seizures; treatment of seizures associated with Lennox-Gastaut syndrome; prophylaxis of migraine headache.

Cautions: hepatic, respiratory, or renal impairment.

Drug interactions: concomitant administration with other CNS depressants and anticholinergic drugs; phenytoin, carbamazepine, digoxin, ethinyl estradiol.

Contraindications: hypersensitivity reactions.

Side effects: dizziness, ataxia, somnolence, nervousness, speech problems, fatigue, nausea, tremor, abnormal vision, upper respiratory infection.

Dose and Administration: *adjunctive therapy for partial onset seizures and adjunctive therapy of primary generalized tonic-clonic seizures:*

Adult: Initial: 25-50mg/day; titrate in increments of 25-50mg per week until an effective daily dose is reached; the daily dose may be increased by 25mg at weekly intervals for the first 4 weeks; thereafter, the daily dose may be increased by 25-50mg weekly to an effective daily dose (usually at least 400mg); usual maximum dose: 1600mg/day

Child 2-16 years: Initial dose titration should begin at 25mg (or less, based on a range of 1-3mg/kg/day) nightly for the first week; dosage may be increased in increments of 1-3mg/kg/day (administer in 2 divided doses) at 1 or 2 week intervals to a total daily dose of 5-9 mg/kg/day.

Adult:*Migraine prophylaxis:* Initial: 25mg/day, titrated at weekly intervals in 25mg increments, up to the recommended total daily dose of 100mg/day given in 2 divided doses.

Storage: store at room temperature.

5.7. Antiparkinson Agents

Antimuscarinic agents are used in Parkinson's disease (idiopathic or primary Parkinsonism) and drug - induced Parkinsonism. Those commonly used are the tertiary amine, benhexol hydrochloride, benzotropine mesylate, orphenadrine hydrochloride, and procyclidine hydrochloride.

In Parkinson's disease, antimuscarinics are generally used in the early stages when the condition is mild and tremor is the predominant symptom as they provide little benefit in bradykinesia. They can also reduce the diarrhoea experienced by patients with this disease.

The most effective form of therapy is a combination of levodopa and peripheral dopa-decarboxylase inhibitor, such as carbidopa. The response to levodopa with carbidopa is a compromise between increased mobility and adverse effects. Dyskinesias may be dose limiting and increasingly frequent with increased duration of treatment. Many factors including tolerance and progression of the disease may result in complications after 2-5 years of treatment. 'End-of-dose' deterioration occurs when there is a reduced duration of benefit from a dose, resulting in disability and dystonias. The 'on-off' phenomenon is characterized by sudden swings from mobility to episodes of akinesia, tremor and rigidity lasting from a few minutes to several hours. Amelioration of these effects can sometimes be achieved by administering levodopa in a sustained-release preparation or in a greater number of fractionated dose throughout the day. Psychiatric symptoms inducing disruption of sleep, vivid dreams and hallucinations are characteristic adverse effects that may occur at any time, especially in the elderly, and may require dose reduction or withdrawal of levodopa.

Amantadine Hydrochloride

Capsule, 100mg

Indications: Parkinson's disease (not for drug - induced Parkinson like syndromes); influenza prophylaxis.

Cautions: epilepsy, confusional or hallucinational states, history of eczema, congestive heart failure and/or peripheral oedema, orthostatic hypotension; renal or liver impairment.

Drug interactions: agents with anticholinergic effects, alcohol, CNS stimulants, hydrochlorothiazide and triamterene.

Contraindication: hypersensitivity to amantadine.

Side effects: livedo reticularis (skin discolouration) mainly of the legs; oedema of the legs. CNS reactions (psychotic episodes, convulsions and nausea), especially when doses exceed 200 mg/day. Mild headache, constipation, insomnia, nervousness, urinary retention, dry mouth, blurred vision as well as neutropenia and skin rashes have occurred.

Dose and Administration: *Oral:* **Adult:** initially 100mg daily, increased to 100mg twice daily after 7 days, maximum 400mg/day. **Elderly (> 65 years):** Maximum 100mg daily.

Storage: store at room temperature.

Benzhexol (Trihexyphenidyl Hydrochloride)

Tablet, 2mg, 5mg

Indications: Parkinsonism; drug induced extrapyramidal symptoms (but not tardive dyskinesia).

Cautions: as antimuscarinics in general (see section 1.3), and cardiovascular disease, hepatic or renal impairment; elderly, avoid abrupt discontinuation of treatment; liable to abuse (may produce euphoric effect)

Drug interactions: as antimuscarinics (section 1.3); antipsychotics, TCAs, antihistamins, amantadine, alcohol, CNS depressants, levodopa.

Contraindications: untreated urinary retention, angle-closure glaucoma, gastrointestinal obstruction, myasthenia gravis.

Side effects: as antimuscarinics (see section 1.3); Common - anticholinergic symptoms such as dry mouth, blurred vision, dizziness, mild nausea or nervousness, CNS stimulation (dose related and in the elderly), manifested by restlessness, confusion, hallucinations or euphoria, amnesia and impaired recall. Constipation and urinary retention or hesitancy may occur, particularly in the elderly. Other effects include tachycardia, drowsiness and raised intraocular pressure. Rare - psychiatric disturbances such as excitation, mania and delusions.

Dose and Administration: *Oral: Adult:* initially, 1-2mg daily with increments of 2 mg every 3-5 days, as required, to 6-10 mg/day in 3-4 divided doses (maximum 15mg/day).

Concomitant with levodopa: usually 1-2 mg 3 times daily is adequate.

Drug-induced Parkinsonism: Effective dosage range varies widely – from 1-15mg/day.

Storage: at room temperature in a tight container.

Bromocriptine

Tablet, 2.5mg, 5mg

Indications: treatment of Parkinson's diseases.

Cautions: monitors for pituitary enlargement, particularly during pregnancy; monitor visual field to detect secondary field loss in macroprolactinoma; contraceptive advice if appropriate (oral contraceptives may increase prolactin concentration).

Drug interactions: inhibitor include azole antifungals, clarithromycin, diclofenac, doxycyclin, erythromycin, isonized, nefazodone, nifedipine, propofol, protease inhibitor, quinidine, telitromycin, and varapamil. Concurrent use of bromocriptin with antihypertensive agents may increase the risk of

hypotension. Concurrent use of levodopa may increase the risk of hallucinations

Contraindications: also hypertension in postpartum women or in puerperium, Hepatic impairment; dose reduction may be necessary, Pregnancy, Breast-feeding; suppresses lactation; avoid breast feeding for about 5 days if lactation prevention fails

Side effects: drowsiness, nasal congestion; less commonly vomiting, postural hypotension, fatigue, dizziness, dry mouth; also, particularly with high doses, confusion, psychomotor excitation, hallucinations; rarely diarrhoea, gastro-intestinal bleeding, gastric ulcer, abdominal pain, tachycardia, bradycardia, arrhythmia, insomnia, psychosis, visual disturbances, tinnitus; very rarely vasospasm of fingers and toes particularly in patients with Raynaud's syndrome, and effects like neuroleptic malignant syndrome on withdrawal; urinary incontinence, leucopenia, thrombocytopenia, hyponatraemia, reversible hearing loss, increased libido, and hypersexuality also reported

Dose and Administration: *Parkinsonism:* 1.25mg twice daily, increased by 2.5mg/day in 2 to 4 week intervals (usual dose range is 30-90mg/day in 3 divided doses), though elderly patients can usually be managed on lower doses.

Diphenhydramine Hydrochloride

Tablet, 250mg, 500mg

Indications: control of Parkinsonism.

Cautions, Drug interactions; Contraindications and Side effects: see section 14.1

Dose and Administration: 50mg 2 to 4 times daily

Benztropine Mesylate

Tablet, 2mg

Injection, 1mg/ml in 2ml ampoule

Indications, Caution, Drug interactions; see under Trihexyphenidyl hydrochloride.

Contraindications: see Trihexyphenidyl Hydrochloride; avoid in children less than 3 years.

Side effects: see trihexyphenidyl Hydrochloride, but causes sedation rather than stimulation.

Dose and Administration: Adult:*Oral:* 0.5 – 1 mg daily usually at bedtime, generally increased, max. 6 mg daily; usual maintenance dose 1 – 4 mg daily in single or divided dose; elderly preferably lower end of range

IM or IV: 1 to 2 mg repeated if symptoms reappear; Elderly preferably lower end of range.

Storage: at room temperature in a well-closed container. Protect from freezing.

Levodopa

Tablet, 250mg, 500mg

Indications: Parkinson's disease (not for drug-induced parkinson like syndromes).

Cautions: asthmatics, patients with chronic obstructive airway disease, renal, hepatic or endocrine diseases, a history of peptic ulceration, open - angle glaucoma, and diabetics

Drug interactions: MAO inhibitors, antipsychotic agents, metoclopramide, antihypertensive agents.

Contraindications: closed-angle glaucoma, a history of malignant melanoma, patients younger than 25 years, psychosis, history of myocardial infarction, particularly residual arrhythmias; convulsive disorders.

Side effects: gastric intolerance, nausea, vomiting, anorexia, peptic ulceration and gastrointestinal bleeding may occur; also psychiatric disturbances including nervousness, mild anxiety and depression to overt psychotic reactions. Complex

involuntary movements. Postural hypotension and dizziness are common during the first few months of therapy. Cardiac arrhythmias, hypertension may occur.

Urinary frequency or retention, visual abnormalities, flushing, blood dyscrasias (thrombocytopenia), raised liver enzymes, increased urea and uric acid serum concentrations, and the development of a scleroderma-like illness.

Dose and Administration: *Oral: Adult:* 500mg to 1g daily administered in 2 or more equally divided doses. Daily dosage may be increased by 100-750mg every 3-7 days until a maximum response is achieved; the maximum recommended daily dosage is 8 g.

Storage: store at room temperature.

Levodopa + benserazide

Tablets, 50mg+12.5mg, 100mg+25mg, 200mg+50mg

Capsules, 50mg+12.5mg, 100mg+25mg, 200mg+50mg

Dose and Administration: Adult: Initially 25/100mg 3 times daily, increased by 25/100mg weekly until desired response is obtained. Usual effective range 100/400 - 200/800 mg/ day

Levodopa + Carbidopa

Tablets, carbidopa 10mg+ levodopa 100mg; carbidopa 25mg+ levodopa 250mg

Dose and Administration: Adult: *10/100 tablets:* initially 50 - 100 mg (with carbidopa 10) 3-4 times daily, increased by 50 - 100 mg daily or alternate days according to response, up to 800 mg (with carbidopa 80) daily in divided doses.

25/250 tablets: initially 12.5/125mg (half a tablet) once or twice daily, increased gradually by 12.5/125mg every day or alternate day. Maximum 200/2000 mg/day (8 tablets).

Orphenadrine hydrochloride

Tablet, 50mg

Indications: Parkinson's disease and drug induced extrapyramidal reactions (but not tardive dyskinesia).

Cautions, Drug interactions, Contraindication and Side effects; see under trihexyphenidyl.

Dose and Administration: Adult: *Oral:* initially 50mg 3 times daily, increased gradually according to the individual response. Usual range, 150 - 250 mg/day (maximum 400mg)

Storage: store at room temperature.

Procyclidine

Injection, 5 mg/ml; 2ml ampoule

Indications: relieves symptoms of parkinsonian syndrome and drug –induced extrapyramidal symptoms.

Cautions: tachycardia, cardiac arrhythmia, hypertension, hypotension, liver or kidney disorder, prostatic hyperplasia, elderly.

Drug interactions: amantadine, narcotic analgesics, phenothiazines, TCA, antiarrhythmics, quinidine, levodopa, digoxin.

Contraindications: angle-closure glaucoma, myasthenia gravis.

Side effects: tachycardia, palpitation, confusion, drowsiness, headache, loss of memory, fatigue, constipation, nausea, vomiting, difficult urination, increased intraocular pain, blurred vision, mydriasis, epigastric stress.

Dose and Administration: Adult: *IM:* 5-10mg may be given as a single injection, repeated if necessary after 20 minutes to a maximum of 20mg daily. Parenteral doses are usually effective within 5 to 10 minutes but may need 30 minutes to produce relief.

5.8. Medicines for Attention Deficit Disorder

Registered medicines in this group include methylphenidate, atomoxetine and dextroamphetamine. They are indicated in attention deficit hyperactivity disorder. Owing to their dependence-producing liability, these drugs should not be used for the relief of fatigue or in the treatment of debility or depression. They should only be used for their specific indications and after careful diagnosis.

Atomoxetine

Capsule, 5mg, 10mg, 18mg, 25mg, 40mg, 60mg

Indications: attention deficit/hyperactivity disorder in children, adolescents and adults.

Cautions: liver dysfunction.

Drug interactions: beta₂ agonists (e.g. salbutamol), pressor agents and drugs that affect noradrenaline; drugs that induce or inhibit CYP2D6; drugs metabolized by CYP3A4, e.g. midazolam; MAO inhibitors.

Contraindications: uncontrolled hypertension, hepatic impairment, narrow angle glaucoma.

Side effects: Children- abdominal discomfort, nausea and vomiting, decreased appetite, dizziness, somnolence, irritability, mood swings and pruritis.

Adult - dry mouth, sinus, headache, nausea, constipation, loss of appetite and weight, insomnia, palpitations, sweating, fatigue, hot flushes and urogenital dysfunction.

Dose and Administration: Adult and (Child/Adolescent ≥ 70 kg): initiate at 40 mg/day for 7 days and titrate gradually up to a maximum of 80mg/day. **Child and (Adolescent < 70kg):** 0.5 mg/kg/day for 7 days followed by gradual titration up to a maximum of 1.2 mg/kg/day.

Storage: store at room temperature.

Dextroamphetamine

Tablet, 5mg, 10mg

Indications: narcolepsy; refractory attention deficit hyperactivity disorder (under specialist supervision)

Cautions: anorexia; mild hypertension (contra-indicated if moderate or severe); psychosis or bipolar disorder; monitor for aggressive behaviour or hostility during initial treatment; history of epilepsy (discontinue if convulsions occur); tics and Tourette syndrome (use with caution)—discontinue if tics occur; monitor growth in children; susceptibility to angle-closure glaucoma; avoid abrupt withdrawal; data on safety and efficacy of long-term use not complete; acute porphyria;

Special cautions in children: Monitor height and weight as growth restriction may occur during prolonged therapy (drug-free periods may allow catch-up in growth but withdraw slowly to avoid inducing depression or renewed hyperactivity);

Driving

Contraindications: cardiovascular disease including moderate to severe hypertension, structural cardiac abnormalities, advanced arteriosclerosis, hyperexcitability or agitated states, hyperthyroidism, history of drug or alcohol abuse, Renal impairment, Pregnancy, Breast-feeding

Side effects: insomnia, restlessness, irritability and excitability, night terrors, euphoria, tremor, dizziness, aggression, paranoia, anxiety, confusion, depression, fatigue, headache; seizures (see also Cautions); dependence and tolerance, psychosis; anorexia, gastro-intestinal symptoms, growth restriction in children (see also under Cautions); dry mouth, sweating, tachycardia (and anginal pain), palpitation, myocardial infarction, hypertension, hypotension; impotence; visual disturbances; alopecia, rash; cardiomyopathy reported with chronic use; cardiovascular collapse; cerebral vasculitis; central stimulants have provoked

choreoathetoid movements and dyskinesia, tics and Tourette syndrome in predisposed individuals (see also Cautions); very rarely angle-closure glaucoma.

Dose and Administration: Narcolepsy, initially 10 mg (elderly 5 mg) daily in divided doses increased at weekly intervals by 10 mg (elderly 5 mg) daily to a max. of 60 mg daily. Refractory attention deficit hyperactivity disorder, adult over 18 years [unlicensed use], initially 5 mg twice daily, increased at weekly intervals according to response; max 60 mg daily; child 6–18 years, initially 5–10 mg daily, increased if necessary at weekly intervals by 5 mg daily, usual max. 1 mg/kg (up to 20 mg) daily (40 mg daily has been required in some children).

Note: Maintenance dose given in 2–4 divided doses.

Methylphenidate

Tablets, 5 mg, 10 mg, 20 mg

Indications: attention deficit hyperactivity disorders in children; narcolepsy.

Cautions: hypertension, vocal or motor tics, epilepsy.

Drug interactions: barbiturates, primidone, phenytoin, phenyl butazone, tricyclic antidepressants, warfarin, and MAO inhibitors.

Contraindications: absolute-history of schizophrenia, drug dependence or personality disorders; patients with glaucoma, thyrotoxicosis, tachyarrhythmias, anxiety, tension or ischaemic heart disease.

Side effects: nervousness, insomnia; weight loss and growth retardation may occur (particularly in children receiving > 30 mg/day for prolonged periods); changes in blood pressure and pulse rate, nausea, drowsiness, dyskinesia, tremor, skin rash and dependence, especially if predisposed.

Dose and Administration: *Oral: Adult:* usually 10 mg 2 to 3 times daily; maximum 60mg/day. **Child over 6 years:** initially

5mg twice daily (at breakfast and lunch), increased at weekly intervals, if necessary, to 20-30mg/day; maximum 1mg/kg/day.

Storage: store in airtight container and at room temperature.

5.9. Medicines for substance Abuse and Dependence

Bupropion

Tablet, 75mg, 100mg

Indications, Cautions, Drug interactions, Contraindications, Side-effects, Dose and Administration and Storage: see section 4.3

Disulfiram

Tablet, 200 mg, 250 mg, 500 mg

Indications: adjunctive treatment of chronic alcoholism.

Cautions: epilepsy, diabetes mellitus, renal or hepatic disease.

Drug interactions: cumulative benzodiazepines such as diazepam and chlordiazepoxide; isoniazid; metronidazole; phenytoin and warfarin; amitriptyline.

Contraindications: cardiac failure, coronary artery disease, psychosis and drug addiction.

Side effects: In the absence of alcohol - drowsiness, headache, an unpleasant taste, impotence, and mild gastrointestinal disturbances, allergic dermatitis. The alcohol - disulfiram reaction may be manifested by facial flushing, throbbing headache, tachycardia and nausea and vomiting. During severe reactions there may be respiratory depression, cardiovascular collapse, arrhythmias, seizures, coma and sudden death.

Dose and Administration: *Oral:* 200 - 400 mg daily or 400 mg on alternate days.

Storage: store at room temperature.

Methadone

Tablet, 50mg, 10mg, 40mg

Concentrated for oral liquid, 5mg/ml, 10mg/ml (Hydrochloride)

Oral liquid, 5mg/5ml, 10mg/5ml

Indications: adjunct in treatment of opioid dependence

Cautions: history of cardiac conduction abnormalities, QT interval prolongation

Contraindications: Opioid analgesics should be avoided in patients with acute respiratory depression and when there is a risk of paralytic ileus. They are also contra-indicated in conditions associated with raised intracranial pressure and in head injury (opioid analgesics interfere with pupillary responses vital for neurological assessment). Comatose patients should not be treated with opioid analgesics.

Side effects: QT interval prolongation, torsade de pointes, hypothermia, restlessness, raised intracranial pressure, dysmenorrhoea, dry eyes, and hyperprolactinaemia

Dose and Administration: Oral or SC or IM: 5–10 mg every 6–8 hours, adjusted according to response; on prolonged use not to be given more frequently than every 12 hours. *Note Child not recommended*

Naltrexone Hydrochloride

Tablet, 50mg

Injection, 380mg/vial

Indications: adjunct to prevent relapse in formerly opioid-dependent patients (who have remained opioid-free for at least 7–10 days)

Cautions: liver function tests needed before and during treatment; test for opioid dependence with naloxone before treatment; avoid concomitant use of opioids but increased dose

of opioid analgesic may be required for pain (monitor for opioid intoxication)

Note: Patients should be warned that an attempt to overcome the blockade of opioid receptors by overdosing could result in acute opioid intoxication

Contraindications: patients currently dependent on opioids, Hepatic impairment, renal impairment, Pregnancy, Breast-feeding

Side effects:nausea, vomiting, abdominal pain, diarrhoea, constipation, reduced appetite, increased thirst; chest pain; anxiety, sleep disorders, headache, reduced energy, increased energy, irritability, emotional lability, dizziness; chills; urinary retention; delayed ejaculation, decreased potency; arthralgia, myalgia; increased lacrimation; rash, and increased sweating; rarely hepatic dysfunction, suicidal ideation, and speech disorders; very rarely hallucinations, tremor, and idiopathic thrombocytopenia

Dose and Administration: Adult over 18 years (initiate in specialist clinics only), 25 mg initially then 50 mg daily; total weekly dose (350 mg) may be divided and given on 3 days of the week for improved compliance (e.g. 100 mg on Monday and Wednesday, and 150 mg on Friday)

Nicotine replacement therapy (NRT)

Chewing Gum, 2mg, 4mg

Transdermal patch, 5mg-30mg/16hrs, 7mg-21mg/24hrs

Indications: treatment to aid smoking cessation for the relief of nicotine withdrawal symptoms (including nicotine craving)

Cautions: severe or unstable cardiovascular disease (including hospitalisation for severe arrhythmias, recent myocardial infarction, or recent cerebrovascular accident)—initiate under medical supervision; uncontrolled hyperthyroidism; diabetes

mellitus (monitor blood-glucose concentration closely when initiating treatment); phaeochromocytoma; oral preparations, oesophagitis, gastritis, peptic ulcers; patches, skin disorders (patches should not be placed on broken skin); hepatic impairment; renal impairment; pregnancy; breast-feeding.

Note: Most warnings under Cautions also apply to continuation of cigarette smoking

Side effects: gastro-intestinal disturbances (including nausea, vomiting, dyspepsia); headache, dizziness; influenza-like symptoms; dry mouth; rash; less frequently palpitation; rarely atrial fibrillation; with nasal spray, sneezing, epistaxis, watering eyes, ear sensations; with lozenges, thirst, paraesthesia of mouth, taste disturbances; with patches, skin reactions (discontinue if severe)—vasculitis also reported, blood pressure changes; with patches or lozenges, sleep disturbances, nightmares, chest pain; with gum or lozenges, mouth ulceration, increased salivation; with gum, lozenge, sublingual tablets, or inhalator, hiccups, throat irritation.

Dose and Administration: *Chewing gum:* smoking cessation, individuals smoking 20 cigarettes or less daily, initially chew one 2-mg piece slowly (chew gum until taste becomes strong, then rest gum between cheek and gum, when taste fades start chewing again) for approx. 30 minutes when urge to smoke occurs; individuals smoking more than 20 cigarettes daily or needing more than 15 pieces of 2-mg gum daily should use the 4-mg strength; max. 15 pieces of 4-mg strength daily; withdraw gradually after 3 months; review treatment if abstinence not achieved within 9 months; **Child** 12–18 years, treatment continued for up to 8 weeks followed by gradual reduction over 4 weeks; review treatment if abstinence not achieved within 3 months Smoking reduction, chew 1 piece when urge to smoke occurs between smoking episodes; reduce smoking within 6

weeks and attempt smoking cessation within 6 months; review treatment if abstinence not achieved within 9 months **Note:** Children under 18 years should consult a healthcare professional before starting smoking-reduction regimen.

*Topical:Transdermal patch:*Dose smoking cessation, Adult over 18 years, apply to dry, nonhairy skin site, removing after 24 hours and siting replacement patch on a different area (avoid using same area for 24 hours); individuals smoking less than 20 cigarettes daily, initially '14-mg'or '21-mg' patch daily (depending on severity of withdrawal symptoms); individuals smoking 20 or more cigarettes daily, initially '21 mg' patch daily; withdraw gradually, reducing dose every 3–4 weeks; review treatment if abstinence not achieved within 3 months; maximum period of treatment should not exceed 6 months.

6. MEDICINES USED in ANAESTHESIA

6.1. General Anaesthetics

General anesthetics are a diverse group of drugs that produce reversible state of unconsciousness (amnesia), analgesia, and muscle relaxation to allow the performance of surgery or interventional procedures. An ideal anesthetic agent would produce unconsciousness, analgesia, and muscle relaxation suitable for all surgical procedures and be metabolically inert and rapidly eliminated. No single agent in safe concentrations fulfills all these requirements and it is customary to employ a number of agents to produce the required conditions

The goal of anesthesia is to provide the desired combination of analgesia, amnesia, and optimal operating conditions while ensuring physiologic homeostasis. The types of anesthesia include general anesthesia, neuraxial anesthesia (spinal and epidural), peripheral nerve blocks, and monitored anesthetic care (sedation). The course of general anesthesia can be divided into three distinct phases: induction, maintenance, and emergence. Induction and Maintenance of anesthesia can be achieved with IV or volatile anesthetics agents. Induction of general anesthesia for adults is usually achieved with the injection of intravenous medications while inhalation anesthetics are particularly useful in the induction of pediatric patients. Maintenance of anesthesia can be achieved with volatile or IV anesthetics. Volatile agents remain a popular because of their ease of delivery, reliable recovery, excellent safety profile, and modest cost. Emergence or "waking up" from general anesthesia is a crucial time in which the patient back to a restored state of consciousness. With this return of consciousness there is a short period of time in which the patient's body is aware of the emergence without a full return to consciousness. This results in autonomic hyper-responsiveness

which may manifest as hypertension, tachycardia, bronchospasm, or laryngospasm. Short acting narcotics, beta blockers, or lidocaine can blunt these responses in patients, when these responses may be harmful (eg ischemic heart disease).

Intravenous anaesthetics: Intravenous anesthetics may be used either to induce anesthesia or for maintenance of anesthesia throughout surgery. Induction of general anesthesia is usually achieved with the injection of intravenous medications such as propofol, thiopental sodium, etomidate, ketamine and narcotics. Propofol is the most commonly used induction agent because of its favorable recovery profile and short elimination half-life (resulting in less prolonged sedation and less nausea than sodium pentothal, a barbiturate induction agent). When used for induction, propofol causes bradycardia and hypotension. Thiopental sodium is a widely used intravenous anesthetic in our country, but it has no analgesic properties. Induction is generally smooth and rapid, but owing to its narrow therapeutic margin, over dosage with cardiorespiratory depression may occur. The reconstituted solution is highly alkaline and therefore irritant on misplaced injection outside the vein; arterial injection is particularly dangerous. Thiopental is contraindicated in porphyria.

Awakening from a moderate dose of thiopental is rapid due to redistribution of the drug in the whole body tissue. Metabolism is, however, slow and some sedative effects may persist for 24 hours. Repeated doses have a cumulative effect.

Ketamine is a phencyclidine derivative and rapid acting dissociative general anesthetic. The benefits of ketamine include significant analgesia and preservation of respiratory drive. It may be used as the sole agent for diagnostic and for painful procedures of short duration such as the dressing of burns, radio

therapeutic procedures, bone marrow sampling and minor orthopedic procedures. It is of particular value in children, it also causes bronchodilation, which may be beneficial in patients with reactive airways. Used alone, it may have cardiovascular stimulant properties and/or unpleasant emergence reactions such as hallucinations, vivid dreams, or delirium. Benzodiazepines can be used in combination with ketamine to reduce these side effects.

Etomidate is used as induction agent. It has minimal respiratory and cardiovascular depressant properties, while causing little 'hangover' effect or histamine release. It has no analgesic properties. A significant cautionary drawback to the use of etomidate is that even a single dose can cause transient adrenal insufficiency.

Opioid analgetics are used in nearly every facet of modern anesthesia practice. They are used as premedicants or sedatives, intravenous anesthetics postoperative analgetics, and intraspinal analgetics. Unfortunately, they are also abused by patients and physicians.

Opioids may be divided into three groups based upon their pharmacodynamic activity: pure agonists (morphine, fentanyl, etc.), pure antagonists (naloxone, naltrexone), and mixed agonist-antagonists (nalbuphine, butorphanol, etc.).

Opioids may also be grouped on the basis of their chemical groups or their postulated interactions with opioid receptor subtypes (μ , κ , δ , σ , ϵ , etc.). Opium is a complex mixture of alkaloids obtained from the seed pods of *Papaver somniferum*, the opium poppy. The two naturally occurring opiate analgetics are the phenanthrene alkaloids, morphine and codeine. The term opioid applies to any natural or synthetic compound that has morphinelike properties. All the clinically available opioids are structurally related to morphine.

Etomidate

Injection, 20 mg/ml in 10ml and 20ml ampoules

Indications: induction agent for general anaesthesia.

Cautions: porphyria, should not be given in repeated doses because it causes adrenal insufficiency

Drug interactions: CNS depressants including alcohol; ketamine.

Contraindication: hypersensitivity to etomidate.

Side effects: pain on injection, a high incidence of involuntary muscle movements (may be reduced by premedication with diazepam or one of the opiates), post-operative nausea and vomiting and brief periods of apnoea. Rare - laryngospasm, skin rashes,

Dose and Administration: *Dose should be individualized.* **Adult:**

Induction: *I V:* 0.2 - 0.3mg/kg slowly over 30 - 60 seconds. Smaller doses may be used as supplements for other anaesthetic agents.

Storage: store at room temperature.

Ketamine Hydrochloride

Injection, 10 mg/ml in 20ml, 50 mg/ml in 20 ml

Indications: Induction, maintenance, analgesia.

Cautions: warn the patient not to drive or operate machinery for about 24 hours of postanaesthesia or avoiding alcohol and other CNS depressants within 24 hours following anaesthesia; pregnancy.

Drug interactions: anaesthetics such as enflurane, isoflurane, methoxyflurane, antihypertensives; CNS depressants, thyroid hormones.

Contraindications: ketamine is contraindicated in any condition in which significant elevation of blood pressure would be hazardous such as severe cardiovascular disease, Heart-failure, severe-hypertension, myocardial infarction, stroke

(history); cerebral trauma, Intracerebral mass or hemorrhage; eye injury, increased cerebrospinal fluid pressure and increased intraocular pressure; psychiatric disorders such as schizophrenia or acute psychosis, thyrotoxic states.

Side effects: increased blood pressure, tachycardia, tonic or clonic muscle movements, emergence reaction (alteration in mood or body image, delirium, dissociative or floating sensation), vivid dreams or illusions, visual hallucinations.

Dose and Administration:Adult:Induction: IV: 1 to 2mg per kg of body weight administered as a single dose or by IV infusion at a rate of 0.5mg per kg of body weight per minute. **IM:** 5-10mg per kg of body weight.

Maintenance: IV: 0.01-0.05mg (base) per kg of body weight by continuous infusion at a rate of 1-2mg per minute.**Child and Elderly:** Same as adult

Storage: at room temperature, protect from light and heat and from freezing.

Propofol

Injection (emulsion), 10mg/ml in 20ml ampoule

Indications: intravenous anaesthesia (both induction and maintenance).

Cautions: cardiac, respiratory, renal or hepatic function impairment, epilepsy, elderly and hypovolaemic or debilitated patients.

Drug interactions: benzodiazepines, opiates, ethanol, narcotics, phenothiazines, fluconazole, ketoconazole, NSAIDs.

Contraindications: hypersensitivity to propofol.

Side effects: hypotension and transient apnoea, bradycardia; headache during recovery; involuntary muscle movements in unpremedicated patients; seizures.

Dose and Administration:Adult: Induction: *Slow IV injection or infusion*, titrated against the response obtained from 40mg every 10 seconds. Most adult patients under 55 years require 1.5 to 2.5mg/kg. Maintenance: continuous infusion, the rate varying from 4 to 12 mg/kg/hour. Alternatively, a technique of repeat bolus injections may be used: increments of 25 - 50mg may be given at intervals determined by clinical signs of lightening anaesthesia (usually every 6 minutes).

Note: Patients over 55 years and high risk patients may require less than the usual doses. For induction: 1- 1.5 mg/kg may be adequate. Maintenance: 2 - 6 mg /kg hour.

Child: over 3 years: Induction: 2.5 mg/kg adjusted as necessary. Maintenance: IV infusion, 9 - 15 mg/kg/hour.

Storage: store at room temperature.

Thiopental sodium

Powder for injection, 0.5 g and 1 g in ampoule

Indications: induction of general anaesthesia; anaesthesia of short duration; control of convulsions (especially in status epilepticus).

Cautions: reduce induction dose in severe liver disease. Extreme care is required in surgery of the mouth, pharynx, or larynx and in patients with acute circulatory failure (shock) or fixed cardiac output, dehydration, hypovolaemia, severe anaemia, hyperkalaemia, toxemia, myasthenia gravis, myoedema or in severe renal disease. Caution should be taken during pregnancy, in geriatric and patients sensitive to any one of barbiturates.

Drug interactions: alcohol, CNS depressant, dopaminergics, antihypertensives, especially diazoxide or ganglionic blockers, & hypotension producing medication, aspirin, probenecid.

Contraindications: porphyria (thiopental sodium may aggravate symptoms by inducing enzymes responsible for porphyria in synthesis).

Side effects: apnea, hypotension, allergic reaction, cardiac arrhythmias, circulatory depression, emergence delirium, and thrombophlebitis.

Dose and Administration: Dosage must be individualized; however, as a general guideline the following can be used.

Adult: *Induction: IV:* 50 to 100 mg (2 to 4 ml of a 2.5 % solution) as require; or 3 to 5mg per Kg of body weight as a single dose. *Maintenance: IV* (Intermittent) 50 to 100 mg (2 to 4 ml of a 2.5 % solution) as required. *Status epilepticus refractory to other treatment: IV,* 2 to 4mg/kg bolus over 20 seconds, then further 50mg boluses every 2-3 minutes until seizures are controlled; then infusion to maintain 1-5 mg/kg/hour using EEG control if possible. **Child up to 15 years of age:** *Induction: IV:* 3 to 5 mg per Kg of body weight. *Maintenance: IV:* (intermittent), about 1 mg per Kg of body weight as required.

Storage: prior to reconstitution, store at room temperature, unless otherwise specified by manufacturer.

Volatile inhalation agents

The most commonly used inhaled anesthetics in modern anesthesia include a single gas (nitouse oxide) and volatile liquids (halothane, isoflurane desflurane and sevoflorane). One of the volatile anesthetics, (with or without nitrous oxide), can be used for induction when intravenous agents are contraindicated and particularly when intubations is likely to be difficult.

If intubation is likely to be difficult, halothane is preferred. It does not augment salivary or bronchial secretions and the incidence of postoperative nausea and vomiting is low. Severe

hepatitis, which may be fatal, sometimes occurs; it is more likely in patients who are repeatedly anaesthetized with halothane within a short period of time.

Isoflurane is an isomer of enflurane. It is more irritant to the airway than halothane and thus unsuitable for inhalational induction. In comparison with the other two, induction of anaesthesia is more rapid, and it is less arrhythmogenic. It is a potent vasodilator with minimal cardiac depressant effect. It is used in neurosurgical anaesthesia because it causes less increase in intracranial blood flow and a smaller subsequent rise in intracranial pressure. Sevoflurane is non-pungent and rapid increase in alveolar anesthetic concentration make it an excellent choice for smooth and rapid inhalation induction in pediatric and adult patients.

Nitrous oxide is used for the maintenance of anaesthesia. It is too weak to be used alone, but it allows the dosage of other anesthetic agents to be reduced. It has a strong analgesic action.

Enflurane

Inhalation, 250ml

Indications: Induction and maintenance of general anaesthesia.

Cautions: increased intracranial pressure, epilepsy, elderly, porphyria

Drug interactions: as for halothane; isoniazid, non-depolarizing muscle relaxants.

Contraindications: history of malignant hyperthermia, or jaundice/hepatic dysfunction (for which no other cause could be established) after exposure to a volatile agent; renal failure.

Side effects: hypotension and tachycardia may occur. Respiratory depression, an increase in salivation and bronchial secretions, and hepatic impairment have been reported.

Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration: Adult: Maintenance range 1-3%.
Child: not used for inhalational induction. Maintenance range 1-3 %.

Ether, anesthetic

Inhalation, 100gm, 250gm

Indications: general anesthesia before surgery.

Cautions: ether is explosive. Mixture of its vapor with oxygen, nitrous oxide or air at certain concentration causes explosion and hence it should be avoided. It should not be used in the presence of open flame or any electrical appliances liable to produce a spark.

Premedication with atropine is necessary to inhibit bronchial and gastric secretion induced by ether.

Drug interactions: avoid concomitant use of ether with competitive muscle relaxants.

Contraindications: diabetes mellitus, impaired kidney function, severe liver disease.

Side effects: irritation on the mucous membrane of the respiratory tract, pharyngeal spasm, decreased blood pressure, capillary bleeding, malignant hyperpyrexia (in some individuals), convulsions in children and young adults.

Dose and Administration:*Inhalation:* Induction: **Adult and Child:** up to 15 % in impaired gases. Maintenance of light anesthesia, 3 to 5 % in air (with or without muscle relaxants); up to 10 % for deep anesthesia.

Halothane

Inhalation, 250 ml

Indications: induction and maintenance of anesthesia in major surgery often combined with nitrous oxide/oxygen mixtures.

Cautions: during pregnancy, breast-feeding, in children and elderly patients.

Drug interactions: sympathomimetics, especially catecholamines such as dopamine, epinephrine, norepinephrine; or cocaine, ephedrine, levodopa, metraminol, methenamine, nephrotoxic agents, xanthines; alcohol, aminoglycosides; capreomycin, citrate-anticoagulated blood, lincomycin (systemic), neuromuscular blocking agents (non depolarizing), polymyxins (systemic). Amiodarone, coumarin or indandione derivative anticoagulants; antihypertensives, especially diazoxide or ganglionic blockers such as guanethidine, guanethidine, mecamylamine or trimethaphan, neostigmine and pyridostigmine.

Contraindications: malignant hyperthermia, biliary tract disease or hepatic function impairment, jaundice or acute hepatic damage; cardiac arrhythmias, head injury or increased intracranial pressure, myasthenia gravis, pheochromocytoma, sensitivity to halothane.

Side effects: hepatotoxicity, impairment of psychomotor skills, emergence delirium (postanaesthesia), shivering or trembling, nausea or vomiting (mild).

Dose and Administration:*inhalation***adult:** Induction: Increase gradually to 2-3% in oxygen or nitrous oxide/oxygen mixture. Maintenance range 0.5-1.5%

Child: Induction: 1.5-2%, though up to 3% may be required. Maintenance: 0.5 to 2%

Storage: at room temperature in a tight, light-resistant container.

Isoflurane

Inhalation, 100 ml

Indications: Inhalational anaesthesia.

Cautions: debilitated patients, elderly, ischaemic heart disease.

Drug interactions: sympathomimetics and xanthines, anticonvulsants, non - depolarizing muscle relaxants, blood pressure lowering agents.

Contraindications: history of malignant hyperthermia

Side effects: respiratory depression and airway irritation (may result in retardation of inhalational induction due to breathholding or coughing if the inspired concentration is increased too rapidly). Increase in heart rate and significant hypotension with increasing concentrations.

Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration:Adult and Child: Maintenance range usually 0.75 to 1.5%.

Storage: store at room temperature.

Nitrous oxide

Inhalation

Indications: maintenance of anaesthesia and, in sub-anaesthetic concentrations, for analgesia. *Nitrous oxide is used for the maintenance of anesthesia. It is too weak to be used alone, but it allows the dosage of other anesthetic agents to be reduced. It has a strong analgesic action.*

Cautions: caution is needed in the presence of air-enclosing cavities (such as pulmonary, renal or occluded middle ear air cysts or air embolism).

Drug interactions: alcohol; alfentanil, fentanyl, sufentanil; amiodarone, anticoagulants (coumarin-or indandione – derivative); antihypertensive agents, especially diazoxide or ganglionic blockers; chlorpromazine; diuretics; CNS depressant, methyl dopa, xanthines.

Contraindications: pneumothorax, head injury or increased intracranial pressure, pre-existing or intracranial lesions, space –

occupying or tumors, history of sensitivity to the anaesthetic being considered for use.

Side effects: mild nausea or vomiting and rarely respiratory depression, neurologic injury, malignant hyperthermic crisis, megaloblastic anaemia.

Dose and Administration: Adult: *Inhalation: Anaesthetic (general):* Induction: 70 % with 30 % of oxygen. Maintenance: 30 to 70 % with oxygen. *For obstetrics or procedures not requiring loss of consciousness:* 25 to 50 % with oxygen. **Child:** Dosage must be individualized.

Storage: store at room temperature, unless otherwise specified by manufacturer.

Sevoflurane

Inhalation, 250ml

Indications: Inhalational anaesthesia

Cautions: porphyria, paediatrics, pregnancy.

Drug interactions: non-depolarizing muscle relaxants, nitrous oxide, opioids and benzodiazepines.

Contraindications: known sensitivity to halogenated agents; history of malignant hyperthermia; liver dysfunction, unexplained fever or leucocytosis occurring after a previous halogenated anaesthetic.

Side effects: may cause dose-dependent cardiorespiratory depression. Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration: Adult: Induction: In adults inspired concentrations of up to 5% usually produce surgical anaesthesia in < 22 minutes. A short acting intravenous induction agent may be used prior to inhalation. Maintenance: Surgical levels of anaesthesia may be sustained with concentrations of 1-3% sevoflurane, with or without the concomitant use of nitrous

oxide. **Child:** Inspired concentrations of up to 6% usually produce surgical anaesthesia in < 2 minutes. Maintenance: 2-3%.

Trichloroethylene

Inhalation

Indications: used for maintenance of light anaesthesia.

Cautions: it should not be used in closed-circuit apparatus.

Drug interactions: sympathomimetics such as adrenaline; alcohol.

Side effects: acute exposure leads to dizziness, lightheadedness, lethargy, nausea and vomiting and hepatic and renal dysfunction. Chronic poisoning may result in visual disturbances, impairment of performance, hearing defects, neuralgia and mild liver function.

Dose and Administration: administered by inhalation.

6.2. Neuromuscular Blockers

One of the most important requirements for optimal operating conditions is that the patient remains still during surgery. This goal can be achieved using different techniques, the most popular of which is neuromuscular blockade. Neuromuscular blocking agents block the acetylcholine receptors at the neuromuscular junctions of striated muscle to provide "relaxation" of the major muscle groups in the body.

These drugs are used as adjuncts to general anaesthesia, particularly to enable adequate muscle relaxation. There are 2 main types of neuromuscular blocking agents: competitive or non-depolarizing agents and depolarizing agents.

Generally, the competitive neuromuscular blocking agents, having a longer duration of action, are used in major operations, while the depolarizing agents, with a much shorter effects, are used for minor operations or manipulations and particularly for

intubations. Following administration of a depolarizing agent, such as suxamethonium, to aid intubation, a longer acting competitive agent may be given to maintain muscle relaxation throughout an operation.

Suxamethonium is the only widely used depolarizing muscle relaxant. It produces rapid, complete paralysis, which is very short-lasting in most patients and is of particular value for laryngoscopy and intubation. Prolonged paralysis may occur in those with low or atypical plasma cholinesterase. Assisted ventilation should be continued until muscle function is restored. Suxamethonium normally produces a phase I (depolarizing) neuromuscular block. After high dose or prolonged use, the nature of the block changes to a phase II (non-depolarizing) block; this phase II block (also known as dual block) is associated with prolonged neuromuscular blockade and apnoea. Non-depolarizing (competitive) muscle relaxants include atracurium besylate, pancuronium bromide, and vecuronium bromide. These agents compete with acetylcholine at the neuromuscular receptor sites. Their action is reversible by anticholinesterase agents, which allow the concentration of acetylcholine to increase at these receptor sites and displace the 'blocker'.

6.2.1. Non-depolarizing muscle relaxants

Atracurium Besylate

Powder for Injection, 10mg/ml in 2.5, 5ml, 25ml ampoules

Indications: adjunct to general anesthesia to facilitate endotracheal intubation and to relax skeletal muscles during surgery.

Cautions: previous anaphylactic reaction.

Drug interactions: aminoglycosides, beta-blockers, clindamycin, calcium channel blocker, ketamine, lidocaine, loop diuretics, theophylline, and sympathomimetics.

Side effects: flushing, bronchial secretion, erythema, itching, wheezing.

Dose and Administration: Adult:IV: usual range initially 0.3 – 0.6 mg/kg, depending on the duration of block required, with supplementary doses of 0.08- 0.2 mg/kg as needed.

Storage: store in refrigeration.

Cisatracurium

Injection, 2mg/ml in 10ml ampoule

Indications: neuromuscular blockade (intermediate duration) for surgery or during intensive care

Cautions: lactation; burn Patients; safety and efficacy have not been determined in children less than 2 years of age.

Side effects: Bradycardia, hypotension, flushing, bronchospasm, rash.

Dose and Administration: IV: Intubation: Adult and Child over 1 month: initially 150 micrograms/kg; maintenance, 30 micrograms/kg approx. every 20 minutes; Child 2–12 years, 20 micrograms/kg approx. every 9 minutes; or maintenance, Adult and Child over 2 years, initially, 3 micrograms/kg/minute, then after stabilisation, 1–2 micrograms/kg/minute; dose reduced by up to 40% if used with isoflurane. Intensive care: Adult: 0.5–10.2 micrograms/kg/minute (usual dose 3 micrograms/kg/minute).

Note: Lower doses can be used for children over 2 years when not for intubation. To avoid excessive dosage in obese patients, dose should be calculated on the basis of ideal body-weight.

Pancuronium bromide

Injection, 2mg/ml in 2ml ampoule

Indications: management of mechanically ventilated patients and used for surgery.

Cautions: renal and hepatic disease.

Drug interactions: aminoglycosides, clindamycin, lincomycin, polymyxin antibiotics, tetracyclines, quinidine, lignocaine, verapamil, lithium, magnesium salts, anaesthetic agents such as enflurane and ether, and potassium - depleting drugs such as amphotericin B and diuretics; digoxin, phenytoin and carbamazepine.

Contraindications: conditions in which tachycardia would be undesirable.

Side effects: tachycardia and a dose - related elevation in blood pressure (due to vagolytic and indirect sympathomimetic effects on the cardiovascular system).

Rarely - hypersensitivity reactions.

Dose and Administration: *IV:Adult:* initially: 0.04 - 0.1mg/kg; further doses of 0.01 - 0.02 mg/kg may be given as required. In intensive care: 0.06 mg/kg every 1 - 1.5 hours. Following administration of suxamethonium, dose should be reduced; 0.02 to 0.06 mg/kg may be adequate for the initial dose. **Child:** over 2 months: 0.04 - 0.1mg/kg; increments of 0.01 - 0.02 mg/kg if required.

Neonates: 0.03 - 0.04 mg/kg with increments of 0.01 to 0.02 mg/kg if needed. Should be used with extreme caution.

Storage: store in refrigerator. Stable at room temperature up to 6 months.

Vecuronium Bromide

Powder for Injection, 10mg in vial

Indications: muscle relaxant during surgery.

Cautions: renal impairment, hepatic impairment, electrolyte disturbances, asthma, pregnancy and breastfeeding.

Drug interactions: carbamazepine, clindamycin, gentamicin, lithium, neostigmine, nifedipine, phenytoin, procainamide, propranolol, pyridostigmine, quinidine, streptomycin, verapamil.

Contraindications: respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorder.

Side effects: hypersensitivity reactions including bronchospasm, hypotension, tachycardia, oedema, erythema, pruritus.

Dose and Administration: *IV: Intubation:* Adult and Child over 5 months: 80-100 mcg/kg; maintenance of relaxation 20-30 mcg/kg. Child under 4 months: initially 10-20mcg/kg, followed by increments according to response. *IV infusion:* Adult: initial bolus 40-100mcg/kg then 0.8-1.4mcg/kg/minute.

Storage: store at room temperature.

6.2.2. Depolarizing muscle relaxant

Suxamethonium Chloride (succinylcholine)

Powder for injection, 50 mg, 100 mg, 500 mg in vial

Injection, 50mg/ml

Indications: rapid and complete depolarizing muscle relaxation of short duration; used mainly for endotracheal intubation.

Cautions: children, during pregnancy, and cardiovascular function impairment. Caution is also required: in conditions that may be adversely affected by increased potassium concentrations (severe burns, digitalis toxicity, or recent digitalization, degenerative or dystrophic neuromuscular disease, paraplegia, pre-existing hyperkalemia, spinal cord injury, severe trauma). Conditions that may lead to low plasma pseudocholine esterase activity (severe anemia, dehydration, exposure to neurotoxic insecticides or other cholinesterase inhibitors, severe hepatic disease or cirrhosis, malnutrition, recessive hereditary trait). Conditions that may be adversely affected by increase in

intraocular pressure (open eye injury, glaucoma, ocular surgery). Fracture or muscle spasm and malignant hyperthermia.

Drug interactions: cholinesterase inhibitor specially echothiopate, demecarium, isofluorophate, cyclophosphamide. Avoid exposure to insecticides such as Malathion. Avoid also simultaneous use of digitalis glycosides, procainamide, physostigmine, calcium salts, and succinylcholine.

Contraindications: allergic to succinylcholine, pulmonary function impairment or respiratory depression, renal function impairment.

Side effects: increased intra ocular pressure, muscle pain and stiffness (postoperative), excessive salivation, cardiac arrhythmias, bradycardia.

Dose and Administration: **Adult:** *IV injection:* initially 0.6-1mg/kg (range 20-100 mg). Subsequent doses must be individualized according to the patient's needs. *IV infusion,* as a 0.1% solution, 2-5 mg/minute for up to 1 hour. **Child:** *IV: 1-12 years,* 1mg/kg; under 1 year, 2mg/kg.

Storage: store between 2 and 8⁰c. Protect from freezing.

6.3. Anesthetic Adjuncts and Adjuvants

A balance combination of agents with different actions is often used to provide the various components of general anesthesia including hypnosis muscle relaxation. This technique has been reported to minimize intra-operative cardiovascular depression, to facilitate a rapid return of consciousness, and to have a low incidence of postoperative adverse effects such as nausea, and vomiting, and excitation.

Antimuscarinics, including atropine, hyoscine, and glycopyrronium, have been used as pre-operative medication to inhibit salivation and excessive secretions of the respiratory tract. This use is less important now that less irritating

anesthetics are used. Atropine, hyoscine and glycopyrronium are also given as premedications to reduce intra-operative bradycardia and hypotension induced by agents such as suxamethonium, halothane, or following vagal stimulation.

At the end of surgery drugs are sometimes administered to accelerate recovery from the effects of the various agents used during anesthesia. Non-depolarizing muscle relaxants may be reversed with anticholinesterases such as neostigmine but concomitant administration of atropine or glycopyrronium is required to prevent bradycardia and other muscarinic actions developing.

Oxygen should be added routinely during anesthesia with inhalational agents, even when air is used as the carrier gas, to protect against hypoxia.

Atropine is now rarely used for premedication but still has an emergency role in the treatment of vagotonic side effects.

Hyoscine effectively reduces secretion and also provides a degree of amnesia, sedation and anti-emesis. Unlike atropine it may produce bradycardia rather than tachycardia. In some patients, especially the elderly, hyoscine may cause the central anti-cholinergic syndrome (excitement, ataxia, hallucinations, behavioral abnormalities and drowsiness) glycopyrronium produces good drying of salivary secretions. When given intravenously it produces less tachycardia than atropine. It is widely used with neostigmine for reversal of non-depolarizing muscle relaxants.

Neostigmine is the specific drug for reversal of non-depolarizing (competitive) blockade. It acts within one minute of intravenous injection and lasts for 20 to 30 minutes; a second dose may then be necessary. Atropine or preferably glycopyrronium should be given before or with neostigmine in

order to prevent bradycardia, excessive salivation; and other muscarinic actions of neostigmine.

Atropine Sulphate

Injection, 1 mg/ml in 1 ml ampoule

Indications: as antisialagogue pre-anaesthetic medication to prevent or reduce salivation and respiratory tract secretions.

Cautions: pregnancy, breastfeeding, in children and elderly patients. Caution is also needed in patients with hyperthyroidism, hepatic or renal disease, hypertension, tachyarrhythmias, congestive heart failure, coronary artery disease, gastric ulcer, esophageal reflex, and cardiac insufficiency. Extreme caution is required in patients with known or suspected GI-infection and with autonomic neuropathy. There should be caution also in debilitated patients with chronic pulmonary disease. Advise patients not to drive vehicle or operate machineries

Drug interactions: atropine with antacids, antidiarrhoeals (adsorbent), other anticholinergic, cyclopropane anaesthesia, ketoconazole.

Contraindications: severe ulcerative colitis, obstructive disease of the GI tract e.g. pylorodeudonal stenosis, achalasia, cardiospasm, paralytic ileus or intestinal atony (especially in geriatric or debilitated patients), known hypersensitivity, angle-closure glaucoma, obstructive uropathy, myasthenia gravis.

Side effects: dryness of mouth, nose and throat, skin; constipation decreased sweating, redness or other signs of irritation at injection site, blurred vision, decreased salivary secretion (difficulty in swallowing), mydriatic effect (increased sensitivity of eyes to light), increased intraocular pressure, bradycardia followed by tachycardia, palpitation and arrhythmias.

Dose and Administration:**Adult:***IV:* 0.3-0.6mg immediately before induction of anaesthesia.*IM:* 0.3 to 0.6mg, 30-60 minutes before induction.

Child:*IM:* 20 micrograms per kg of body weight

Storage: store at room temperature protect from freezing.

Droperidol

Injection, 2.5 mg/ml

Indications: antiemetic in surgical and diagnostic procedures; preoperative medication in patients when other treatments are ineffective or inappropriate.

Cautions: hypokalemia, hypomagnesemia, pheochromocytoma, alcoholism (acute), Parkinsonism

Drug interactions: anesthetics, bromocriptine, levodopa, CNS depression - producing medications, epinephrine, extrapyramidal reaction, hypotension- producing medications, propofol.

Contraindications: hypersensitivity to droperidol.

Side effects: akathisia, anxiety, hypertension, dystonia, hyperpyrexia, oculogyric crisis, hypotension, tachycardia, excessive sedation.

Dose and Administration: *Nausea and Vomiting: IM, IV:Adult:* initial; 2.5mg; additional doses of 1.25mg may be administered to achieve desired effect; administer additional doses with caution.

Child 2-12 years: 0.05-0.06mg/kg (maximum initial dose: 0.1mg/kg).

Storage: store at room temperature.

Fentanyl

Injection, 0.05mg/ml in 2ml ampoule

Indications: general or local adjunct anesthesia, pain of labor and vaginal delivery.

Cautions: cardiac bradyarrhythmias, hepatic impairment, hypothyroidism, renal functions impairment, respiratory impairment, elderly.

Drug interactions: antihypertensives, diuretics, benzodiazepines, cimetidine, erythromycin, CNS depression-producing medications, MAO inhibitors, nalbuphine, pentazocine, naloxone, naltrexone, neuromuscular blocking agents, nitrous oxide, phenothiazines.

Contraindications: hypersensitivity reaction to fentanyl.

Side effects: drowsiness, nausea or vomiting, brady cardia, hypotension, respiratory depression, cardiac arrhythmia, biliary spasm, changes in vision, chills, constipation, ureteral spasm, urinary retention.

Dose and Administration: *IV:Adult: Spontaneous respiration:* initially 50 - 200mcg, and 50mcg as supplements when needed.*Assisted respiration:* Initially 300-3500mcg (up to 50mcg/kg), then 100-200mcg as required.**Child over 2 years:** *Spontaneous respiration:* 1-3mcg/kg in small increments, and supplements of 1mcg/kg as required.

Assisted respiration: initially 10 - 15 mcg/kg, followed by 1 - 3 mcg/kg as required.

Storage: store at room temperature and protect from light.

Glycopyrronium Bromide (Glycopyrrolate)

Injection, 0.2 mg/ml in 1 ml and 3 ml ampoules

Indications: as antisialagogue in preanesthesia. Also, indicated as anti-arrhythmic in pre-anesthesia, anesthesia, and surgery. In addition, indicated to prevent aspiration pneumonitis during anesthesia. May be used as antidiarrheal and for cholinesterase inhibitor toxicity

Cautions: close supervision is recommended for infants, children and geriatric patients. Cardiovascular disease, prostatic enlargement, ulcerative colitis, and pyloric stenosis; pregnancy and breast-feeding.

Drug interactions: anti-cholinergics, cyclopropane, ketoconazole (*Note: patients should be advised to take this medication at least two hours after ketoconazole*), potassium chloride (especially wax –matrix preparations).

Contraindications: symptomatic reflux, paralytic ileus, glaucoma, cardiac disease, hemorrhage, myasthenia gravis, prostate hypertrophy.

Side effects: constipation; blurred vision; clumsiness or unsteadiness, confusion; difficulty in breathing; dryness of mouth, nose, or throat; drowsiness; muscle weakness; tiredness; tachycardia, hesitate micturation

Dose and Administration: Adult: *Anticholinergic – prophylaxis of excessive salivation and respiratory tract secretions, in anesthesia; and prophylaxis of gastric hypersecretory conditions, in anesthesia: IM: 4.4 mcg (0.004mg) per kg of body weight one-half to one hour before induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered.*

Antiarrhythmic, in anesthesia; or Antiarrhythmic, in surgery: IV: 100 mcg (0.1mg), the dosage being repeated if necessary at two to three minute intervals.

Cholinergic adjunct (curariform block): IV: 200mcg (0.2 mg) for each 1 mg of neostigmine or 5 mg of pyridostigmine given simultaneously; may be mixed in the same syringe.

Note: Geriatric patients may be more sensitive to the effects of the usual adult dose.

Child: *Anticholinergic Prophylaxis of excessive salivation and respiratory tract secretions, in anaesthesia; and Prophylaxis of*

gastric hypersecretory conditions, in anaesthesia; IM, 4.4 to 8.8 mcg (0.0044 to 0.0088 mg) per kg of body weight one half to one hour before induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered

Antiarrhythmics, in anesthesia; or Antiarrhythmics, in surgery: IV: 4.4 mcg (0.0044 mg) per Kg of body weight up to a maximum of 100 mcg (0.1 mg) the dosage being repeated, if necessary, at two-to three minute intervals.

Cholinergic adjunct (curariform block) *IV* – the same as usual adult and adolescent dose.

Storage: store at room temperature unless otherwise specified by manufacturer.

Hyoscine Hydrobromide

Injection, 0.4 mg/ml, 0.6 mg/ml, 1mg/ml in 1 ml ampoule

Indications: as antisialogogue pre anaesthetic medication to prevent or reduce salivation and respiratory tract secretion.

Parental administration of scopolamine in combination with morphine or mepridine is indicated in pre-anaesthesia to reduce excitement and produce amnesia.

Cautions: pregnancy and breast-feeding, in children and elderly patients. Advise patients to avoid alcohol, driving vehicle and operating machineries.

Drug interactions: antacids, antidiarrhoeals (adsorbents), other anticholinergics, cyclopropane anaesthesia, CNS depressants.

Contraindications: angle closure glaucoma, pyloric obstruction, urinary bladder neck obstruction, tachycardia, paralytic ileus, hypersensitivity to the drug, ulcerative colitis.

Side effects: constipation decreased sweating, drowsiness, dryness of mouth, skin, throat and nose, loss of memory, redness or other signs of irritation at injection site.

Dose and Administration:Adult: *Prophylaxis of excessive salivation and respiratory tract secretion in anaesthesia: IM* 0.2-0.6mg, 30 minutes to 1 hour before induction of anaesthesia.*Anaesthetic Adjunct - sedation - hypnosis: IM, IV or SC:* 0.6mg three or four times a day.*Amnesia:IM, IV, SC:* 0.32 to 0.05mg. **Child:** *Prophylaxis of excessive salivation and respiratory tract secretion in anaesthesia: IM:* administered 45 minutes - 1 hour before induction of anaesthesia. Child (4-7 months) 0.1mg. Child (7months - 3 years) - 0.15mg, Child (3-8 years) - 0.2mg, Child (8-12 years) 0.3mg.

Storage: store at room temperature in light-resistant container, protect from light.

Neostigmine

Injection (Methylsulphate), 0.5 mg/ml, 2.5 mg/ml in 1 ml ampoule

Indications: for reversal of the effects of Non-depolarizing Neuromuscular blocking agents (e.g. tubocurarine, metocurine, gallamine or pancuronium) after surgery; in the treatment of post-operative non-obstructive urinary retention; for prevention and treatment of post-operative gastro intestinal ileus and prevention of postoperative distention and urinary retention.

Cautions: caution should be taken during near term pregnancy, in elderly and in those patients with epilepsy, bronchial asthma, bradycardia, recent coronary occlusion, vagotonia, hyperthyroidism, cardiac arrhythmias, or peptic ulcer.

Drug interactions: anticholinergics especially atropine and related compounds, local and some general anaesthetics such as chloroform, cyclopropane, enflurane, halothane, lidocaine; systemic aminoglycosides, succinylcholine or decamylthonium; other cholinesterase inhibitors including demecarium, echothiopate isophlurophate, edrophonium; ganglionic blocking

agents such as guanethidine, mecamylamine, trimethaphan; procainamide.

Contraindications: intestinal or urinary tract obstruction (mechanical), hypersensitivity to the drug or bromide, peritonitis, urinary tract infection.

Side effects: diarrhoea, increasing sweating, increasing of watering of mouth, nausea, vomiting, stomach cramp, frequent urge to urinate, increased bronchial secretion, miosis, bradycardia, bronchospasm, weakness, muscle cramp, fasciculation, hypotension.

Dose and Administration:Adult: *Antidote (to non-depolarizing neuromuscular blocking agents) after surgery: IV: 0.5mg - 2mg administered slowly, repeated as required up to a total dose of 5mg.*

Note: 0.6mg to 1.2mg of atropine is administered prior to or concurrently with neostigmine to counteract its muscarinic side effect.Prevention of post-operative distention or retention:IM or SC 0.25mg immediately following surgery, repeated every four to six hours for 2 or 3 days.Prevention of post-operative distention:IM or SC- 0.5mg as needed.

Prevention of urinary retention:IM or SC - 0.5mg; dose repeated every 3 hours for at least five doses after patient has voided or the bladder has been emptied.

Note: If urination doesn't occur within one hour following the initial 0.5mg per dose, the patient should be catheterized.

Child:*Antidote (to non-depolarizing neuromuscular blocker) after surgery:IV,0.04mg per kg of body weight administered with 0.02mg of atropine per kg of body weight.*

Storage: at room temperature. Protect from freezing and light.

Oxygen (white-colored cylinder)

Indications: oxygen is given by inhalation to correct hypoxia in conditions causing under ventilation of the lungs, such as

exacerbations of chronic bronchitis, pneumonia, or pulmonary oedema, where bronchospasm causes hypoxia, as in asthma, in extensive fibrosing alveolitis after general anaesthesia and in conditions where the oxygen content of the air breathed is inadequate as at high altitudes.

Cautions: any fire or spark is highly dangerous in the presence of increased oxygen concentrations especially when oxygen is used under pressure.

Metal cylinders containing oxygen should be fitted with a reducing valve by which the rate of flow can be controlled.

Side effects: CNS, toxicity (nausea, mood change, vertigo, twitching, convulsions, loss of consciousness), pulmonary toxicity (decrease in vital capacity, cough, substernal distress, and later atelectasis), retinopathy of prematurity.

Dose and Administration: *by inhalation.* It is administered by means of nasal catheter, facemask, endotracheal tube, or oxygen tent.

Concentration of oxygen in inspired anesthetic gases should never be less than 29-30% and use sodalime (carbondioxide absorbent).

Soda lime, Carbon Dioxide Adsorbent

Used to absorb carbondioxide, for instance in closed-circuit anaesthetic apparatus.

6.4. Local Anesthetics

The local anesthetics are compounds which produce reversible loss of sensation by preventing or diminishing the conduction of sensory nerve impulses near to the site of their application or injection. Local anesthetics could also be described as local analgesics as they are most often used to produce loss of pain without loss of nervous control. Also because their mode of action is to decrease permeability of the nerve cell membrane to sodium ions they are considered to

have a membrane stabilizing effect. Local anesthetics are used very widely in dental practice, for brief and superficial interventions for obstetric procedures, and for specialized techniques of regional anesthesia calling for highly developed skills. Where patient cooperation is required the patient must be psychologically prepared to adopt the proposed procedure. Facilities and equipment for resuscitation should be readily available at all times. Care must always be taken to avoid inadvertent intravascular injection. The drugs used vary widely in their potency, toxicity, duration of action, stability in water, and ability to penetrate mucous membranes. These variations determine their suitability for use by various routes, e.g. topical (surface), infiltration, plexus, epidural (extradural) or spinal block. The cold sensation produced by ethyl chloride spray is used to test the onset of regional anaesthesia.

Local infiltration anesthesia. Many simple surgical procedures that neither involve the body cavities nor require muscle relaxation can be performed under local infiltration anesthesia. Lower segment caesarean section can also be performed under local infiltration anesthesia. The local anesthetic drug of choice is lidocaine 0.5 % with or without epinephrine. No more than 4 mg/Kg of plain lidocaine or 7 mg/kg of lidocaine with epinephrine should be administered on any one occasion. The addition of epinephrine (adrenaline) diminishes local blood flow, slows the rate of absorption of the local anesthetic, and prolongs its effect. Care is necessary when using epinephrine for this purpose since, in excesses, it may produce ischaemic necrosis. And should not be injected with epinephrine at end arterial sites (Finger, earlobe, penis, etc).

Surface anesthesia: Topical preparations of lidocaine are available and topical eye drop solutions of tetracaine are used for local anaesthesia of the cornea and conjunctiva.

Regional Block: A regional nerve block can proceed safe and effective anesthesia but its execution requires considerable training and practice. Nevertheless, where the necessary skills are available, techniques such as axillary's, ankle block, etc can be invaluable.

Either lidocaine 1 % or bupivacaine 0.5 % is suitable. Bupivacaine has the advantage of a longer duration of action.

Spinal Anesthesia: This is one of the most useful of all anaesthetic techniques and can be used widely for surgery of the abdomen and the lower limbs. It is a major procedure requiring considerable training and practice. Either lidocaine 5 % in glucose or bupivacaine 0.5 % in glucose can be used but the latter is often chosen because of its longer duration of action.*Epidural anesthesia and analgesia:* Local anesthetic agents are popular alone or with opioids or epidural anesthesia and analgesia in suitable surgical procedures and laboring mother.

Bupivacaine

Injection, 0.25%, 0.5%

Indications: the 0.5% solution is chiefly indicated for peripheral nerve blocks, eye blocks, spinal and epidural (including caudal) anesthesia. Diluted solutions (0.25%) have been used for local infiltration. Bupivacaine is particularly useful for producing prolonged analgesia during labour, where the interval between doses is usually 2-3 hours.

Cautions: respiratory impairment; hepatic impairment; epilepsy; porphyria; myasthenia gravis; pregnancy and breastfeeding.

Drug interactions: hyaluronidase.

Contraindications: adjacent skin infection, inflamed skin, concomitant anticoagulant therapy, severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient.

Side effects: cardiac arrest, hypotension, bradycardia, seizures, restlessness, anxiety, dizziness, nausea, vomiting, blurred vision, tinnitus and apnea.

Dose and Administration:Adult:*Dosage depends on site of injection, procedure used, and the status of the patient:* Not more than 2mg/kg (with or without adrenaline) should be

administered in any 4 hour period, and in 24 hours the total amount should not exceed 400mg. **Child:** *Local infiltration:* 2mg/kg. Regional anaesthesia: 2.5mg/kg
Storage: store at room temperature.

Cocaine Hydrochloride

Topical solution, 4% (40mg/ml), 10 % (100mg/ml)

Indications: provide local anesthesia and vasoconstriction of accessible mucous membranes, especially in the oral, laryngeal, and nasal cavities

Cautions: Pregnancy, breast feeding and severely traumatized mucosa and sepsis.

Contraindications: known history of hypersensitivity to the drug or to the components of the topical solution.

Side effects: nausea, nervousness, unusual feelings of well-being, or restlessness

Dose and Administration: *The dosage varies and depends upon the area to be anesthetized, vascularity of the tissues, individual tolerance, and the technique of anesthesia. The lowest dose needed to provide effective anesthesia should be administered. Dose should be reduced for children and for elderly and debilitated patients. Cocaine hydrochloride topical solution can be administered by means of cotton applicators or packs, instilled into a cavity, or as a spray.*

Storage: Store at room temperature.

Ethyl Chloride

Spray, 50ml

Indications: as a local anaesthetic in minor operative procedures such as incision of boils and removal of localized growths.

Cautions: during application, the skin adjacent to the area being treated should be covered with vaseline to protect against tissue sloughing. Inhalation of ethyl chloride should be avoided.

Contraindications: broken skin or mucous membrane.

Side effects: freezing may injure cells, decrease resistance to infections, and delay healing. The frozen tissue may be painful, as it gets warm. And cutaneous sensitization may occur rarely.

Dose and Administration: the container should be held about 12 inches (30 cm) from the area being treated and the spray directed downward until light frosting appears. Because the local anaesthetic effect is very brief, incision should be made as soon as the tissue become white.

Storage: at room temperature, in tight containers, away from fire. Protect from light.

Lidocaine Hydrochloride

Ointment, 5 % in 10 g; Jelly, 2% in 30 ml; Cartridge, 2% in 1.8 ml ampoule; Spray, 2%, 4 %, 10 % in 80 g; Viscous, 2 % in 100 ml; Injection, 0.5 %, 1 %, 2 %, 5 %

Indications: surface anaesthesia of mucous membranes; infiltration anesthesia; peripheral and sympathetic nerve block; dental anaesthesia; spinal anaesthesia; intravenous regional anaesthesia; arrhythmias.

Cautions: caution in patients with inflammation and/or infections at site of injection, and in very young, the elderly, acutely ill, or weak patients.

Drug interactions: avoid simultaneous use of lidocaine with vasoconstrictors (e.g. adrenaline) on the extremities such as the finger, toes etc.

Contraindications: known hypersensitivity.

Side effects: a transient burning sensation may occur at the site of injection.

Dose and Administration:*Note: Intradermally, subcutaneously, or submucosally (local infiltration). Inject indirectly into the tissue to be incised or in the immediate surgery area. It should be injected slowly, with frequent aspirations before and during the injection, to reduce the risk of inadvertent intravascular administration.*

The total dose should not exceed 300mg/dose (4.5mg/kg of body weight). Children should receive smaller amounts of lidocaine, generally in lower concentration than adults. *By injection*, infiltration anesthesia, according to patient's weight and nature of procedure, max, 300 mg. Ointment, *Topical*, **Adult** and **Child** 2 years of age and older as a 5 % ointment, to the affected area three or four times a day as needed. *Jelly, Topical, Adult*, to the affected area three or four times a day as needed. *Spray, Topical, Adult*, sprayed and/or applied to affected area three or four times a day as needed.

Storage: at room temperature. Protect from freezing.

Lidocaine Hydrochloride and Adrenaline

Injection, 1 % + 1:200,000 in 30 ml Vial

Injection, 2 % + 1:200,000 in 20 ml vial

See under Lidocaine Hydrochloride

Dose and Administrations: *Dental Anaesthesia (for infiltration or nerve block)*. **Adult:** 20 to 100 mg (1 to 5 ml) of lidocaine hydrochloride as 2 % solution with epinephrine 1:2000,000; **Child,** 4 to 5 mg of Lidocaine Hydrochloride per kg of body weight or 100 to 150 mg as a single dose. Local infiltration or nerve block 7 mg of lidocaine hydrochloride per kg of body weight as a 0.25 to 1 % solution with epinephrine 1:200,000.

Storage: at room temperature protect from light and freezing.

Tetracaine hydrochloride

Injection, 0.5%, 2%, 4% in 2ml vial

Indications: spinal anesthesia.

Dose and Administration: Adult: *Subarachnoid injection:* 5-20mg.

7. MEDICINES for MUSCLOSKELETAL and JOINT DISEASE

7.1. Antirheumatics

Many different drugs have been used for rheumatoid arthritis. The choice of drugs for relief of pain depends up on the severity of symptoms. In mild cases an analgesic alone may be all that is required but most patients need the additional anti-inflammatory effect provided by a NSAID (see also notes in section5.1).

Acemetacin

Capsule, 30mg, 60mg 90mg, (D/R)

Indications: pain and inflammation in rheumatic disease and other musculoskeletal disorders; postoperative analgesia.

Cautions and Side effects: see under Indometacin and notes in section 5.1

Drug interactions: coumarin or indandione derivative anticoagulants, heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasias causing medications and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes in section 5.1

Dose and Administration: 120 mg daily in divided doses with food, increased if necessary to 180 mg daily; child not recommended.

Acetylsalicylic acid

Tablet, 75 mg, 100 mg (soluble), 300 mg, 324 mg (microfined), 500 mg (enteric coated)

Indications, Cautions, Drug interactions, Contraindications, Side effects, Dose and Administration and Storage: see section 5.1

Acetylsalicylic acid + Caffeine + Paracetamol

Tablet, 250mg+65mg+250mg

Indications: temporary relief of the pain of headache, mild to moderate pain associated with migraine headache, pain due to sinusitis or colds, muscular aches, pain of menstrual discomfort, toothaches and minor arthritis pain and pain accompanied by fever.

Cautions: see notes above, also in dehydrated patients, particularly children, gout, coagulation or platelet function disorder.

Drug interactions: anticoagulants, anti-inflammatory, phenothiazines, oral hypoglycemic, insulin, sulfinpyrazone, urinary alkalinizers and acidifiers, diuretics, bronchodilators, caffeine containing beverages.

Contraindications: hypersensitivity (including asthma, angioedema, urticaria, or rhinitis) to acetylsalicylic acid or any other NSAID; active peptic ulceration.

Dosage and Administration: see section 5.1. Adults and Children over 12 Years of Age: 2 tablet with a full glass of water after meal every 6 hours while symptoms persist, not to exceed 8 tablets in 24 hours. *Note: The patient should be instructed not to lie down for 15-30 minutes following drug intake in order to reduce the risk of esophageal irritation and ulceration.*

Diclofenac Diethylamine

Gel, 1%, 30gm

Indications: For the relief of aches and pain associated with acute, localized muscle or joint injuries such as sprains, strains or sports injuries (e.g. sprain of ankle, strain of shoulder or back muscles). Rest may also be helpful to assist the relief of associated discomfort.

Cautions, Contraindications and Side effects: see section 5.1

Drug interactions: anticoagulants (blood thinners), or heparin or thrombolytic agents, antihypertensives, oral antidiabetic agents, fluoroquinolone antibiotics (ofloxacin) aspirin and anti-inflammatory, colchicine, lithium, methotrexate, probenecid. See section 5.1

Dose and Administration: Adults and adolescents 16 years and older: apply Diclofenac diethylamine gel 3 to 4 times a day. Gently rub a small amount of Diclofenac diethylamine gel into the skin where you have pain or swelling. The amount needed will vary depending upon the size of the painful or swollen area. Usually, a strip approximately 2 cm long will be sufficient to cover a 200cm² area. Wash your hands after rubbing in Diclofenac diethylamine gel, unless of course they are the site being treated. The gel should not be used for more than 7 days for muscle and joint injuries, unless recommended.

Diclofenac sodium

Capsule(S/R), 75mg

Injection, 25 mg/ml in 3 ml ampoule, 75mg/ml

Tablet (e/c), 25 mg, 50 mg

Tablet 75mg (S/R) ,100mg(S/R)

Sachet, 50mg (as potassium)

Suppository, 12.5mg, 25mg, 50mg, 100 mg

Gel, 1%, 3%

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout; postoperative pain.

Cautions: See notes in section 5.1

Drug interactions: coumarin or indandione derivative anticoagulants, or heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene, aspirin and anti-inflammatory, blood dyscrasia causing medications and

bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: See also notes in section 5.1, porphyria.

Side effects: see notes above; suppositories may cause rectal irritation, injection site reactions.

Dose and Administration:Adult: *Oral: Rheumatoid arthritis:* 150-200mg per day in three or four divided doses, initially. After a satisfactory response has been obtained, dosage should be reduced to the minimum dose that provides continuing control of symptoms, usually 75 – 100 mg a day in 3 divided doses.

Deep IM injection into the gluteal muscle: *acute exacerbations and post-operative:* 75 mg once daily (twice daily in severe cases) for maximum of 2 days.

Ureteric colic: 75 mg then a further 75 mg after 30 minutes if necessary.*IV infusion* (in hospital setting), 75 mg repeated if necessary after 4 – 6 hours for maximum 2 days.*Prevention of postoperative pain,* initially after surgery 25 to 50 mg over 15 – 60 minutes then 5 mg/hour for maximum 2 days.*Rectum in suppositories,* 75 to 150 mg daily in divided doses. Maximum total daily dose by any route 150 mg.**Child** 1 – 12 years, *juvenile arthritis, Oral or rectum:* 1 – 3 mg/kg daily in divided doses (25 mg e/c tablets, 12.5 mg and 25 mg suppositories only).

Storage: at room temperature in a tight container, protect from moisture.

Diclofenac sodium + Misoprostol

Tablet, 50mg + 200mcg, 75mg+200mcg

Indications: the diclofenac component is indicated for the treatment of osteoarthritis and rheumatoid arthritis; the

misoprostol component is indicated for the prophylaxis of NSAID-induced gastric and duodenal ulceration.

Dose and Administration:*Oral:Adult: Osteoarthritis:* 50 mg/200 mcg three times daily. For patients experiencing intolerance, 50 mg/200 mcg or 75 mg/200 mcg twice daily can be used, but is less effective at preventing ulcers. *Dosages of diclofenac higher than 150 mg/day and misoprostol 800 mcg/day in osteoarthritis are not recommended.**Rheumatoid arthritis:* 50 mg/200 mcg three or four times daily. For patients experiencing intolerance, 50 mg/200 mcg or 75 mg/200 mcg twice daily can be used, but is less effective at preventing ulcers.

Etofenamate

Gel, 5%, 10%

Cream, 10%

Lotion, 10%

Spray, 100mg/ml (18mg/dose)

Indications: treatment of soft tissue rheumatic disorders of musculoskeletal system: muscular rheumatism muscle hardening which occurs with frozen shoulder (periarthritis of the shoulder), lumbago, sciatica, tenosynovitis, bursitis, disorders caused by overstraining and erosion of the spinal column or joints (spondylosis, osteoarthritis), treatment of blunt injuries (sport injuries such as bruises, sprains and strains)

Caution: do not apply to damaged, eczematous inflamed skin, to the mucus membranes, to the eyes and any other open skin

Contraindications: hypersensitivity to etofenamate, flufenamic acid, or any other NSAID pregnancy and breast feeding, children

Side effects: reddening of the skin, allergic skin reactions (intense itching, rashes, erythema, swelling, blistering).

Dose and administration: for rheumatic disorders, apply strip of gel 5 to 10 cm long (corresponding to approximately 1.7 to

3.3 mg per administration three to four times a day for 3 to 4 weeks and for sports injuries up to 2 weeks depending on the size of the painful areas and rub over in over as large as an area of the skin as possible

Storage: do not store above 25 °C

Ibuprofen

Capsule, 300 mg

Tablet, 200 mg, 400 mg (enteric coated, optional)

Syrup, 100mg/5ml

Indications, Cautions Drug interactions, Contraindications Side effects and Dose and Administration: see section 5.1.

Indomethacin

Capsule, 25 mg, 50mg, 75mg

Suppository, 100 mg

Syrup, 25mg/5ml, 100mg/5ml

Tablet, 25mg (enteric coated, optional)

Indications: acute or chronic rheumatoid arthritis, for relief of acute or chronic osteoarthritis and for relief of acute or chronic ankylosing spondylitis; acute gout (section 6.2). It is also indicated for relief of acute or chronic juvenile arthritis and in the treatment of psoriatic arthritis.

Cautions: see notes above, also epilepsy, Parkinsonism, psychiatric disturbances, during prolonged therapy ophthalmic and blood examinations particularly advisable; avoid rectal administrations in proctitis and haemorrhoids. Dizziness may affect performance of skilled tasks (e.g. driving)

Drug interactions: coumarin or indandione derivative anticoagulants, heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasias causing medications

and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes above

Side effects: see notes above; frequently gastrointestinal disturbances (including diarrhea, headache, dizziness, and light-headedness; also gastro-intestinal ulceration and bleeding; rarely, drowsiness, confusion, insomnia, convulsions, psychiatric disturbances, depression, syncope, blood disorders (particularly thrombocytopenia), hypertension, hyperglycaemia, blurred vision, corneal deposits, peripheral neuropathy, and intestinal strictures; suppositories may cause rectal irritation and occasional bleeding.

Dose and Administration: **Adult:** *Anti-rheumatic:Oral:* initially 25 to 50mg two or four times a day, if well tolerated, the dosage per day may be increased by 25 or 50mg at weekly intervals until a satisfactory response is obtained or up to a maximum dose of 200mg per day.*Rectal:* 50mg four times a day. **Child:** *Anti-rheumatic:Oral:* 1.5 to 2.5mg per kg of body weight, per day, administered in three or four divided doses, up to a maximum of 4mg per kg of body weight per day or 150 to 200mg per day, whichever is less.*Rectal:* same as oral (for children).

Storage: store at room temperature in a well-closed container.

Leflunomide

Tablet, 10mg, 20mg, 100mg

Indications: treatment of active rheumatoid arthritis; indicated to reduce signs and symptoms, and to retard structural damage and improve physical function.

Cautions: hepatic disease, patients with severe immune deficiency, uncontrolled infection; hematologic abnormalities; renal impairment.

Drug interactions: NSAIDs, methotrexate, rifampin.

Contraindications: pregnancy, hypersensitivity reaction.

Side effects: diarrhea, respiratory tract infection, hypertension, chest pain, headache, dizziness, fever, sleep disorder, rash, alopecia, eczema, nausea, weight loss, anorexia, vomiting, bronchitis, cough.

Dose and Administration: *Oral: Adult:* Initial: 100mg/day for 3 days, followed by 20mg/day; dosage may be decreased to 10 mg/day in patients who have difficulty tolerating the 20mg dose.

Storage: store at room temperature and protect from light.

Meloxicam

Tablet, 7.5mg, 15mg

Indications: Pain and inflammation in rheumatic disease; exacerbation of osteoarthritis (short-term); ankylosing spondylitis

Cautions: renal impairment; hepatic impairment; cardiac disease; elderly; pregnancy and breastfeeding; coagulation defects; allergic disorders.

Drug interactions: coumarin or indandione derivative anticoagulants, heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasias causing medications and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid, sulfonyleurea antidiabetic agents.

Contraindications: hypersensitivity (including asthma, angioedema, urticaria, orrhinitis) to acetylsalicylic acid or any other NSAID; active peptic ulceration.

Side effects: Gastro-intestinal disturbances including discomfort, nausea, diarrhoea, and occasionally bleeding and ulceration occur. Systemic as well as local effects of NSAIDs

contribute to gastro-intestinal damage; taking oral formulations with milk or food, or using enteric-coated formulations, or changing the route of administration may only partially reduce symptoms such as dyspepsia. Other side-effects include hypersensitivity reactions (particularly rashes, angioedema, and bronchospasm), headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances such as tinnitus, photosensitivity, and haematuria. Blood disorders have also occurred. Fluid retention may occur (rarely precipitating).

Dose and Administration: *Oral: Osteoarthritis:* Adult and child over 16 years: 7.5 mg once daily, increased if necessary to max. 15 mg once daily.

Rheumatoid arthritis, ankylosing spondylitis: Adult and Child over 16 years: 15 mg once daily, may be reduced to 7.5 mg once daily; elderly 7.5 mg daily; Child 12-18 years and body weight under 50kg – 7.5mg once daily; Child 12-18 years and body weight over 50kg – 15mg once daily.

Storage: store it at room temperature and away from excess heat and moisture

Naproxen

Tablet, 200mg, 220mg, 250mg, 375mg, 500mg

Suspension, 125/5ml

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; dysmenorrhoea; acute gout.

Cautions, Drug interactions, Contraindications and Side effects: See under meloxicam.

Dose and Administration: Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

Rheumatic disorders the usual initial dose of naproxen is 250 mg, twice daily, adjusted to 500 mg to 1g daily in two divided doses. Acute gout, an initial dose of 750 mg followed by 250 mg every 8 hours has been suggested; while in dysmenorrhoea 500 mg may be given initially, followed by 250 mg every 6 to 8 hours. A dose of 10 mg per body weight daily, in two divided doses has been used in children over 5 years of age with juvenile rheumatoid arthritis. The elderly are at increased risk of the serious consequences of adverse reactions. If NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

Storage: store in a dry place below 25°C. Protect from light. Keep container tightly closed.

Nimesulide

Tablet, 100mg, 200mg

Indications: treatment of acute pain, symptomatic treatment of painful osteoarthritis, primary dysmenorrhea

Cautions: Nimesulide containing medical products should be use for the shortest possible duration as required by the clinical situation. May cause hepato toxicity, gastrointestinal bleeding or ulceration, may interfere with platelet function, and may impair female fertility, co administration of NSAIDs or other analgesics with Nimesulide is not recommended.

Contraindication: known hypersensitivity to Nimesulide, history of hypersensitivity reactions to other NSAIDs, history of hepatic reactions to Nimesulide, active gastric or duodenal ulcer, severe coagulation disorders, severe heart failure, severe renal impairment, and severe renal impairment, children under 12 years old.

Piroxicam

Capsule, 10 mg, 20 mg

Tablet, 10 mg, 20 mg

Suppository, 20 mg

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout.

Cautions: CHF, hypertension, dehydration, history of GI disease.

Drug interactions: lithium, methotrexate, amiodarone, fluoxetine, glimepiride, glipizide, phenytoin, sertraline, warfarin, and other CYP2C8/9 substrates; diuretics; beta-blockers; aspirin; antacids, and cholestyramine.

Contraindications: hypersensitivity to piroxicam, aspirin or other NSAIDs; active GI bleeding; pregnancy (3rd trimester or near term).

Side effects: dizziness, rash, abdominal cramps, heartburn, indigestion, nausea, headache, nervousness, itching, fluid retention, vomiting and tinnitus.

Dose and Administration: *Oral, Rectum: Adult: Rheumatic disease:* initially 20 mg daily, maintenance 10 - 30 mg daily, in single or divided doses.

Childover 6 years: *Oral: juvenile arthritis,* less than 15 kg, 5 mg daily; 16 - 25 kg, 10 mg; 26-45 kg, 15mg; over 46kg, 20 mg. *Acute musculoskeletal disorders:Adult:* 40 mg daily in single or divided doses for 2 days, then 20 mg daily for 7 - 14 days. *Acute goute:Adult:* 40 mg initially, then 40 mg daily in single or divided doses for 4 - 6 days.

Sulphasalazine

Tablet (e/c), 500mg

Indications: severe rheumatoid arthritis.

Cautions: renal or hepatic impairment, or urinary tract obstruction, pregnancy and breast-feeding, glucose-6-phosphate dehydrogenase(G6PD) deficiency, intestinal obstruction, blood dyscrasias, porphyria.

Drug interactions: digoxin, diuretics, oral contraceptives, oral antidiabetic agents, phenytoin or phenobarbital, pyrimethamine, warfarin, zidovudine and lamivudine.

Contraindications: hypersensitivity to salicylates and sulphonamides; child under 2 years of age.

Side effects: nausea, vomiting, diarrhea and anorexia; reversible oligospermia and infertility are common in males; haematological disturbances, hypersensitivity reactions and hepatic function disturbances. Photosensitivity may occur.

Dose and Administration:Adult:Oral: initially 500mg daily, increased by 500mg at intervals of 1 week to a maximum of 2-3g daily in divided doses.

Storage: protect from light.

Tenoxicam

Tablet, 20mg

Suppository, 20mg

Indications: symptomatic management of osteoarthritis and rheumatoid arthritis and also in the short term management of soft-tissue injury.

Cautions and Side effects: as for non-steroidal anti-inflammatory drug in general.

Drug interactions: see under indomethacin

Dose and Administrations: Oral: as a single daily dose usually of 20mg. In acute skeletal disorders treatment for up to 7 days is usually sufficient but in severe cases it may be given for up to a maximum of 14 days. Dose similar to those given by mouth have been given *by rectal* suppository. Child not recommended.

Tolmetin sodium

Capsule, 200 mg, 400 mg

Tablet, 200 mg

Indications: treatment of rheumatoid arthritis and osteoarthritis, juvenile rheumatoid arthritis.

Cautions: as piroxicam.

Drug interactions: digoxin, methotrexate, cyclosporine,

Contraindications: hypersensitivity to tolmetin, aspirin, or other NSAIDs, pregnancy (3rd trimester or near term).

Side effects: chest pain, hypertension, edema, headache, dizziness, drowsiness, depression, skin irritation, weight gain/loss, heartburn, abdominal pain, diarrhea, flatulence, vomiting, constipation, gastritis, peptic ulcer, nausea, urinary tract infection, visual disturbances, tinnitus.

Dose and Administration: *Oral: Adult:* 400 mg 3 times /day; usual dose: 600 mg to 1.8 g/day; maximum; 2 g/day. **Child ≥ 2 years:** *Anti-inflammatory:* initial: 20 mg/kg/day in 3 divided doses, then 15-30 mg/kg/day in 3 divided doses. *Analgesic:* 5-7 mg/kg/dose every 6-8 hours.

7.2. Medines used for Gout

It is important to distinguish drugs for the treatment of acute attacks of gout from those used in the long-term control of the disease. The latter exacerbate and prolong the acute manifestations if started during attack.

Acute gout: Acute attacks of gout are usually treated with high doses of NSAIDs such as indomethacin (150 - 200 mg daily in divided doses), ibuprofen has weaker anti-inflammatory properties than other NSAIDs and is therefore unsuitable for treatment of gout. Salicylates, including acetylsalicylic acid are also not suitable because they may increase plasma-urate

concentrations. Colchicine is an alternative for those patients in whom NSAIDs are contraindicated. Its use is limited by toxicity with high doses. It does not induce fluid retention and can therefore be given to patients with heart failure; it can also be given to patients receiving anticoagulants.

Chronic gout: For long-term control of gout in patients who have frequent attacks, the xanthine oxidase inhibitor allopurinol may be used to reduce production of uric acid. It should not be used to treat an acute attack since it may prolong it indefinitely. Treatment for chronic gout should not be started until after an acute attack has completely subsided, usually 2 - 3 weeks. The initiations of allopurinol treatment may precipitate an acute attack therefore colchicines or a suitable NSAIDs should be used as a prophylactic and continued for at least one month after the hyperuricaemia has been corrected. If an acute attack develops during treatment for chronic gout, then allopurinol should continue at the same dosage and the acute attack should be treated in its own right. Treatment for chronic gout must be continued indefinitely to prevent further attacks of gout.

Note: Administer, prophylactic colchicine or non-steroidal anti-inflammatory drugs (not aspirin or salicylates) until at least 1 month after hyperuricemia corrected, ensure adequate fluid intake (2 liters/day). In neoplastic conditions treatment with allopurinol should be commenced before cytotoxic drugs are given.

Allopurinol

Tablet, 100 mg

Indications: long-term management of hyperuricemia associated with primary or secondary gout; to control hyperuricemia secondary to blood dyscrasias such as polycythemia vera, myeloid metaplasia, or their treatment.

Note: Allopurinol is not effective in the treatment of acute gout attacks because it has no anti-inflammatory action, and may intensify and prolong inflammation during the acute phase.

Cautions: renal and hepatic function impairment, diabetes mellitus, and hypertension

Drug interactions: coumarin or indandione derivative anticoagulants, mercaptopurine, alcohol, xanthenes such as aminophylline, oxtriphylline, theophylline, furosemide, diazoxide, ethacrinic acid and thiazide diuretics.

Contraindications: sensitivity to allopurinol, acute gout.

Side effects: dermatitis allergic (skin rash, hives or itching), agranulocytosis (chills, fever or sore throat), angitis (vasculitis), hypersensitivity (chills, fever, sore throat muscle ache, pain or weakness, shortness of breath, troubled breathing, tightness in chest, wheezing), diarrhoea, drowsiness, headache.

Dose and Administration: Adult: Antic gout: Initial - Oral, 100mg once a day, to be increased by 100mg per day at one week intervals until the desired serum uric acid concentration is attained. Maximum - 800mg per day. Maintenance - Oral, 100 - 200mg two or three times a day or 300mg as a single dose once a day.

Child: Antihyperuricemic, in neoplastic disease therapy:

Child (up to 6 years)- Oral, 50mg three times a day; 6-10 years of age, oral, 100mg three times a day or 300mg as a single dose once a day.

Note: Drink large amounts of fluids.

Storage: at room temperature in a well-closed container.

Colchicine

Injection, 0.5 mg/ml in 2 ml ampoule

Tablet, 0.5mg

Indications: acute gout, short-term prophylaxis during initial therapy with allopurinol and uricosuric drugs; prophylaxis of familial Mediterranean fever (recurrent polyserositis).

Cautions: elderly, gastro-intestinal disease, cardiac, hepatic and renal impairment

Drug interactions: cyclosporin

Contraindications: pregnancy and breast-feeding

Side effects: most common are nausea, vomiting, and abdominal pain, excessive doses may also cause profuse diarrhea, gastro-intestinal hemorrhage, rashes, renal and hepatic damage. Rarely peripheral neuritis, myopathy, alopecia, and blood disorder with prolonged treatment.

Dose and Administration: Acute gout: Oral: 0.5 - 1mg initially, followed by 500 micrograms every 2 - 3 hours until relief of pain is obtained, or vomiting or diarrhea occurs; maximum total dose 6 mg, the course should not be repeated within 3 days. Prevention of gout attacks during initial treatment with allopurinol, 500 micrograms 2 - 3 times daily continuing for at least 1 month after hyperuricaemia has been corrected.

Storage: at room temperature. Protect from freezing. Protect from light.

Ibuprofen

Tablet, 200 mg, 400 mg (enteric coated, optional)

Indications: for relief of the pain and inflammation of acute gout arthritis.

Cautions, Drug Interactions, Contraindications, Side effects,

Storage; See section 6.1 under Ibuprofen.

Dose and Administrations: Treatment of acute migraine attack: Oral: preferably with or after food,

Adult: 400–600 mg at first sign of attack may be repeated every 6–8 hours if necessary, maximum 2.4 g daily; **Children:** 8–12

years 200 mg at first sign of attack, may be repeated every 6–8 hours if necessary

Indomethacin

Capsule, 25 mg

Suppository, 100 mg

Indications: for relief of the pain and inflammation of acute gouty arthritis.

Cautions, Drug interactions, Contraindications, Side effect, and Storage; see section 6.1, under indomethacin.

Dose and Administration: Adult: Antigout: Oral: 100mg initially, then 50mg three times a day until pain is relieved, with the dosage then being reduced until medication is discontinued. *Rectal:* the total daily dose may be given as 100mg in the morning and at night. The total daily combined dose by mouth and by rectum should not exceed 200mg. In acute gout the daily dose is 150-200mg in divided doses until all symptoms and signs subside. In Child dose not recommended.

Probenecid

Tablet, 500 mg

Indications: long-term management of hyperuricemia associated with chronic gout.

Note: It is not effective in the treatment of acute gout attacks and does not eliminate the need to use colchicine or non-steroidal anti-inflammatory drugs to relieve an attack.

Cautions: children (younger than 2 years of age), in patients with peptic ulceration, renal function impairment, blood dyscrasias.

Drug interactions: antineoplastic (rapidly cytolytic), zidovudine, indomethacin, ketoprofen, aspirin or other

salicylates (including bismuth subsalicylate), cephalosporines or penicillines, heparin, and nitrofurantoin.

Contraindications: probenecid is contraindicated in any condition in which there is an increased risk of uric acid renal calculi formation or urate nephropathy such as cancer chemotherapy with rapidly cytolytic antineoplastic agents, radiation therapy for malignancy, moderate to severe renal function impairment, history of blood dyscrasias nephrolithiasis, porphyria, acute gout attacks.

Side effects: acute gout, arthritis attack (joint pain, redness, swelling) headache, loss of appetite, nausea or vomiting (mild), dizziness, flushing or redness of face, urinary frequency, sore gums, aplastic anaemia, nephrotic syndrome (cloudy urine, swelling of face).

Dose and Administration:Adult: *Antigout:* *Oral:* Initial 250mg two times a day for one week. Maintenance 500mg two times a day.

Child: dosage has not been established.

Storage: at room temperature in a well-closed container.

7.3. Skeletal Muscle Relaxants

Centrally acting muscle relaxants have a selective action on the central nervous system and are used in the management of spasticity due to neuromuscular and musculoskeletal disorders and for relief of painful muscle spasm. Diazepam and baclofen are effective for the control of muscle spasm in a variety of disorders. The efficacy of agents such as methocarbamol and orphenadrine is controversial; they may be no more clinically useful than adequate analgesia alone. Significant adverse effects (e.g. sedation, hepatotoxicity, immunological reactions) may occur. Dantrolene acts uniquely outside the CNS and used in the

treatment of malignant hyperthermia and in selected instances of skeletal muscle spasticity.

Muscle relaxants should be used with caution if muscle spasticity plays a role in sustaining upright posture and balance. A reduction in muscle tone may cause a loss of the splinting action of the spastic muscles and lead to increased disability and instability.

Baclofen

Tablet, 5mg, 10mg

Indications: relief of muscle spasticity due to spinal cord injury or disease, especially multiple sclerosis; pain relief in trigeminal neuralgia; stiff - man syndrome.

Cautions: epilepsy, peptic ulcer disease, renal impairment, cerebrovascular disease or pre - existing psychiatric disturbances.

Drug interactions: other CNS depressants; antihypertensive agents. **Contraindications:** hypersensitivity to baclofen.

Side effects: drowsiness, dizziness, ataxia, nausea, constipation or diarrhea, confusion, hypotension, allergic skin reactions; psychiatric disturbances (e.g. depression, hallucinations, euphoria) occur occasionally in the elderly or in patients with psychiatric or brain disorders.

Dose and Administration: *Oral: Adult:* initially 5mg 3 times daily; preferably with meals, increased by 5mg /dose every 3 days until the desired response is obtained, usually with 30 - 75mg/day. Maximum 100 mg/day.

Child: 1 to 1.5mg/kg daily. Maximum doses: 2 - 7 years, 30 - 40 mg/day; over 8 years, 60mg/day.

Storage: store at room temperature.

Chlormezanone + Paracetamol

Tablet, 100mg + 450mg

Indications: relief of generalized pain associated with tension.

Cautions: do not use continuously for more than 10 days without consulting your doctor; liver or kidney disease.

Drug interactions: other tranquilizers or antidepressants.

Contraindications: sensitivity to Paracetamol. Safety in pregnancy and lactation has not been established.

Side effects: sensitivity reactions resulting in reversible skin rash or blood disorders; drowsiness, weakness, nausea, dizziness, flushing of the skin, excitement, depression, skin rash, confusion, dryness of the mouth and difficulty in micturition; cholestatic jaundice may occur. The patient should not drive a vehicle or operate machinery, if dizziness or drowsiness occurs.

Dose and Administration:Adult: 1 tablet 3-4 times daily as required. **Child 9-12 years:** ½ tablet 3 - 4 times daily as required. *Not for children under 9 years of age.*

Storage: store below 25°C. Protect from light.

Dantrolene sodium

Capsule, 25mg, 50mg

Indications: treatment of spasticity associated with spinal cord injury, stroke, cerebral palsy, or multiple sclerosis; treatment of malignant hyperthermia.

Cautions: impaired cardiac function or pulmonary functions; hepatic disease.

Drug interactions: estrogens, CNS depressants, MAO inhibitors, phenothiazines, clindamycin, verapamil, warfarin, clofibrate, tolbutamide,azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin,

aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin and rifamycins.

Contraindications: active hepatic disease; should not be used where spasticity is used to maintain posture or balance.

Side effects: drowsiness, dizziness, lightheadedness, fatigue, rash, diarrhea, vomiting, muscle weakness, chills, fever, headache, insomnia, nervousness, mental depression, constipation, anorexia, stomach cramps, blurred vision, respiratory depression.

Dose and Administration: Oral: *Spasticity*: **Adult:** 25mg/day to start, increase frequency to 2 - 4 times/day, then increase dose by 25mg every 4 - 7 days to a maximum of 100mg 2 - 4 times / day or 400mg/day.

Child: initial 0.5mg/kg/dose twice daily, increase frequency to 3 - 4 times/day at 4 - 7 day intervals, then increase dose by 0.5mg/kg to a maximum of 3mg/kg /dose 2 - 4 times/day up to 400mg/day.

Malignant hyperthermia:

Adult and Child: *preoperative prophylaxis:* 4 to 8 mg/kg/day in 4 divided doses, begin 1 to 2 days prior to surgery with last dose 3 - 4 hours prior to surgery.

Storage: store at room temperature.

Diazepam

Tablet, 2 mg, 5 mg, 10 mg

Syrup, 2 mg / 5 ml

Injection, 10 mg/ml, in 2 ml ampoule

Indications: muscle spasm of varied etiology, including tetanus; other indications (section 4.2, section 4.4).

Cautions: see section 4.2; special precautions for intravenous injection.

Contraindications, Side effects, see section 4.2; also hypotonia.

Dose and Administration:*Oral:* 2 - 15 mg daily in divided doses, increased if necessary in spastic conditions to 60 mg daily according to response.

Cerebral spasticity in selected cases:

Child: 2 - 40 mg daily in divided doses. IM or slow IV injection (into a large vein at a rate of not more than 5 mg/minute), in acute muscle spasm, 10 mg repeated if necessary after 4 hours. Tetanus: Adult and Child: IV injection: 100 - 300 micrograms/kg repeated every 1 - 4 hours; IV infusion (or by nasoduodenal tube): 3 - 10 mg/kg over 24 hours, adjusted according to response. *Note: Only use IM route when oral and IV routes not possible.*

Methocarbamol

Injection, 1g in 10ml vial

Tablet, 500mg

Indications: treatment of muscle spasm associated with acute painful musculo skeletal conditions; supportive therapy in tetanus.

Cautions: renal or hepatic impairment, seizures.

Drug interactions: CNS depressants, ethanol.

Contraindications: hypersensitivity to methocarbamol.

Side effects: flushing of face, bradycardia, hypotension, syncope, drowsiness, dizziness, lightheadedness, convulsion, vertigo, headache, fever, amnesia, confusion, insomnia, sedation, allergic dermatitis, urticaria, pruritus, rash, nausea, vomiting, metallic taste, dyspepsia, leukopenia, jaundice, thrombophlebitis, blurred vision, renal impairment, conjunctivitis and nasal congestion.

Dose and Administration:*Muscle spasm: Adult and Child > 16 years:* *Oral:* 1.5g 4 times /day for 2 -3 days (up to 8g/day may be given in severe conditions) then decrease to 4 – 4.5 g /day in 3 - 6 divided doses.

I.M, I.V: 1 g every 8 hours if oral not possible; injection should not be used for more than 3 consecutive days. If condition persists, may repeat course of therapy after a drug- free interval of 48 hours.

Elderly: *oral:* initial: 500mg 4 times /day.

Storage: Store at controlled room temperature.

Orphenadrine Citrate

Tablet, 100 mg

Drop, 2.5 mg/ml

Injection, 30 mg/ml

Indications: to relieve pain due to spasm of skeletal muscle (see notes above).

Cautions, Drug interactions, Contraindications, Side effects; see section 4.5 under orphenadrine hydrochloride.

Dose and Administration:Adult: *Oral:* 100 mg twice daily IM *or slow IV* (over a period of 5 minutes) injection in a dose of 60 mg which is repeated every 12 hours, as needed.

Storage: at room temperature, protect from light and freezing.

Other centrally acting muscle relaxants include

Orphenadrine citrate + Paracetamol

Tablet, 35mg + 450mg

Indications: generalised pain and the relief of muscle spasm associated with acute painful musculo-skeletal conditions.

Cautions: cardiac disease or arrhythmias, especially tachycardia.

Drug interactions: orphenadrine may increase central nervous system depression if taken concurrently with alcohol or central nervous system depressants. Anticholinergic effects may be intensified if orphenadrine is taken concurrently with anticholinergics or medication with anticholinergic effects.

Contraindications: hypersensitivity to any of the ingredients; severe liver function impairment; prostatic enlargement, achalasia, bladder neck obstruction, glaucoma, myasthenia gravis, peptic ulcer or stenosing and pyloric or duodenal obstruction; safety in pregnancy and lactation has not been established; porphyria.

Side effects: see under individual preparations.

Dose and Administration:Adult: 2 tablets 3 times a day. Do not exceed the recommended dosage.

Storage: store below 25°C. Protect from light.

7.4. Cholinergic and Anticholinesterase Agents

Parasympathomimetics may be classified into 2 distinct pharmacological groups. Cholinergic agonists, such as bethanechol, which act directly on effector cells to mimic the effects of acetylcholin. Anticholinesterases (neostigmine, pyridostigmine and edrophonium) which inhibit the enzymic hydrolysis of acetylcholin by acetylcholinesterase and other cholinesterases, thereby prolonging and enhancing its actions in the body.

Bethanechol

Tablet, 10mg, 25mg

Injection (chloride), 5 mg/ml in 1 ampoule

Indications: nonobstructive urinary retention and retention due to neurogenic bladder.

Cautions: hyperthyroidism, peptic ulcer disease, epilepsy, obstructive pulmonary disease, bradycardia, vasomotor instability, atrioventricular conduction defects, hypotension, or Parkinsonism.

Drug interactions: procainamide, quinidine, atropine, antihistamines, TCAs, phenothiazines.

Contraindications: hypersensitivity to bethanechol; mechanical obstruction of the GI or GU tract.

Side effects: hypotension, tachycardia, bradycardia, flushed skin, head ache, malaise, abdominal cramps, diarrhea, nausea, vomiting, salivation, eructation, urinary urgency, lacrimation, miosis, asthmatic attacks, branchial constriction, diaphoresis.

Dose and Administration:

Adult: urinary retention, neurogenic bladder, and/or bladder atony: *Oral:* initial, 10 – 50 mg 2- 4 times/day. To determine effective dose, may initiate at a dose of 5 - 10mg, with additional doses of 5 - 10 mg hourly until an effective cumulative dose is reached.

SC: Initial: 2.575mg, may repeat in 15 - 30 minutes; (maximum cumulative initial dose: 10.3mg); subsequent doses may be given 3 - 4 times daily as needed.

Storage: store at room temperature.

Edrophonium

Injection, 10mg/ml in 1ml ampoule

Indications: diagnosis of myasthenia gravis, differentiation of cholinergic crises from myasthenia crises, reversal of non depolarizing neuromuscular blockers, adjunct treatment of respiratory depression caused by curare overdose.

Cautions: bronchial asthma and those receiving a cardiac glycoside; atropine sulfate should always be readily available as an antagonist.

Drug interactions: digoxin, succinylcholine, decamethonium, pancuronium, vecuronium, acetazolamide, neostigmine, physostigmine, atropin, nondepolarizing muscle relaxants, procainamide, and quinidine.

Contraindications: hypersensitivity to edrophonium, GI or GU obstruction.

Side effects: bradycardia, hypotension, decreased carbon monoxide, tachycardia, convulsions, dizziness, loss of consciousness, drowsiness, headache, skin rash, thrombophlebitis, urticaria, hyperperistalsis, nausea, vomiting, salivation, diarrhea, stomach cramps, dysphagia, flatulence, urinary urgency, muscle cramps, spasms, small pupils, lacrimation, increased bronchial secretions, laryngospasm, respiratory muscle paralysis, dyspnea, bronchospasm.

Dose and Administration: Adult: *Diagnosis:IV:* 2 mg test dose administered over 15 - 30 seconds; 8 mg given 45 seconds later if no response is seen; test dose may be repeated after 30 minutes.*IM:* Initial: 10mg, if no cholinergic reaction occurs; administer 2mg 30 minutes later. Titration of oral anticholinesterase therapy: 1 - 2mg 1 hour after oral dose of anticholinesterase. Reversal of non-depolarizing neuromuscular blocking agents:*I V:* 10mg over 30 - 45 seconds, may repeat every 5 - 10 minutes up to 40mg. *Termination of paroxysmal atrial tachycardia:* IV rapid injection: 5- 10mg. *Differentiation of cholinergic from myasthenic crisis:* IV: 1mg; may repeat after 1 minute. **Child:** *Diagnosis:*Initial; 0.04 mg/kg over 1 minute followed by 0.16 mg/kg if no response, to a maximum total dose of 5mg for children < 34kg, or 10mg for children > 34kg. *Titration of oral anticholinesterase therapy:* 0.04 mg/kg once given 1 hour after oral intake of the drug being used in treatment.

Infant: *IM:* 0.5 to 1 mg. *I.V:* Initial 0.1 mg, followed by 0.4mg if no response; total dose to 0.5mg.

Storage: protect from light.

Neostigmine

Tablet (Bromide), 15 mg

Injection (Methylsulphate), 0.5 mg/ml, 2.5 mg/ml in 1 ml ampoules

Indications: in the treatment of conditions such as myasthenia gravis and to reverse muscle relaxation produced by competitive (non-depolarizing) muscle relaxant.

Cautions, Contraindications, Drug interactions, Side effects; see section 5.3 under neostigmine.

Dose and Administrations:*Oral:* as neostigmine bromide, **Adult:** 15 to 30 mg at suitable intervals throughout day, total daily dose 75 - 300 mg; but doses above 180 mg daily not usually tolerated.

Child: up to 6 years, initially 7.5 mg, 6 – 12 years, initially 15 mg, total daily dose usually 15 – 90 mg in divided doses at appropriate intervals.

SC or IM injection: as neostigmine methylsulphate,

Adult: 0.5 to 2.5 mg as required, total daily dose 5 to 20 mg.

Neonate: 50 - 250 micrograms 30 minutes before feeds (not usually required beyond 8 weeks of age);

Child: 200 - 500 micrograms as required.

Pyridostigmine bromide

Tablet, 10mg, 25mg, 60mg, 180mg (sustained release)

Injection, 1mg/ml, 5mg/ml in 1ml ampoule

Indications: myasthenia gravis.

Cautions: asthma, urinary tract infection, cardiovascular disease including arrhythmias, hypotension, peptic ulcer,

epilepsy, parkinsonism, avoid intravenous injection, renal impairment, pregnancy and breastfeeding.

Drug interactions: alcuronium, atropine, biperiden, chloroquine, clindamycin, gentamicin, lithium, procainamide, propranolol, quinidine, streptomycin, suxamethonium, vecuronium.

Contraindications: recent intestinal or bladder surgery, mechanical intestinal or urinary tract obstruction, after suxamethonium, pneumonia, and peritonitis.

Side effects: muscarinic effects generally weaker than with neostigmine, increased salivation and bronchial secretions, sweating, nausea and vomiting, abdominal cramps, diarrhoea, miosis, muscle spasm, bradycardia, bronchospasm, allergic reactions, hypotension, cholinergic crisis on overdose, thrombophlebitis, and rash associated with bromide salt.

Dose and Administration: *Oral:* **Adult:** 30 - 120mg at 4 - 6 hourly intervals, total daily dose 120 -720mg, adjusted to individual response. **Child:** 7mg/kg/ day in 5-6 divided doses.*I.M:* **Adult:** 2mg every 2 - 3 hours;

Neonate:50 to 150 micrograms before feeds (but neostigmine usually preferred). **Child:** total daily dose 1 to 12 mg given in divided doses at appropriate intervals.

Storage: store at room temperature and protect from light.

7.5. Disease Modifying Antirheumatic Medicines

Leflunomide

Tablet, 10mg, 20mg, 100mg

(See section 6.1)

Methotrexate

Tablet, 2.5mg, 5mg, 7.5mg,

10mg, 15mg

Powder for Injection, 5mg,

50mg in vial (See section antineoplastic)

7.6. Medicines for the relief of soft tissue inflammation

Enzymes

Hyaluronidase is used to render the tissues more easily permeable to injected fluids, e.g. for introduction of fluids by subcutaneous infusion (termed hypodermoclysis).

Hyaluronidase

Powder for injection, 1500 units in ampoule

Indications: enhance permeation of subcutaneous or intramuscular injections, local anesthetics and subcutaneous infusions; promote resorption of excess fluids and blood.

Cautions: infants or elderly (control speed and total volume and avoid overhydration especially in renal impairment).

Contraindications: do not be apply direct to cornea; avoid sites where infection or malignancy; not for anaesthesia in unexplained premature labour; not to be used to reduce swelling of bites or stings; not for intravenous administration.

Drug interactions: anticoagulants, antiplatelet.

Side effects: edema, flushing, hypotension, dizziness, headache, itching, rash, local (erythema, pain, rash, swelling).

Dose and Administration: *SC or IM:* 1500 units dissolved directly in solution to be injected (ensure compatibility) with local anaesthetics, 1500 units mixed with local anaesthetic solution (ophthalmology, 15 units/ml). *Hypodermoclysis,* 1500 units dissolved in 1 mL water for injections or 0.9% sodium chloride injection, administered before start of 500-1000mL infusion fluid. *Extravasation or haematoma,* 1500 units dissolved in 1mL water for injections or 0.9% sodium chloride injection, infiltrated into affected area (as soon as possible after extravasation).

Storage: store at 20 C to 80 C.

7.7. Bone modulating Medicines

Alendronate Sodium

Tablet, 70mg

Indications: Treatment of postmenopausal osteoporosis and osteoporosis in men, Prevention of postmenopausal osteoporosis, Prevention and treatment of corticosteroid-induced osteoporosis

Cautions: upper gastro-intestinal disorders (dysphagia, symptomatic oesophageal disease, gastritis, duodenitis, or ulcers—see also under Contra-indications and Side-effects); history (within 1 year) of ulcers, active gastro-intestinal bleeding, or surgery of the upper gastro-intestinal tract; renal impairment; correct disturbances of calcium and mineral metabolism (e.g. vitamin-D deficiency, hypocalcaemia) before starting and monitor serum-calcium concentration during treatment; consider preventive dental treatment before initiating bisphosphonate (risk of osteonecrosis of the jaw, see notes above); exclude other causes of osteoporosis; atypical stress fractures reported (discontinue unless benefits of continued treatment clearly outweigh risks)

Contraindications: abnormalities of oesophagus and other factors which delay emptying (e.g. stricture or achalasia), hypocalcaemia, pregnancy and breast-feeding.

Side effects: oesophageal reactions (see below), abdominal pain and distension, dyspepsia, regurgitation, melaena, diarrhoea or constipation, flatulence, musculoskeletal pain, headache; rarely rash, pruritus, erythema, photosensitivity, uveitis, scleritis, transient decrease in serum calcium and phosphate; nausea, vomiting, gastritis, peptic ulceration, hypersensitivity reactions (including urticaria and angioedema), and atypical stress fractures with long-term use also reported; myalgia, malaise,

and fever at initiation of treatment; very rarely severe skin reactions (including Stevens-Johnson syndrome), osteonecrosis. Oesophageal reactions: Severe oesophageal reactions (oesophagitis, oesophageal ulcers, oesophageal stricture and oesophageal erosions) have been reported; patients should be advised to stop taking the tablets and to seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, new or worsening heartburn, pain on swallowing or retrosternal pain.

Drug interactions: Aminoglycosides, NSAIDs, bisphosphate derivatives, antacids (Aluminum, Calcium, magnesium) oral calcium salts, oral iron salts and oral magnesium salt.

Dose and Administration: *Treatment of postmenopausal osteoporosis and osteoporosis in men, 10 mg daily or (in postmenopausal osteoporosis) 70 mg once weekly. Prevention of postmenopausal osteoporosis, 5 mg daily. Prevention and treatment of corticosteroid-induced osteoporosis, 5 mg daily (postmenopausal women not receiving hormone replacement therapy, 10 mg daily). Note: Tablets should be swallowed whole with plenty of water while sitting or standing; to be taken on an empty stomach at least 30 minutes before breakfast (or another oral medicine); patient should stand or sit upright for at least 30 minutes after taking tablet.*

Ibandronate

Tablet, 2.5mg, 50mg, 150mg

Indications: reduction of bone damage in bone metastases in breast cancer and treatment of postmenopausal osteoporosis.

Cautions: consider preventive dental treatment before initiating bisphosphonate (risk of osteonecrosis of the jaw, see notes above); renal impairment; monitor renal function and serum calcium, phosphate and magnesium; cardiac disease (avoid fluid overload).

Contra-indications: pregnancy; breastfeeding

Drug interactions: see under Alendronate Sodium

Side effects: hypocalcaemia, hypophosphataemia, influenza-like symptoms (including fever, chills, and muscle pain), bone pain; oesophageal reactions (see below), diarrhoea, nausea, vomiting, gastritis, abdominal pain, dyspepsia, pharyngitis; headache, asthenia, rash; rarely anaemia, hypersensitivity reactions (pruritus, bronchospasm and angioedema reported); urticaria; injection-site reactions; very rarely osteonecrosis. Oesophageal reactions Severe oesophageal reactions reported with all oral bisphosphonates; patients should be advised to stop tablets and seek medical attention for symptoms of oesophageal irritation such as dysphagia, pain on swallowing, retrosternal pain, or heartburn

Dose and Administration: *Reduction of bone damage in bone metastases in breast cancer: Oral: 50 mg daily*

*Treatment of postmenopausal osteoporosis: Oral: 150 mg once a month.***Child: not recommended**

Note: Tablets should be swallowed whole with plenty of water while sitting or standing in an empty stomach at least 30 minutes (tablets, 50 mg) or 1hour (tablets, 150 mg) before breakfast or another oral medicine; patient should continue to fast, and stand or sit upright for at least 30 minutes (50-mg tablet) or 1 hour (150-mg tablet) after taking tablet

Pamidronate

Injection, 30mg, 90mg

Indications: Treatment of hypercalcemia associated with malignancy; treatment of osteolytic bone lesions associated with multiple myeloma or metastatic breast cancer; moderate to severe Paget's disease of bone.

Cautions: Invasive dental procedures should be avoided during treatment ,renal impairment and avoid in severe renal

impairment, patients with pre-existing anemia leucopenia, or thrombocytopenia, monitor serum electrolytes especially in the elderly, severe bone, joint and muscle pain.

Drug interactions: See under Alendronate Sodium

Contraindication: Hypersensitivity to pamidronate, other bisphosphonates, or any component of the formulation; pregnancy.

Side effects: fatigue, fever, headache, anxiety, insomnia, hypophosphatemia, nausea, vomiting, abdominal pain, leucopenia, myalgia, arthralgia, dyspnea, cough, constipation, back pain, painful or swollen gums, loosening of the teeth, numbness or heavy feeling in the jaw, poor healing of the jaw, bloody or black and tarry stools, shortness of breath, fast heartbeat, numbness or tingling around the mouth, eye pain or tearing.

Dose and Administration: Drug must be diluted properly before administration and infused intravenously slowly. Due to risk of nephrotoxicity, doses should not exceed 90mg.IV. **Adult:** *Hypercalcemia of malignancy:*

Moderate cancer-related Hypocalcaemia (corrected serum calcium: 12-13.5mg//dL): 60-90mg, as single dose.

Severe cancer- related Hypocalcaemia (corrected serum calcium :> 13.5mg//dL): 90mg, as single dose. A period of 7 days should elapse before the use of second course; repeat infusions every 2-3 weeks have been suggested, however, could be administered every 2-3 months according to the degree and of severity of hypercalcemia and/or the type of malignancy. *Osteolytic bone lesions with multiple myeloma:* 90mg monthly. *Osteolytic bone lesions with metastatic breast cancer:* 90mg repeated every 3-4 weeks. *Paget's disease:* 30mg for 3 consecutive days. **Elderly:** Begin at lower end dosing range.

8. ANTI-INFECTIVES

8.1. Antibacterials

8.1.1. Penicillins

Penicillins can be classified into four broad categories, each covering a different spectrum of activity. The natural penicillins (penicillin G and penicillin V) have activity against many gram-positive organisms, gram-negative cocci and some other gram-negative organisms. The aminopenicillins (ampicillin and amoxicilline) have activity against penicillin-sensitive gram-positive bacteria, as well as *Escherchia coli*, *Proteus mirabilis*, *Salmonella sp.*, *Shigella sp.* and *Haemophilus influenza*. The antistaphylococcal penicillins (cloxacillin, dicloxacillin, etc) are also active against beta – lactamase producing staphylococci. The antipseudomonal penicillins have less activity against gram-positive organisms than the natural penicillins or aminopenicillins.

Benzylpenicillin can be considered the parent compound of the penicillins and is inactivated by penicillinase producing bacteria and because of its instability in gastric acid it is usually injected. Long acting preparations include procaine penicillin and benzathine penicillin which slowly release benzylpenicillin after injection. Phenoxymethyl penicillin is acid stable and therefore given by mouth but it is also inactivated by penicillinase. It is generally used for relatively mild infections.

The isoxazolyl penicillins such as cloxacillin, dicloxacillin are resistant to penicillinase & gastric acid.

Ampicillin has a broader spectrum of activity than benzylpenicillin; although generally less active against gram-positive bacteria, some gram-negative organisms including *Escherichia coli*, *Haemophilus influenzae*, and *Salmonella spp.* are sensitive although resistance is being reported increasingly, *Pseudomonas spp* are not sensitive. Ampicillin is

acid stable and can be given by mouth but is destroyed by penicillinase. Amoxicillin, only differs from ampicillin by the addition of a hydroxyl group, but is better absorbed from the gastro-intestinal tract.

The most important side effect of the penicillins is hypersensitivity reaction which cause rashes and anaphylaxis, which can be fatal. Individuals who have experienced anaphylaxis, urticaria, or rash immediately after penicillin administration are at increased risk of immediate hypersensitivity to penicillin; these individuals should not receive a beta-lactam antibiotic. Patients who are allergic to one penicillin will be allergic to all because the hypersensitivity is related to the basic penicillin structure.

A rare but serious toxic effect of the penicillins is encephalopathy due to cerebral irritation. This may result from excessively high doses or in patients with severe renal failure. The penicillins should not be given by intrathecal injection because they can cause encephalopathy which may be fatal.

Another problem relating to high doses of penicillin, or normal dose given to patients with renal failure, is the accumulation of electrolyte since most injectable penicillins contain either sodium or potassium.

Diarrhea frequently occurs during oral penicillin therapy. It is most common with broad- spectrum penicillins, which can also cause antibiotic associated colitis.

Amoxicillin

Tablet, 500 mg

Capsule, 250 mg, 500 mg

Injection, 250 mg, 500 mg in vial

Syrup, 125mg/5ml, 250 mg/5ml

Indications: urinary tract infections, upper respiratory tract infections, bronchitis, pneumonia, otitis media, dental abscess, osteomyelitis, Lyme disease in children, endocarditis prophylaxis, post-splenectomy prophylaxis, gynaecological infections, gonorrhoea, and *Helicobacter pylori* eradication (section 1.2)

Cautions: history of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukaemia, and possibly HIV infection.

Drug interactions: probenecid (except in cases of gonorrhoea and other STD), allopurinol, oral contraceptives, methotrexate, warfarin.

Contraindications: known hypersensitivity (allergy) to any penicillines.

Side effects: allergic reaction, specifically anaphylaxis (bronchospasm, sudden or severe decrease in blood pressure), skin rash, joint pain, fever, GIT reaction (mild diarrhoea, nausea, vomiting), oral candidiasis (sore mouth or tongue), pseudomembranous colitis (severe abdominal or stomach cramps and pain, abdominal tenderness, watery and severe diarrhoea).

Dose and Administrations:*Infections due to sensitive organisms: Oral:Adult and Child* over 10 years, 250 mg every 8 hours, doubled in severe infections; **Child** up to 10 years, 125mg every 8 hours, doubled in severe infections. *Severe or recurrent purulent respiratory-tract infections:Oral:Adult:* 3 g every 12 hours.*Pneumonia:Oral:Adult:* 0.5 to 1 g every 8 hours. *Short Course Oral therapy.Dental abscess:Adult:* 3 g repeated after 8 hours. *Urinary tract infections:Adult:* 3 g repeated after 10 – 12 hours.*Otitis media: Child* 3 – 10 years, 750 mg twice daily for 2 days.*IM:* 500 mg every 8 hours; **Child**, 50 to 10 mg/kg daily in divided doses.*IV injection or infusion:*

500 mg every 8 hours increased to 1g every 6 hours. **Child**, 50 to 100 mg/kg daily in divided doses

Adults*Meningitis (in combination with another antibiotic if necessary): IV infusion: 2 g every 4 hours for at least 5 days in meningococcal disease or for 10 – 14 days in listerial meningitis. Enterococcal endocarditis (in combination with another antibiotic if necessary): IV infusion: 2 g every 4 hours.*

Storage: at room temperature in a tight container; oral suspension remains stable for 14 days at room temperature or if refrigerated.

Note: Reconstitution and Administration: According to manufacturer's directions.

Amoxicilline and Clavulanic acid

Tablet (Chewable), 125 mg + 31.25 mg, 250mg +62.5 mg, (film coated), 250 mg + 125 mg, 500 mg + 125 mg

Capsule, 500mg +125mg, 875mg +125mg

Oral Suspension, 125 mg + 31.25 mg in each 5 ml, 250 mg + 62.5 mg in each 5 ml, 228mg/5ml ,457mg/5ml

Injection, 500 mg + 100mg, 1 g + 200 mg

Indications: infection due to beta-lactamase-producing bacteria including respiratory tract infections, genito-urinary and abdominal infections, cellulites, animal bites, severe dental infections, and surgical prophylaxis.

Cautions: during pregnancy, hepatic impairment and nursing women, history of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukemia & HIV infection.

Drug interactions: allopurinol, disulfiram, probenecid, anticoagulants, anti-inflammatory drugs, platelet aggregation inhibitor, contraceptives, heparin, thrombolytic agents, sulfipyrazone.

Contraindications: penicillin hypersensitivity, history of amoxicilline + clavulanic acid associated or penicillin associated jaundice or hepatic dysfunction.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, anorexia and flatulence, rash and urticaria, pseudomembraneous colitis, headache, dizziness.

Dose and Administration: Note: All doses expressed as amoxicillin. *Infections due to susceptible beta-lactamase producing organisms:* **Oral: Adult and Child** over 12 years, 250mg every 8 hours, doubled in severe infections; Child under 1 year, 20mg/kg daily in 3 divided doses; Child 1-6 years, 125mg every 8 hours; 6-12 years, 250mg every 8 hours. *Severe dental infections:* **Oral: Adult** 250mg every 8 hours for 5 days. *Infections due to susceptible beta-lactamase producing organisms: slow IV injection: Adult and Child* over 12 years, 1g every 8 hours, increased to 1g every 6 hours in severe infections; **Neonate and Premature Infant** 25mg/kg every 12 hours; Infant up to 3 months, 25mg/kg every 8 hours; **Child** 3 months to 12 years, 25mg/kg every 8 hours increased to 25 mg/kg every 6 hours in more severe infections. *Surgical prophylaxis: IV injection: Adult* 1g at induction, with up to 2 to 3 further doses of 1g every 8 hours (if increased risk of infection).

Storage: in tight containers at a temperature less than 24°C; exposure to excessive humidity should be avoided. *Following reconstitution, oral suspension of amoxicillin and clavulanate potassium should be stored at 2 – 8 °C, and unused suspension should be discarded after 10 days.*

Ampicillin

Capsule, 250 mg, 500 mg

Oral suspension; 125 mg/5ml, 250 mg/5ml

Drop, 100 mg/ml

Injection, (sodium), 250 mg, 500 mg, 1 g in vial

Indications: broad spectrum activity against several Gram-positive organisms, Gram-negative cocci and some bacilli. Used in respiratory tract infections, cholecystitis and gastrointestinal tract infections, including typhoid

Cautions, Drug interactions, Contraindications and Side effects; see under Amoxicillin and see notes above.

Dose and Administration:Adult:Oral:250-500mg 6 hourly (up to 1g 6 hourly for severe infections).**IM:** 500mg 6 hourly. **IV:** by slow injection or infusion over 30-60 minutes, 500mg 4-6 hourly (up to 12g daily for severe infections).**Meningitis/septicaemia:IV:** 1-2g 3-4 hourly; maximum 300 mg/kg/day or 16g.Renal impairment: GFR 10 to 50ml/min, dose interval 6-12 hours; GFR <10ml/min, 12-24 hours.**Child: Oral, IM or IV:** under 20kg, 10-25 mg/kg/dose 6 hourly; over 20kg, as for adults.**Meningitis or severe infections:IV:**50mg/kg dose 6 hourly. **Neonates:IM or IV:** 50mg/kg/dose (meningitis 100mg/kg/dose) 12 hourly in the first week of life, 8 hourly from 1-3 weeks old, 6 hourly thereafter.

Storage: at room temperature; after reconstitution oral suspension is stable for 7 days at room temperature or for 14 days under refrigeration.*Note: Reconstitution and Administration: According to manufacturer's directions.*

Ampicillin sodium and sulbactam sodium

Injection, 1 g + 0.5g, 2 g + 1 g

Indications: in the treatment of intra abdominal infections such as abscess, female pelvic infections & infections caused by ampicilline susceptible organisms and as a secondary agent in the treatment of genito-urinary tract infections, skin and soft

tissue infections, including burn wound infections, and bone and joint infections.

Cautions: renal function impairment, congestive heart failure, and gastrointestinal disease.

Drug interactions: see notes under amoxicilline and clavulanic acid.

Contraindications: Allergy of penicillines, infectious mononucleosis.

Side effects: allergic reactions, specially anaphylaxis; serum sickness like reactions (skin rash, joint pain, fever), chest pain pseudomembraneous colitis, oral candidiasis, vaginal candidiasis, clostridium difficile colitis, dysuria, edema, erythemamultiforme, hepatic dysfunction, glossitis, leukopenia, platelet dysfunction and seizures.

Dose and Administration:Adult: *IM or IV:* 1.5 to 3 grams (1 to 2 grams, Ampicillin and 500 mg to 1 gram, sulbactam) every six hours.

Gonorrhea: *IM:* 1.5 grams (1 gram of Ampicilline and 500 mg of sulbactam) as a single dose with 1 gram of oral probenecid.*Note: Adults with impaired renal function may require a reduction in dose.* Usual adult prescribing limits up to a maximum of 4 grams (sulbactam) daily.

Child: Dosage has not been established in children up to the age of 12 years. However, doses of 200 to 400mg per kg of body weight of ampicillin and 100 to 200 mg per kg of body weight of sulbactam per day, administered in divided doses, have been used.

Storage: Prior to reconstitution, do not store above 30°C, unless otherwise specified by the manufacturers.

Carbenicillin

Tablet (Indanyl sodium), 382 mg

Injection 1g, 5 g in vial

Indications: treatment of serious urinary tract infections and prostatitis caused by susceptible gram-negative aerobic bacilli.

Cautions: impaired renal and/or hepatic function.

Drug interactions: heparin or oral anticoagulants, aminoglycosides, methotrexate probenecid, disulfiram, tetracyclines.

Contraindications: hypersensitivity to carbenicillin, penicillins, or any component of the formulation.

Side effects: diarrhea, nausea, bad taste, vomiting, flatulenc, glossitis, anemia, epigastric distress, headache, hematuria, hypersensitivity reactions, hyperthermia, hypokalemia, rash, thrombocytopenia and urticaria.

Dose and Administration: *Urinary tract infections:*

Oral: Adult: 1 - 2 tablets every 6 hours for urinary tract infections or 2 tablets every 6 hours for prostatitis.

Child: 30 - 50 mg/kg/day divided every 6 hours; maximum dose: 2 - 3 g/day. *IM: Adult:* 1 to 2g every 6 hours. *Child:* 50-100mg/kg daily in divided doses.

Storage: temperature not exceeding 30°C and injections at 2-8°C.

Cloxacillin sodium

Capsule, 250mg, 500mg

Syrup, 125mg, 250mg in each 5ml

Injection, 250mg, 500mg in vial

Indications: infections due to beta-lactamase-producing staphylococci including impetigo, cellulitis and other soft-tissue infections; staphylococcal endocarditis, septicaemia, pneumonia and osteomyelitis.

Cautions: history of allergy, renal and hepatic function impairment, GIT disease especially ulcerative colitis, and

regional enteritis, antibiotic associated colitis, heart failure; pregnancy and breastfeeding.

Drug interactions: probenecid, chloramphenicol, erythromycin, sulfonamide, and tetracyclines.

Contraindications: known hypersensitivity or allergy to penicillines.

Side effects: nausea and vomiting, diarrhea, hypersensitivity reactions including urticaria, fever, joint pain, rashes, angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis; neutropenia, thrombocytopenia, coagulation disorders; antibiotic-associated colitis; hepatitis and cholestatic jaundice may be delayed in onset; electrolyte disturbances; pain, inflammation, phlebitis or thrombophlebitis at injection sites.

Dose and Administration:Adult: *Oral:* 250 to 500mg (base) every six hours. Maximum dose up to 6 gm (base) a day.*IV* 250 to 500mg (base) every six hours maximum 6gms (base) daily.**Child:** Infants and children up to 20kg of body weights: *Oral:* 6.25 to 12.5mg (base) per kg of body weight every six hours or *IV:* 6.25 to 12.5mg (base) per kg of body weight every six hours.*Note: continue medicines for full time of treatment and take on empty stomach.*

Storage: store at room temperature. *After reconstitution, solutions retain their potency for 14 days if refrigerated.*

Flucloxacillin

Capsule, 250 mg, 500 mg

Injection, 250 mg, 500 mg in vial

Syrup, 125 mg/5ml

Indications: for treatment of infections due to staphylococci resistant to benzylpenicillin these include bone and joint

infections, endocarditis, peritonitis, pneumonia, skin infections, surgical infection and toxic shock syndrome.

Cautions: older patients and those receiving fluoxacillin for more than 2 weeks.

Drug interactions: see benzylpenicillin.

Side effects: hepatitis, cholestatic jaundice, agranulocytosis and neutropenia occur.

Dose and Administration: Adult: *Oral, IM:* 250mg four times daily. It is given intravenously in a dose of 0.25 to 1 g four times daily by slow injection over 3 to 4 minutes or by IV infusion.

Storage: store at room temperature.

Mezlocillin

Powder for injection, 0.5 g, 1g, 2 g, 3 g, 4 g, /vial

Intravenous (IV) infusion, 2 g, 3 g, 4 g

Indications: treatment of infections caused by susceptible gram negative aerobic bacilli (*Klebsiella, Proteus, Eschericia coli, Enterobacter, Pseudomonas aeruginosa, Serratia*) involving the skin and skin structure, bone and joint, respiratory tract, urinary tract, gastrointestinal tract, as well as septicemia.

Cautions: hypersensitivity to mezlocillin, any component, or penicillins.

Drug interactions: as for benzylpenicillin. Clavulanic acid, methotrexate, probenecid

Side effects: as for carbenicillin.

Dose and Administration: Adult: *Serious infection: IV:* 200 to 300mg/kg daily in divided doses, for life-threatening infections, up to 350mg/kg daily may be used, but total dose should not exceed 24g. *Urinary- tract infection: IM or IV:* 1.5 to 2g every 6 hours.

Storage: store in airtight container.

Penicillin G, Benzathine

Injection, 0.6, 1.2, 2.4 million IU in Vial

Indications: streptococcal pharyngitis, diphtheria carrier state, syphilis and other treponemal infections (yaws, pinta, bejel); rheumatic fever prophylaxis.

Cautions: history of allergy (see notes above); renal failure; pregnancy and breast feeding

Drug interactions: methotrexate

Contra indications: see under penicillin G, sodium crystalline; and neurosyphilis

Side effects: see under penicillin G, sodium crystalline

Dose and Administrations: *deep IM injection. Streptococcal pharyngitis: primary prophylaxis of rheumatic fever:* Adult and Child over 30 Kg body-weight, 900 mg as a single dose. Child under 30 Kg body – weight, 450 – 675 mg as a single dose.

Secondary prophylaxis of rheumatic fever: Adult and Child over 30 Kg body-weight, 900 mg once every 3 – 4 weeks; Child under 30 Kg body-weight, 450 mg once every 3 – 4 weeks. *Early syphilis:* Adult 1.8 g as a single dose, divided between 2 sites. *Late syphilis:* Adult 1.8 g divided between two sites, once weekly for 3 consecutive weeks. *Congenital syphilis (where no evidence of CSF involvement):* Child up to 2 years, 37.5 mg/kg as a single dose. *Yaws, Pinta, and bejel:* Adult: 900 mg as a single dose; Child 450 mg as a single dose.

Reconstitution and Administration. *According to manufacturer's directions.*

Storage: store between 2 and 8°C.

Penicillin G, Sodium crystalline

Injection, 1 million IU, 10 million IU, 20 million IU in vial. 1 million unit equivalent to 600 mg

Indications: throat infections, pneumonia, otitis media, lyme disease in children; streptococcal endocarditis; meningococcal disease; necrotizing enterocolitis, necrotizing fasciitis; leptospirosis, neurosyphilis, anthrax; actinomycosis; brain abscess; gas gangrene; cellulitis; osteomyelitis.

Cautions: history of allergy (see notes under 8.1.1); renal failure; heart failure; pregnancy and breastfeeding.

Drug interactions: methotrexate, probenecid (decrease renal tubular secretion of the penicillins), aminoglycosides (inactivated by high doses of IV benzylpenicillin; should not be administered in same giving set).

Contraindications: penicillin hypersensitivity (see notes under 8.1.1); avoid intrathecal route

Side effects: hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness like reactions, hemolytic anemia and interstitial nephritis; neutropenia, thrombocytopenia, coagulation disorders and central nervous system toxicity including convulsions reported (especially with high doses or in severe renal impairment), paraesthesia with prolonged use; diarrhea and antibiotic associated colitis; see also notes above.

Dose and Administration: *Mild to moderate infections due to sensitive organisms: IM or slow IV injection or infusion: Adult:* 0.6 – 2.4 g daily in 2 – 4 divided doses, with higher doses in severe infections and duration of treatment depending on disease. **Neonate:** 50 mg/kg daily in 2 divided doses; **Infant 1 to 4 weeks,** 75 mg/kg daily in 3 divided doses; **Child 1 month to 12 years,** 100 mg/kg daily in 4 divided doses, with higher doses in severe infections. *Bacterial endocarditic: slow IV injection or infusion:* Adult up to 7.2g daily in 6 divided doses. *Meningococcal meningitis: slow IV injection or infusion: Adult up to 14.4 g daily in divided doses;*

Premature infant and Neonate 100 mg/kg daily in 2 divided doses; **Infant** 150 mg/kg daily in 3 divided doses; **Child** 1 month to 12 years, 180 – 300 mg/kg daily in 4 – 6 divided doses. *Suspected meningococcal disease (before transfer to hospital): IM or slow IV injection:* Adult and Child over 10 years, 1.2 g; Child 1 to 9 years, 600 mg; Child less than 1 year, 300 mg. *Neurosyphilis: slow IV injection:* Adult: 1.8 – 2.4 g every 4 hours for 2 weeks. *Congenital syphilis, IM or slow IV injection:* Child up to 2 years, 30 mg /kg daily in 2 divided doses for 10 days, Child over 2 years, 120 – 180 mg/Kg (to maximum of 1.44g) daily in divided doses for 14 days.

Reconstitution and Administration: According to manufacturer's directions

Storage: at room temperature. Prior to reconstitution

Phenoxymethyl Penicillin

Tablet, 125 mg, 250 mg, 500,000 IU

Oral suspension, 125 mg/5ml, 50000 IU/ml

250mg = 400,000 units

Indications: streptococcal pharyngitis; otitis media; erysipelas; mouth infection; secondary prophylaxis of rheumatic fever; post-splenectomy prophylaxis.

Cautions, Contraindications, Drug interactions, Side effects; see under penicillin G, sodium crystalline

Dose and Administration: Infections due to sensitive organisms:
Oral: Adult: 500 mg every 6 hours increased up to 1 g every 6 hours in severe infections; **Child up to 1 year**, 62.5 mg every 6 hours; Child 1 – 5 years, 125 mg every 6 hours; Child 6 – 12 years, 250 mg every 6 hours. *Secondary prophylaxis of rheumatic fever: Oral:* Adult: 500 mg twice daily; Child 1 – 5 years, 125 mg twice daily; Child 6 – 12 years, 250 mg twice daily.

Patient advice: Phenoxymethyl penicillin should be taken at least 30 minutes before or 2 hours after food.

Storage: at room temperature in a tight container.

Phenoxymethyl penicillin, potassium

Tablet, 390 mg

Suspension, 195 mg/5ml

See under Phenoxymethyl penicillin

Piperacillin

Powder for injection (as sodium salt), 1g, 2g in vial

Indications: infections due to *P. aeruginosa* - usually in combination with an aminoglycoside for synergistic effect.

Cautions: known hypersensitivity to any penicillin or cephalosporin.

Drug interactions: probenecid, aminoglycosides, oral contraceptives.

Side effects: the high sodium content may cause fluid retention and hypokalaemia. Piperacillin has a potential for provoking a bleeding diathesis. Neutropenia, leucopenia and thrombocytopenia have been reported. Other effects include thrombophlebitis at the injection site, neuromuscular excitability with high doses, cholestatic jaundice, bloody diarrhea, and reversible elevation of serum urea and creatinine levels.

Dose and Administration: Adult:*IV:* usually 2-4g, 6 - 8 hourly, injected over 3-5 minutes, or infused over 20 - 40 minutes; maximum 24 g/day.*IM:* 2g, 8 - 12 hourly (i.e. 4 to 6 g/day).*Single doses over 2g must be given intravenously; the IV route is preferred in severe infections.* Child: *IV:* 2 months - 12 years, 50 - 100mg/kg/dose 6-8 hourly (Maximum dose 2 - 4g). Give 12 hourly in the first week of life.

Storage: store in airtight containers.

Procaine Penicillin, Fortified

Injection (buffered), 4,000,000 IU

Indications: for the treatment of respiratory infections (e.g. pneumonia), acute otitis media, skin structure infections, uncomplicated urogenital gonorrhea, and syphilis.

Cautions: same as penicillin G benzathine and also caution in the treatment of gonococcal infections during pregnancy and in children.

Drug interactions: see under penicillin G, sodium crystalline

Contraindications: known hypersensitivity to any penicillin and/ or procaine.

Side effects: hypersensitivity reactions such as skin rash, fever, joint pains, edema and anaphylaxis may occur.

Dose and Administration: *IM injection* only. Adult:

Gonorrhea (acute, uncomplicated): 4,800,000 IU (2,400,000 IU in each buttock). Repeat the same dose next day. *Syphilis—Primary, secondary, or latent (of not more than 2 years duration):* 600,000 IU daily for 8 days. Tertiary (2 year and more)- 600,000 IU daily for 10-15 days. *Pneumonia, acute otitis media, skin or skin structure infections:* **Adult and child** (12 years and over): 600,000-1,200,000 IU daily for 5- 7days. Maximum dose –100,000 IU of penicillin G /kg of body weight in divided doses. **Child (below 12 years):** Treatment is given daily for 5 to 7 days: 1-5 months of age, (3-5kg) 100,000 IU daily; 6-12 months of age, (6-10kg) 200,000 IU daily; 1- 6 years of age, (11-20kg) 300,000 IU daily; 1-5 years of age, (21-30kg) 400,000 IU daily. *Note: Remember to treat always the sexual partner.*

Storage: At room temperature. After reconstitution, it should be used within 14 days provided it is stored between 2-4°C or within 4 days at about 20°C.

Sultamicillin (Ampicillin Sodium and Sulbactam Sodium double ester)

Tablet, 375 mg, 750mg

Indications; Cautions; Drug interactions; Contraindications; Side effects: see under Ampicillin sodium + Sulbactam sodium.

Dose and Administration: *Oral:* 375-750mg twice daily.

8.1.2. Cephalosporins, carbapenems, and other beta-lactams

Cephalosporins: 1st, 2nd, 3rd, 4th

Cephalosporins are bactericidal and they act by inhibiting synthesis of the bacterial cell wall. The most widely used system of classification of cephalosporins is by generations and is based on the general features of their antibacterial activity.

First generation cephalosporins: They usually are active against a wide spectrum of Gram-positive bacteria including penicillinase-producing and non penicillinase producing organisms. But not active against enterococci including oxacilline-resistant staphylococci (formerly known as meticillin-resistant staphylococci). Their activity against Gram-negative bacteria is modest. Cefadroxil and cefalexin are available in oral formulations, while cefazolin is administered parenterally and widely used for surgical prophylaxis.

Second generation cephalosporins: They have similar or slightly less activity than first generations against Gram-positive bacteria, but greater stability to hydrolysis by beta lactamases produced by Gram-negative bacteria and enhanced activity against many of the Enterobacteriaceae and Haemophilus influenzae (including ampicillin-resistant strains). Cefaclor, Cefprozil and Cefuroxime are second-generation cephalosporins.

Third generation cephalosporins: They are sometimes referred to as extended-spectrum cephalosporins. Compared with the earlier generations of cephalosporins they have a wider spectrum and greater potency of activity against Gram-negative organisms, including most clinically important Enterobacteriaceae. Their activity against Gram-positive bacteria is said to be less than that of the first-generation drugs, but they are very active against *streptococci*. Cefotaxime has good activity against most Gram-positive and Gram-negative organisms. It is useful in treating infection due to *H. influenzae* (including beta-lactamase-producing strains), *Salmonella spp* and *N. gonorrhoeae*. It is ineffective against *P.aeruginosa*. Ceftazidime is effective against many strains of *P.aeruginosa*. It is not adequate for *S.pneumoniae* or other streptococci. Ceftriaxone has activity similar to that of cefotaxime. Its longer half-life allows once or twice daily dosing. There is concern that widespread use of these agents could lead to increasing resistance, particularly among pneumococci.

Fourth generation Cephalosporins: Cefepime, classified as a fourth-generation cephalosporin, has an extended spectrum of activity against both gram-positive and gram-negative organisms, including *P aeruginosa*.

First Generation Cephalosporins

Cefadroxil

Capsule/ Tablet, 500mg, 1gm

Oral suspension, 125mg/5ml, 250mg/5ml

Indications: treatment of susceptible bacterial infections, including those caused by group A beta-hemolytic *Streptococcus*; prophylaxis against bacterial endocarditis in

patients who are allergic to penicillin and undergoing surgical or dental procedures.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, anticoagulants.

Contraindications: hypersensitivity to cefadroxil or other cephalosporins.

Side effects: diarrhea, abdominal pain, agranulocytosis, anaphylaxis, angioedema, arthralgia, cholestasis, dyspepsia, erythema multiforme, fever, nausea, neutropenia, pruritus, pseudomembranous colitis, rash, serum sickness, Stevens-Johnson syndrome, thrombocytopenia, transaminases increased, urticaria, vaginitis, vomiting.

Dose and Administration: *Oral:* **Adult:** 1-2 g/day in 2 divided doses. **Child:** 30 mg/kg/day divided twice daily up to a maximum of 2g/day. *Prophylaxis against bacterial endocarditis:* **Adult:** 2g 1 hour prior to the procedure. **Child:** 50mg/kg 1 hour prior to the procedure.

Storage: store at room temperature.

Cephalexin

Capsule, 250 mg, 500 mg

Syrup, 125 mg/5ml

Indications: treatment of susceptible bacterial infections including respiratory tract infections, otitis media, skin and skin structure infections, bone infections and genitourinary tract infections, including acute prostatitis, alternative therapy for acute bacterial endocarditis prophylaxis.

Cautions: severe renal impairment, penicillin allergy.

Drug interactions: probenecid, aminoglycosides.

Contraindications: hypersensitivity to cephalexin or other cephalosporins.

Side effects: agitation, confusion, dizziness, fatigue, hallucinations, headache, angioedema, erythema multiforme, rash, Stevens-Johnson syndrome, urticaria, abdominal pain, diarrhea, dyspepsia, gastritis, pseudomembranous colitis, genital pruritus, genital moniliasis, vaginitis, vaginal discharge, thrombocytopenia; arthritis, joint-disorder.

Dose and Administration: *Oral:Adult:* 250 to 1000 mg every 6 hours; maximum: 4 g/day.*Streptococcal pharyngitis, skin infections:* 500 mg every 12 hours.

Uncomplicated cystitis: 500 mg every 12 hours for 7 - 14 days.*Prophylaxis of bacterial endocarditis:* 2g 1 hour prior to procedure.**Neonates:** 25mg/kg, every 6 - 12 hours.**Child 1 month to 1 year:** 125mg every 12 hours.

Child > 1 year: 25 to 50 mg/kg/day every 6 - 8 hours, more severe infections; 50 - 100 mg/kg/day in divided doses every 6 - 8 hours; maximum: 4 g/24 hours.

Otitis media: 75 to 100mg/kg/day in 4 divided doses.

Streptococcal pharyngitis, skin infections: 25-50 mg/kg /day divided every 12 hours.*Uncomplicated cystitis:***Child >15 years:** Refer to Adults dosing.*Prophylaxis of bacterial endocarditis:* 50 mg/kg 1 hour prior to procedure (maximum: 2 g).

Storage: store capsules and powder for oral suspension at room temperature. After reconstitution of oral suspension store in airtight containers at 2-8 °C and discard if not used within 2 weeks.

Cephazoline Sodium

Injection, 250 mg, 500 mg, 1g in vial

Indications: treatment of respiratory tract, skin and skin structure, genital, urinary tract, biliary tract, bone and joint infections, septicemia, preoperative prophylaxis.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, aminoglycosides, warfarin.

Contraindications: hypersensitivity to cefazolin sodium or other cephalosporins.

Side effects: fever, seizure, rash, pruritus, Stevens-Johnson syndrome, diarrhea, nausea, vomiting, abdominal cramps, anorexia, pseudomembranous colitis, oral candidiasis, vaginitis, hepatitis, eosinophilia, neutropenia, thrombocytopenia, leukopenia, thrombocytosis, pain at injection site, phlebitis, renal failure; BUN increased, serum creatinine increased.

Dose and Administration: *IM, IV:* **Adult:** 250 mg to 2 g every 6 - 12 (usually 8) hours, depending on severity of infection; maximum dose: 12g/day. **Child**>1 month: 25 - 100 mg/kg/day divided every 6 - 8 hours; maximum: 6 g/day.

Storage: store intact vials at room temperature and protect from temperature exceeding 40°C.

Cephradine

Capsule, 250 mg, 500 mg

Intravenous (I.V) Infusion, 2g, 4g/100ml

Powder for injection, 250mg, 500mg, 1g/vial

Syrup, 125 mg/5ml; 250 mg/5ml

Indications: treatment of infections when caused by susceptible strains in respiratory, genitourinary, gastrointestinal, skin, bone and joint infections; treatment of susceptible gram-positive bacilli and cocci; some gram-negative bacilli.

Cautions: renal impairment, penicillin allergy.

Drug interactions: probenecid, aminoglycosids.

Contraindications: hypersensitivity to cephradine or other cephalosporins.

Side effects: dizziness, rash, pruritus, diarrhea, nausea, pseudomembranous colitis, leukopenia, neutropenia, eosinophilia, joint pain, BUN increased, creatinine increased.

Dose and Administration: Adult: *Oral:* 250 to 500 mg every 6 - 12 hours. *In severe infection: deep IM or IV by slow injection* over 3-5 minutes or by infusion, in doses of 2-4 g daily in 4 divided doses; up to 8g daily. **Child 1 - 8 months:** 12.5mg/kg twice daily (total daily dose may alternatively be given in 3-4 divided doses). **Child \geq 9 months:** *Oral:* Usual dose: 25 - 50 mg/kg/day in divided doses every 6 hours. *Otitis media:* 75 -100 mg/kg/day in divided doses every 6 or 12 hours (maximum: 4g/day). *Injection:* 50-100mg/kg daily may be given in 4 divided doses, increasing to 300mg/kg daily in severe infections.

Storage: store at controlled room temperature.

Second Generation Cephalosporins

Cefaclor

Capsules, 250 mg, 500 mg

Suspension, 125 mg/5ml, 250 mg/5ml

Indications: treatment of susceptible bacterial infections including otitis media, lower respiratory tract infections, acute exacerbations of chronic bronchitis, pharyngitis and tonsillitis, urinary tract infections, skin infections.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: hypersensitivity to cefaclor or other cephalosporins.

Side effects: rash, diarrhea, vaginitis, eosinophilia, transaminases increased, agitation, agranulocytosis, anaphylaxis, angioedema, aplastic anemia, cholestatic jaundice, CNS irritability, confusion, dizziness, hallucinations, hemolytic anemia, hepatitis.

Dose and Administration:*Oral:Adult:* 250 - 500 mg every 8 hours. **Child**>1 month: 20 - 40 mg/kg/day divided every 8 - 12 hours; Maximum dose: 1 g/day.

Otitis media: 40 mg/kg/day divided every 12 hours

Pharyngitis: 20 mg/kg/day divided every 12 hours.

Storage: store at controlled room temperature. Refrigerate suspension after reconstitution and discard after 14 days. Do not freeze.

Cefprozil

Tablet, 500mg, 1g

Oral solution, 125mg/5ml, 250mg/5ml

Indications: treatment of otitis media, infections involving respiratory tract and skin and skin structure; active against methicillin –sensitive staphylococci, many streptococci, and various gram-negative bacilli including *E.coli*, some *Klebsiella*, *P. mirabilis*, *H. influenzae* and *Moraxella*.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: cephalosporin hypersensitivity.

Side effects: dizziness, diaper rash, diarrhea, nausea, vomiting, abdominal pain, vaginitis, transaminases increased, and superinfection.

Dose and Administration: *Oral:Pharyngitis/tonsillitis:*

Adult and Child >13 years: 500 mg every 24 hours for 10 days.**Children 2-12 years:** 7.5 to 15 mg/kg/day divided every 12 hours for 10 days; maximum: 1 g/day.

Uncomplicated skin and skin structure infections:

Adult and Child >13 years: 250mg every 12 hours, or 500 mg every 12-24 hours for 10 days.**Child 2-12 years:** 20mg/kg every 24 hours for 10 days; maximum: 1 g/day.*Secondary bacterial infection of acute bronchitis or acute bacterial exacerbation of*

chronic bronchitis: 500mg every 12 hours for 10 days. **Infants and Child > 6 months to 12 years**: Otitis media: 15mg/kg every 12 hours for 10 days.

Storage: store at room temperature.

Cefuroxime

Tablet, 125 mg, 250 mg

Powder for injection, 250 mg/vial, 750 mg/vial, 1.5 g/vial, Oral suspension, 125mg/ml

Indications: bone and joint infections; upper respiratory tract infections (pneumonia or bronchitis) caused by *S.Pyogenes*, *H.influenza* (beta-lactamase negative and beta-lactamase positive strains), sinusitis caused by *M. Catarrhalis*, *S.Pneumonia* or *H.Influenzae*, Lower respiratory tract infections (pneumonia or bronchitis), skin structure infections caused by *S.Aureus*, *S.Pyogenes* or *S.Agalactiae*; Gonorrhoea

Cautions: penicillin sensitivity; renal impairment; pregnancy and breast feeding (but appropriate to use); false positive urinary glucose (if tested for reducing substances) and false positive coombs' test.

Drug interactions: anticoagulants

Contraindications: cephalosporin hypersensitivity; porphyria.

Side effects: diarrhea and rarely antibiotic associated colitis, nausea and vomiting, abdominal discomfort, headache, allergic reactions including rashes, pruritus, urticaria, serum sickness like reactions with rashes, fever and arthralgia, and anaphylaxis, erythema multiforme, toxic epidermal necrolysis, transient hepatitis and cholestatic jaundice, eosinophilia and blood disorders (including thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia and hemolytic anaemia),reversible interstitial nephritis, hyperactivity,

nervousness, sleep disturbances, confusion, hypertonia, and dizziness.

Dose and Administration:*Oral:*(as cefuroxime axetil), 250 mg twice daily in most infections including mild to moderate lower respiratory – tract infections (e.g. bronchitis); doubled for more severe lower respiratory-tract infections or if pneumonia suspected.*Urinary-tract infection*, 125 mg twice daily, doubled in pyelonephritis.

Gonorrhoea, 1 g as a single dose; **Child** over 3 months, 125 mg twice daily, if necessary doubled in child over 2 years with otitis media.*Lyme disease*,**Adult and Child** over 12 years, 500 mg twice daily for 20 days.

IM or IV injection or infusion: 750 mg every 6 – 8 hours; 1.5 g every 6 – 8 hours in severe infections; single doses over 750 mg intravenous route only. Child usual dose 60 mg/kg daily (range 30 – 100 mg/Kg daily) in 3- 4 divided doses (2- 3 divided doses in neonates).*Gonorrhoea*, 1.5 g as a single dose by intramuscular injection (divided between 2 sites). *Surgical prophylaxis*, 1.5 g by intravenous injection at induction; may be supplemented with 750mg intramuscularly 8 and 16 hours later abdominal, pelvic, and orthopedic operations) or followed by 750 mg intramuscularly every 8 hours for further 24 – 48 hours (cardiac, pulmonary, oesophageal, and vascular operations).*Meningitis*, 3 g intravenously every 8 hours; **Child**, 200 to 240 mg/kg daily (in 3 – 4 divided does) reduced to 100 mg/kg daily after 3 days or on clinical improvement; Neonate, 100 mg/kg daily reduced to 50 mg/kg daily.

Storage: at room temperature.

Third Generation Cephalosporins

Cefditoren

Tablet, 200mg, 400mg

Indications: acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia, pharyngitis/tonsillitis, and uncomplicated skin and skin-structure infections

Cautions: pregnancy and lactation, renal impairment, hepatic impairment

Contraindications: known hypersensitivity reaction to cefditoren or any other cephalosporin, carnitine deficiency, milk protein hypersensitivity (not lactose intolerance), children younger than 12 years of age,

Drug interactions: antacids and H₂ receptor antagonists, probenecid, oral contraceptives

Dose and Administration: orally with meals (to enhance GI absorption). *Adults: Pharyngitis and Tonsillitis:* 200 mg twice daily for 10 days; *Acute Bacterial Exacerbations of Chronic Bronchitis:* 400 mg twice daily for 10 days; *Community-acquired Pneumonia:* 400 mg twice daily for 14 days; *Skin and Skin Structure Infections:* 200mg twice daily for 10 days

Children ≥12 years of age: Pharyngitis and Tonsillitis: 200 mg twice daily for 10 days; Acute Bacterial Exacerbations of Chronic Bronchitis: 400 mg twice daily for 10 days; *Community-acquired Pneumonia:* 400 mg twice daily for 14 days; *Skin and Skin Structure Infections:* 200 mg twice daily for 10 days.

Cefepime

Powder for injection, 500mg, 1gm/vial, 2gm/vial

Indications: uncomplicated urinary tract infections, uncomplicated skin and skin structure infections, moderate to severe pneumonia, complicated intra-abdominal infections (in combination with metronidazole) and in children 2 months to 16 years: febrile neutropenia, uncomplicated skin/soft tissue infections pneumonia, complicated /uncomplicated urinary tract infections

Cautions: pregnancy and lactation, renal impairment, may cause antibiotic associated colitis

Drug interactions: probenecid, aminoglycosides

Contraindications: hypersensitivity to Cefepime or any other cephalosporin group

Dose and administration: *Usual Dose Range:* **Adults:** IV 1-2 gm/kg every 6-12 hours; **children:** IV 50 mg/kg every 8-12 hours (above two months of age or less than 40 kg body weight). Indication specific dosing: *febrile neutropenia:* 50mg/kg every 8 hours for 7-10 days; *uncomplicated skin/soft tissue infections, pneumonia, complicated/uncomplicated UTI* 50mg/kg twice daily; *mild to moderate UTI* IM,IV 500-1000mg every 12 hours; peritonitis (spontaneous) IV 2 gm every 12 hours with metronidazole; otitis externa (malignant), pneumonia IV, 2 gm every 12 hours; septic lateral/cavernous sinus thrombosis IV 2gm every 6 hours; with metronidazole for lateral.

Cefixime

Tablet, 200mg, 400mg

Indications: treatment of urinary tract infections, otitis media, respiratory infections due to susceptible organisms; uncomplicated cervical/urethral gonorrhea due to *N. gonorrhoeae*.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides, warfarin.

Contraindications: cephalosporin hypersensitivity.

Side effects: diarrhea, abdominal pain, nausea, dyspepsia, flatulence, loose stools, acute renal failure, anaphylactic reactions, angioedema, dizziness, drug fever, headache, rash, seizure, Stevens-Johnson syndrome.

Dose and Administration: *Oral: Adult and Child* > 50kg or >12 years: 400mg/day divided every 12-24 hours. *Uncomplicated cervical/urethral gonorrhea due to N. gonorrhoeae:* 400mg as a single dose. **Child** ≥ 6 months: 8mg/kg/day divided every 12-24 hours.

Cefotaxime

Injection, as sodium, 0.5 g, 1 g in vial

Indications: susceptible infections in respiratory tract, skin, bone and joint, urinary tract, gynecologic as well as septicemia, and documented or suspected meningitis and other infections due to gram-negative bacilli, gram-positive cocci and penicillin-resistant pneumococci

Cautions: severe renal impairment, patients with colitis, a history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: hypersensitivity to cefotaxime or other cephalosporins.

Side effects: rash, pruritus, diarrhea, nausea, vomiting, colitis, pain at injection site, anaphylaxis, arrhythmia, candidiasis, fever, headache, interstitial nephritis, neutropenia, Stevens-Johnson syndrome, thrombocytopenia, urticaria, vaginitis, agranulocytosis, aplastic anemia, cholestasis, hemolytic anemia, hemorrhage, renal dysfunction, seizure, superinfection, toxic nephropathy.

Dose and Administration: Adult and Child >12 years:

Uncomplicated infections: I.M, I.V: 1 g every 12 hours.

Moderate/severe infections: I.M, I.V: 1 - 2 g every 8 hours. *Infections commonly needing higher doses (e.g. septicemia): I V:* 2 g every 6 - 8 hours. *Gonorrhoeae and associated infections:* 500mg IM single dose. *Life-threatening infections: I.V:* 2 g every 4 hours. *Preop: I.M, I.V:* 1 g 30 - 90

minutes before surgery. *C-section*: 1 g as soon as the umbilical cord is clamped, then 1g *I.M.*,\

I.V at 6 and 12 hour intervals. **Neonates, Infants and Children up to 12 years:** *I.M.*, *I.V.*: <50Kg: 50 to 180 mg/kg/day in divided doses every 4-6 hours.

Meningitis: 200 mg/kg/day in divided doses every 6 hours.

Storage: store at a temperature not exceeding 8 °C.

Cefpodoxime

Tablet, 100mg, 200mg

Indications: treatment of susceptible acute, community acquired pneumonia caused by *S. pneumoniae* or non-betalactamase producing *H.influenzae*; acute uncomplicated gonorrhea caused by *N. gonorrhoeae*; uncomplicated skin and skin structure infections caused by *S. aureus* or *S.pyogenes*; acute otitis media caused by *S.pneumoniae*, *H.influenzae* or *M.catarrhalis*; pharyngitis or tonsillitis; and uncomplicated UTI caused by *E.coli*, *Klebsiella*, and *Proteus*.

Cautions: renal impairment, prolonged use may result in superinfection, use with caution in patients with a history of penicillin allergy especially IgE-mediated reactions (eg anaphylaxis, urticaria)

Drug interactions: probenecid, furosemide, aminoglycosides, antacids and H₂-receptor antagonists.

Contraindications: hypersensitivity to cephalosporins

Side effects: diaper rash, diarrhea in infants, headache, rash, nausea, abdominal pain, vomiting.

Dose and Administration: *Oral: Adult and Child ≥ 12 years:* *Acute community-acquired pneumonia and bacterial exacerbations of chronic bronchitis:* 200 mg every 12 hours for 14 days and 10 days, respectively

Acute maxillary sinusitis: 200mg every 12 hours for 10 days. *Skin and skin structure*: 400mg every 12 hours for 7-14 days. *Uncomplicated gonorrhoea (male and female) and rectal gonococcal infections (female)*: 200mg as a single dose. *Pharyngitis/tonsillitis*: 100mg every 12 hours for 5-10 days. *Uncomplicated urinary tract infection*: 100mg every 12 hours for 7 days. **Child 2 months to 12 years**: *Acute otitis media*: 10mg/kg/day divided every 12 hours (400mg/day) for 5 days (maximum: 200mg/dose). *Acute maxillary sinusitis*: 10mg/kg/day divided every 12 hours for 10 days (maximum: 200mg/dose). *Pharyngitis/tonsillitis*: 10mg/kg/day in 2 divided doses for 5-10 days (maximum: 100mg/dose)

Ceftazidime

Injection, 0.5 g, 1 g, 2 g in vial

Indications: infections due to sensitive bacteria, especially those due to pseudomonas spp. and including those resistant to aminoglycosides.

Cautions: penicillin sensitivity, renal impairment, pregnancy and breast-feeding, false positive urinary glucose and false positive coombs' test.

Drug interactions: contraceptives (oral), furosemide, warfarin.

Contraindications: cephalosporin hypersensitivity; porphyria.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, headache, rarely, antibiotic associated colitis (particularly with higher doses), allergic reactions including rashes, pruritus, urticaria, serum sickness like reaction, fever and arthralgia, and anaphylaxis, erythema multiforme, toxic epidermal necrolysis, disturbances in liver enzymes, transient hepatitis, cholestatic jaundice eosinophilia and blood disorders (including thrombocytopenia, leukopenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia); reversible interstitial

nephritis, nervousness, sleep disturbances, confusion, hypertonia, and dizziness.

Dose and Administration: **Adult:** *IM, IV:* 500mg to 2g every 8-12 hours. *Urinary tract infections:* 250-500mg every 12 hours. **Neonates:** 30mg/kg IV every 12 hours

Infants and Children up to 12 years: *IV:* 30-50mg/kg/dose every 8 hours; maximum dose: 6g/day.

Storage: store between (-25) and (-10) °C unless otherwise specified by manufacturer. After thawing, solutions retain their potency for 24 hours at room temperature or for 7 days if refrigerated.

Ceftriaxone

Injection, 0.25g, 0.5 g, 1 g, 2 g in vial

Indications: serious infections due to sensitive bacteria, including septicaemia, pneumonia, and meningitis, surgical prophylaxis, prophylaxis of meningococcal meningitis, gonorrhoea.

Cautions: penicillin sensitivity; renal and hepatic impairment; premature neonates, may displace bilirubin from serum albumin; pregnancy and breast feeding; false positive urinary glucose and false positive coombs' test.

Drug interactions: furosemide and warfarin. Do not admix with aminoglycosides in same bottle/bag.

Contraindications: cephalosporin hypersensitivity, porphyria, neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding.

Side effects: diarrhea, nausea and vomiting, abdominal discomfort, headache, antibiotic-associated colitis, allergic reactions including rashes, pruritus, urticaria, serum sickness-like reactions, fever and arthralgia, and anaphylaxis, erythema multiforme, toxic epidermal necrolysis, disturbances in liver

enzymes, transient hepatitis and cholestatic jaundice, eosinophilia and blood disorders, reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, confusion, hypertonia and dizziness, calcium ceftriaxone precipitates in urine or in gall bladder - consider discontinuation if symptomatic, rarely prolongation of prothrombin time, pancreatitis.

Dose and Administration:*Infections due to susceptible organisms: IM, IV injection (over 3 - 4 minutes) or IV infusion: Adult:* 1 g daily; severe infections 2 - 4 g daily.

Infant and Child: 20 - 50 mg/kg daily, up to 80 mg/kg daily in severe infections; by *IV infusion* (over 60 minutes). **Neonate:** less than 1 week 20 - 50 mg/kg once daily, **Neonates:** 1-4week and weigh 2kg or less 50mg/kg. If above 2kg, 50-75mg/kg once daily.

Uncomplicated gonorrhea: IM: Adult: 250 mg, adolescent: 125mg as a single dose. *Surgical prophylaxis: IM, IV injection* (over at least 2 to 4 minutes), 1 g as a single dose. *Colorectal surgery (with antibacterial active against anaerobes), IM or IV* (over at least 2 - 4 minutes), or *by IV infusion*, 2 g as a single dose.

Storage: prior to reconstitution, store at room temperature. Premixed solution store at -20°C; once thawed, solutions are stable for 3 days at room temperature of 25°C or for 21 days refrigerated at 5°C. Do not refreeze.

Imipenem and Cilastatin

Powder for Infusion, 500 mg (500mg+500mg), 250mg (250mg+250mg)

Indications: for treatment respiratory tract, urinary tract, intra-abdominal, gynecologic, bone and joint, skin structure and polymicrobial infections as well as bacterial septicemia and

endocarditis. Antibacterial activity includes resistant gram-negative bacilli (*Pseudomonas aeruginosa* and *Enterobacter* sp), gram-positive bacteria (methicillin-sensitive *Staphylococcus aureus* and *Streptococcus specius* and anaerobes, treatment of aerobic and anaerobic Gram-positive and Gram-negative infections; hospital-acquired septicaemia; ***not indicated*** for CNS infections.

Cautions: Renal impairment, pregnancy, breastfeeding, prolonged use may result in superinfection, in patients with a history of seizures or hypersensitivity to beta-lactams, elderly patients, pediatric CNS infections, IV and IM preparations cannot be interchanged.

Drug interactions: Ganciclovir, Valproate, Typhoid Vaccine (oral),

Contraindications: Hypersensitivity to the medicine or any component of the formulation; sensitivity to beta-lactam antibacterials (avoid if history of immediate hypersensitivity reaction); CNS disorders (e.g. epilepsy); severe renal impairment, Pregnancy.

Side-effects: nausea (may reduce rate of infusion), vomiting, diarrhoea (rarely antibiotic-associated colitis), eosinophilia, rash (rarely toxic epidermal necrolysis and Stevens-Johnson syndrome); *less commonly* hypotension, seizures, myoclonic activity, dizziness, drowsiness, hallucinations, confusion, leucopenia, thrombocytopenia, thrombocytosis, positive Coombs' test; *rarely* taste disturbances, hepatitis, encephalopathy, anaphylactic reactions, paraesthesia, tremor, acute renal failure, polyuria, tooth, tongue or urine discoloration, hearing loss; *very rarely*, abdominal pain, heartburn, glossitis, tachycardia, palpitation, flushing, cyanosis, dyspnoea, hyperventilation, headache, asthenia,

haemolyticaemia, aggravation of myasthenia gravis, polyarthralgia, tinnitus, hypersalivation, hyperhidrosis

Dose and Administration: By intravenous infusion, in terms of imipenem, 500 mg every 6 hours *or* 1 g every 8 hours; less sensitive organisms or life-threatening infection, 1 g every 6 hours; 1 year and older, 15 mg/kg (max. 500 mg) every 6 hours; less sensitive organisms or life-threatening infection, 25 mg/kg (max. 1 g) every 6 hours. **Children 3 months and older:** IV 15 to 25 mg/kg every 6 hours for non-CNS infections. Max dose, 2 g/day for fully susceptible organisms, 4 g/day for infections with moderately susceptible organisms. Doses up to 90 mg/kg/day have been used in older children with cystic fibrosis. **Infants 4 week to 3 month** (at least 1.5 kg):IV 25 mg/kg every 6 h for non-CNS infections.

Neonates 1 to 4 wk (weighing at least 1.5 kg):IV 25 mg/kg every 8 h for non-CNS infections. **Neonates younger than 1 wk** (weighing at least 1.5 kg):IV 25 mg/kg IV every 12 hours for non-CNS infections.

Storage: Should be stored at $<25^{\circ}\text{C}$

Meropenem

Powder for injection, 500mg, 1gm

Indications: treatment of intra-abdominal infections (complicated appendicitis and peritonitis), bacterial meningitis in pediatric patients, ≥ 3 months caused by *S. pneumonia*, *H. influenza*, and *N. meningitides*; complicated skin and skin infections caused by susceptible organism.

Cautions: breast feeding, renal impairment, children < 3 months of age.

Drug interactions: probenecid may increase meropenem serum concentration; meropenem may decrease valproic acid serum concentration.

Contraindications: hypersensitivity to meropenem, any component of the formulation or other carbapenems; patients who have experienced anaphylactic reactions to other beta-lactams.

Side effects: headache, pain, rash, pruritus, diarrhea, constipation, oral moniliasis (pediatric patients), injection site reaction

Dose and Administration:*IV (infusion over 15 to 30 minutes; bolus injection over 3 to 5 minutes):* **Adult:** *Intraabdominal Infection:* 1 g IV every 8 hours for 7 to 14 days. *Meningitis:* 1 to 2 g IV every 8 hours for 7 to 21 days. *Skin or Soft Tissue Infection:* Complicated infection: 500 mg IV every 8 hours. *Duration of therapy should generally be continued for approximately 7 to 10 days, or for 3 days after the acute inflammation disappears, depending on the nature and severity of the infection. For more severe infections, such as diabetic soft tissue infections, 14 to 21 days of therapy may be required.*

Pediatric: *Intraabdominal Infection:* 3 months or older: 20 mg/kg IV every 8 hours; Maximum dose: 3 g/day. **Children** 50 kg or more: 1 g IV every 8 hours. *Meningitis:* 3 months or older: 40 mg/kg IV every 8 hours, Maximum dose: 6 g/day. Children 50 kg or more: 2 g IV every 8 hours. *Skin and Structure Infection, complicated:***3 months or older:** 10 mg/kg IV every 8 hours. Maximum dose: 1.5 g/day.

Children 50 kg or more: 500 mg IV every 8 hours

Storage: store at 20⁰c to 25⁰c.

Gemifloxacin

Tablet, 320mg

Indications: respiratory tract infections; acute exacerbations of chronic bronchitis, mild to moderate community acquired pneumonia

Cautions: hepatic and renal impairment, patients with creatinine clearance less than 40ml/minute

Drug interactions: antacids, cimetidine, corticosteroids, didanosine, digoxin, hormonal contraceptives, omeprazole, probenecid, sucralfate, theophylline, warfarin, drugs that prolong QT interval, drugs metabolized by hepatic enzymes

Contraindications: pregnancy and lactation, or adolescents younger than 18 years of old (safety and efficacy not established)

Dose and administration: Adults \geq 18 years: *acute exacerbations of chronic bronchitis:* 320mg once daily for 5 days; mild to moderate community acquired pneumonia: 320mg once daily for 5-7 days.

8.1.3. Macrolides

The macrolides are bacteriostatic or bactericidal, depending on the concentration and type of micro-organism, and are thought to interfere with bacterial protein synthesis. Their antimicrobial property is similar to benzylpenicillin but they are also active against organisms such as *Legionella pneumophila*, *Mycoplasma pneumoniae*, and some rickettsias, chlamydias, and chlamydophilas. Macrolides have postantibiotic effect: that is, antibacterial activity persists after concentrations have dropped below the minimum inhibitory concentration.

Azithromycin

Capsule, 250 mg

Powder for oral suspension, 200 mg/5ml

Indications: treatment of acute otitis media, pharyngitis/tonsillitis, mild to moderate upper and lower respiratory tract infections, infections of the skin, community - acquired pneumonia, pelvic inflammatory disease, sexually-

transmitted diseases (urethritis/cervicitis), genital ulcer, acute bacterial exacerbations of chronic obstructive pulmonary disease (COPD), acute bacterial sinusitis.

Cautions: hepatic and renal dysfunction, prolonged cardiac repolarization.

Drug interactions: pimoziide, phenytoin, ergot alkaloids, alfentanil bromocriptine, carbamazepine, cyclosporine, digoxin, disopyramide, triazolam; nelfinavir, aluminium and magnesium containing antacids.

Contraindications: hypersensitivity to azithromycin.

Side effects: diarrhea, nausea, abdominal pain, cramping, vomiting, acute renal failure, allergic reaction, aggressive behaviour, anaphylaxis, angioedema, arrhythmia, cholestatic jaundice, deafness, enteritis, erythema multiforme, headache, hearing loss, hepatic necrosis.

Dose and Administration: *Oral: Adolescents \geq 16 years and Adults: Respiratory tract, skin and soft tissue infections:* 500 mg on day 1 followed by 250 mg/day on days 2 – 5. *Alternative regimen: Bacterial exacerbation of COPD:* 500 mg/day for a total of 3 days. *Bacterial sinusitis:* 500 mg/day for a total of 3 days.

Urethritis/cervicitis: Due to C.trachomatis: 1 g as a single dose; *due to N.gonorrhoeae:* 2 g as a single dose

Chancroid due to H-ducreyi: 1 g as a single dose. **Child \geq 6 months:** *Community - acquired pneumonia:* 10 mg/kg on day 1 followed by 5 mg/kg/day once daily on days 2 to 5. *Bacterial Sinusitis:* 10 mg/kg once daily for 3 days. *Otitis media:* 1 day regimen: 30 mg/kg as a single dose; 3 days regimen: 10 mg/kg once daily for 3 days; 5day regimen: 10 mg/kg on day 1 followed by 5 mg/kg/day once daily on days 2 to 5. **Child \geq 2 years:** *pharyngitis, tonsillitis:* 12 mg/kg/day once daily for 5 days.

Storage: Suspension: store dry powder below 30⁰c; following reconstitution, store suspension at 5⁰c to 30⁰c.

Clarithromycin

Tablet, 250 mg, 500 mg

Granules for oral suspension, 125 mg/5ml, 250 mg/5 ml

Powder for IV infusion, 500 mg/vial

Indications: respiratory tract infections, mild to moderate skin and soft tissue infections, adjunct in the treatment of duodenal ulcers by eradication of *Helicobacter pylori* and *ycobacterium avium* infections, in combination with ethambutol.

Cautions: severe renal impairment.

Drug interactions: cisapride, pimozone, sparfloxacin, thioridazine, benzodiazepines, calcium channel blockers, cyclosporine, quinidine, sildenafil, midazolam, triazolam, cisapride, ergot alkaloids, neuromuscular - blocking agents and warfarin, amprenavir, azole antifungals, ciprofloxacin, diclofenac, doxycycline, erythromycin, isoniazid, nefazodone, propofol.

Contraindications: hypersensitivity to clarithromycin, or any macrolide antibiotics, use with ergot derivatives, pimozone, cisapride.

Side effects: headache, rash, diarrhea, vomiting, nausea, abnormal taste, heartburn, abdominal pain, prothrombin time increased, BUN increased.

Dose and Administration:Adult: *Oral:* 250-500mg twice daily. *IV infusion* over 60 minutes, 500mg twice daily.*M.avium complex (MAC) infections in AIDS:* 500mg twice daily plus ethambutol.*H. pylori:Oral:* 500 mg twice daily (see under omeprazole dose and admenstration). **Child:Oral:** 7.5-15 mg/kg/dose (maximum 500 mg) 12 hourly.

Storage: store at room temperature.

Erythromycin

Tablet (stearate), 250mg, 500mg

Capsule, 250mg

Oral suspension, 125mg/5ml, 200mg/5ml, 250mg/5ml

Injection, 50mg/ml in 2ml ampoule

Indications: conjunctivitis in newborns, genitourinary tract infection during pregnancy, pneumonia in infants, prophylaxis of bacterial endocarditis, gonorrhoea, legionnaires disease, pharyngitis, sinusitis and for long term prophylaxis of rheumatic fever, syphilis.

Cautions: pregnancy and breast-feeding, renal and hepatic function impairment, cardiac arrhythmias (prolongation of QT interval), porphyria, in neonates less than two weeks risk of hypertrophic pyloric stenosis.

Drug interactions: alfentanil, carbamazepine, chloramphenicol, itraconazole, cyclosporins, terfenadin, warfarin, xanthines such as aminophylline, caffeine, oxtriphylline, and theophylline.

Side effects: Nausea, Vomiting, diarrhoea, abdominal, stomach cramping and discomfort, reversible loss of hearing, recurrent fainting, hypersensitivity (skin rash, redness or itching), cholestatic jaundice (dark or amber urine, pale stools, stomach pains), inflammation or phlebitis at injection site.

Dose and Administration: Adult: *Antibacterial (systemic): Oral:* 250mg (base) every 6 hours, or 500mg every 12 hours if twice a day dosage is required. Maximum: up to 4 grams (base) daily. *IV infusion:* 250-500mg (base) every 6 hours. Maximum up to 4 grams.

Endocarditis (prophylaxis): In patients with heart disease or rheumatic or other acquired valvular heart disease who undergo dental procedures or surgical procedure of the upper respiratory tract, Oral, 1gm (base) one hour prior to the procedure, and 500mg 6 hours following the procedure. *Genitourinary tract*

8. Anti-Infectives

infection, including chlamydial: Oral: 500mg (base) every six hours for at least seven days. For patients unable to tolerate the higher dosage regimen, the dosage may be halved and given for at least fourteen days. *Legionnaires' disease: Oral: 500mg (base) to 1gm(base) every six hours.* *Streptococcal (prophylaxis) - continuous prophylaxis of streptococcal infections in patients with a history of rheumatic heart disease: Oral: 250mg (base) every twelve hours.* **Child:** *Antibacterial (systemic): oral: 7.5mg to 12.5mg (base) per kg of body weight every 6 hours, or 17 to 25mg per kg of body weight every 12 hours. Severe infection: 15 to 25mg (base) per kg of body weight every six hours.* *Antibacterial (systemic): IV infusion, 3.75 to 5mg (base) per kg of body weight every 6 hours.* *Conjunctivitis, chlamydial: oral: 12.5mg (base) per kg of body weight every 6 hours for at least two week.* *Endocarditis prophylaxis: in patients with heart disease are rheumatic or other acquired valvular heart disease who undergo dental procedures or surgical procedures of the upper respiratory tract: Oral: 20mg (base) per kg of body weight one hour prior to the procedure, and 10mg per kg of body weight six hours following the procedure.* *Pertusis: oral: 10 to 12.5mg (base) per kg of body weight every 6 hours for 14 days.*

Pneumonia, chlamydial: oral: 12.5mg (base) per kg of body weight every 6 hours for two weeks.

Streptococcal pharyngitis: oral: 5-12.5mg (base) per kg of body weight every 6 hours for at least 10 days.

Neonates: *oral: 7.5mg to 12.5mg (base) per kg of body weight every 6 hours*

Note: For oral dosage- continue medicine for full time of treatment

Storage: at room temperature in tight container.

8.1.4 Aminoglycosides

Aminoglycosides, such as amikacin, gentamicin, neomycin and tobramycin have a similar antimicrobial spectrum and act by interfering with bacterial protein synthesis by binding irreversibly to the 30s and 50s portions of the bacterial ribosome. They are most active against Gram-negative rods. Aminoglycosides show enhanced activity with penicillins against some enterococci and streptococci.

Gentamicin

Injection, 40mg/ml; 80mg/ 2ml; 20mg/2ml

Indications: biliary tract infection, bone and joint infection, meningitis, ventriculitis, urinary tract infection, peritonitis, bacterial septicemia.

Cautions: in premature infants and neonates, elderly, patients with renal function impairment (check renal function test) or dehydration, and in those with eighth-cranial nerve impairment. Prolonged use should be avoided.

Drug interactions: avoid concurrent and/or sequential use of two or more aminoglycosides or aminoglycosides with capreomycin, antimyasthenic, methoxyflurane or polymyxin, cephalosporins, ciclosporin, cisplatin, neostigmine, pyridostigmine, suxamethonium, vecuronium, furosemide, penicillines and indomethacin.

Contraindications: pregnancy, myasthenia gravis, previous allergic reaction to one aminoglycoside.

Side effects: nephrotoxicity, increased thirst, loss of appetite, nausea or vomiting; neurotoxicity (muscle twitching, numbness, seizures, tingling); ototoxicity, auditory damage (loss of hearing, ringing or buzzing a feeling of fullness in the ears), vestibular damage (clumsiness, dizziness, nausea, vomiting, unsteadiness)

Dosage and Administration:**Adult:***Antibacterial (systemic):IM or IV infusion:* 1-1.7mg (base) per kg of body weight every eight hours for seven to ten days or more.*Urinary tract infection (bacterial, uncomplicated):IM or IV infusion:* Adults (< 60kg body weight) - 3mg (base) per kg of body weight once a day, or 1.5mg per kg of body weight every 12 hours. Adults (\geq 60kg of body weight)160mg (base) once a day, or 80mg every 12 hours.Usual adult prescribing limit - up to 7mg (base) per kg of body weight daily in severe, life threatening infections.**Child:** *Antibacterial (systemic):IM or IV infusion:* premature or full term neonates up to 1 week of age: 2.5mg (base) per kg of body weight every 12 or 24 hours for seven to ten days or more.**Older neonates and infants:** 2.5mg (base) per kg of body weight every 8 to 16 hours for 7-10 days or more.**Child:** 2 to 2.5mg (base) per kg of body weight every 8 hours for 7-10 days or more.

Storage: store at room temperature and protect from freezing.

Neomycin

Tablet, 500 mg

Indications: To prepare GI tract for surgery; treatment of diarrhea caused by *E.Coli*; adjunct in the treatment of hepatic encephalopathy; bladder irrigation, ocular infections.

Cautions: renal impairment, pre-existing hearing impairment, neuromuscular disorders.

Drug interactions: oral anticoagulants, digoxin, methotrexate.

Contraindications: hypersensitivity to neomycin or other aminoglycosides.

Side effects: nausea, diarrhea, vomiting, irritation or soreness of the mouth or rectal area, dyspnea, eosinophilia, nephrotoxicity, neurotoxicity, ototoxicity.

Dose and Administration: *Oral:Preoperative intestinal antisepsis:* **Adult:** 1 g each hour for 4 doses then 1 g every 4

hours for 5 doses, or 1 g at 1 PM, 2 PM, and 11 PM on day preceding surgery as an adjunct to mechanical cleansing of the bowel and oral erythromycin; or 6g/day divided every 4 hours for 2-3 days. **Child:** 90 mg/kg/day divided every 4 hours for 2 days; or 25 mg/kg at 1 PM, 2 PM and 11 PM on the day preceding surgery as an adjunct to mechanical cleansing of the intestine and in combination with erythromycin base. *Hepatic encephalopathy:* **Adult:** 500-2000mg every 6-8 hours or 4 to 12g/day divided every 4-6 hours for 5 - 6 days. **Child:** 50 to 100 mg/kg/day in divided doses every 6 - 8 hours or 2.5 to 7 g/m²/day divided every 4 to 6 hours for 5 - 6 days not to exceed 12 g/day.

Chronic hepatic insufficiency: **Adult:** 4 g/day for an indefinite period.

Storage: store in airtight containers and at room temperature.

Tobramycin

Injection, 40 mg/ml

Indications: infections caused by susceptible gram-negative bacilli including *Pseudomonas aeruginosa*.

Cautions: renal impairment, pre-existing auditory or vestibular impairment, patients with neuromuscular disorders.

Drug interactions: penicillins, neuromuscular blockers, amphotericin B, cephalosporins, and loop diuretics.

Contraindications: hypersensitivity to tobramycin and other aminoglycosides, pregnancy.

Side effects: confusion, disorientation, dizziness, fever, headache, lethargy, vertigo, exfoliative dermatitis, itching, rash, urticaria, serum calcium, magnesium, potassium, and/or sodium decreased, diarrhea, nausea, vomiting, anemia, eosinophilia, granulocytopenia, leukocytosis, leukopenia, thrombocytopenia,

hearing loss, tinnitus, ototoxicity, roaring in the ears, BUN increased, serum creatinine increased, oliguria, proteinuria.

Dose and Administration: *I.M, I.V:Adult:Severe life - threatening infections:* Conventional dosing: 2 to 2.5 mg/kg/dose. High dose: some clinicians suggest a daily dose of 4 - 7 mg/kg for all patients with normal renal function. *Urinary tract infection:* 1.5 mg/kg /dose. **Neonates:** preterm <32 weeks 4- 5mg/kg every 36 hours

Preterm >32 weeks 4-5mg/kg every 24 hours. **Term neonates, Infant and Child**<5 years:2- 25 mg/kg/dose every 8-12 hours. *Cystis fibrosis:* 2.5 - 3.3 mg/kg every 6 - 8 hours.

Storage: store at room temperature.

8.1.5. Quinolones

Nalidixic acid and Norfloxacin are effective in uncomplicated urinary tract infections. Ciprofloxacin is active against both Gram-Positive and Gram – Negative bacteria. It is particularly active against Gram – negative bacteria, including *Salmonella, Shigella, Campylobacter, Neisseria, and Pseudomonas*, Ciprofloxacin has only moderate activity against Gram-positive bacteria such as *streptococcus pneumoniae* and *Enterococcus faecalis*; it is not the drug of first choice for *Pneumococcal pneumonia*. It is active against *Chlamydia* and some mycobacteria. Most anaerobic organisms are not susceptible.

Sparfloxacin is antibacterial agent similar to ciprofloxacin. It has been reported to be more active in vitro than ciprofloxacin against some organisms, including staphylococci and mycobacteria, and has a much longer plasma half-life.

Cautions, Quinolones should be used with caution in patients with a history of epilepsy or conditions predisposing to seizures; convulsions may be induced in patients with or without a history of convulsions; also, use with caution in G6PD deficiency,

pregnancy or breast feeding; use in children has been associated with an increased risk of adverse effects involving joints and surrounding tissue structures May impair ability to perform skilled tasks, such as operating machinery, driving Exposure to sunlight should be avoided (discontinue if photosensitivity occurs).

Side effects, Adverse effects of quinolones include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, and rarely antibiotic associated colitis; headache, dizziness, sleep disorders, rash (rarely stevens-Johnson Syndrom and toxic epidermal necrolysis), and pruritus; less commonly, anorexia, transient disturbances in liver enzymes and bilirubin and increases in blood urea and creatinine; drowsiness, restlessness, depression, confusion, hallucinations, convulsions, paraesthesia; photosensitivity; hypersensitivity reactions including fever, urticaria, angioedema, arthralgia, myalgia, and anaphylaxis, blood disorders; disturbances in vision, taste, hearing, and smell; isolated reports of tendon inflammation and damage; if psychiatric, neurological, or hypersensitivity reactions occur discontinue the drug.

Drug interactions, Quinolones may interact with the various compounds including analgesics, anticoagulants, ciclosporin (increased risk of nephrotoxicity) and theophylline.

Ciprofloxacin

Tablet (as hydrochloride), 250 mg, 500mg, 1000mg

Capsule, 500mg, 1000mg

Injection Infusion (as lactate), 2 mg/ml in 50 ml and 100 ml bottle

Indications: gastroenteritis including cholera, shigellosis, travellers' diarrhoea, campylobacter and salmonella enteritis; typhoid; gonorrhoea; chancroid; legionnaires' disease;

meningitis (including meningococcal meningitis prophylaxis); respiratory-tract infections—including pseudomonal infections in cystic fibrosis, but not pneumococcal pneumonia; urinary-tract infections; bone and joint infections; septicaemia; anthrax; skin infections; prophylaxis in surgery

Cautions: history of epilepsy or conditions that predispose to seizures, G6PD deficiency, myasthenia gravis (risk of exacerbation), pregnancy, breastfeeding, children or adolescents (see below); avoid exposure to excessive sunlight (discontinue if photosensitivity occurs); rarely, tendon damage—discontinue at first sign of pain or inflammation and rest affected limb; hepatic impairment; renal failure; avoid excessive alkalinity of urine and ensure adequate fluid intake as risk of crystalluria

Children: Ciprofloxacin can be used in children over 1 year for complicated urinary-tract infections, for pseudomonal lower respiratory-tract infections in cystic fibrosis, for prophylaxis and treatment of inhalational anthrax; and for other infections where the benefit is considered to outweigh the potential risk.

Drug interactions: see notes above

Contraindications: Absolute- known allergy to ciprofloxacin or other quinolones. Pregnancy and lactation, inpatients with history of tender disorder.

Side effects: nausea, vomiting, dyspepsia, abdominal pain, diarrhea, headache, dizziness, weakness, sleep disorders, rash, and pruritus, increase in blood urea and creatinine; metabolic acidosis; drowsiness, restlessness, asthenia, depression, confusion, hallucinations, convulsions, paraesthesia, raised intracranial pressure, cranial nerve palsy; photosensitivity, fever, urticaria, angioedema, arthralgia, myalgia, anaphylaxis, eosinophilia, leukopenia, thrombocytopenia, disturbances in vision, taste, hearing smell; haemolytic anaemia, renal failure, interstitial nephritis, hepatitis and cholestatic jaundice

Dose and Administration: Adult: *Oral: Infections due to susceptible organisms:* 250 – 750 mg twice daily.

Acute uncomplicated cystitis: 100 mg twice daily for 3 days. *Chronic prostatitis:* 500 mg twice daily for 28 days. *Gonorrhoea, chancroid, shigellosis, or cholera:* 500 mg as a single dose. *Pseudomonal lower respiratory– tract infection in cystic fibrosis:* 750 mg twice daily;

Child: 5 to 17 years, up to 20 mg/kg twice daily (maximum 1.5 g daily). *Most other infections:* 500 to 750 mg twice daily. *Surgical prophylaxis:* 750 mg 60- 90 minutes before procedure. *IV infusion* (over 30 – 60 minutes ; 400 mg over 60 minutes), 200–400 mg twice daily pseudomonal lower respiratory –tract infection in cystic fibrosis, 400 mg twice daily; Child 5-17 years, up to 10mg/kg 3 times daily (max. 1.2g daily). *Urinary tract infections:* 100 mg twice daily. *Gonorrhoea:* 100 mg as a single dose. *Note: Child not recommended (see cautions and contraindications above) but where benefit outweighs risk, by mouth, 10 – 30 mg/kg daily in 2 divided doses or by intravenous infusion, 8-16 mg/kg daily in 2 divided doses.*

Storage: Tablet: store below 30°C in a well-closed container. Injection: Store in a cool place (between 8 and 15°C) or at controlled room temperature (between 20 and 25°C). Protect from light and freezing.

Nalidixic acid

Tablet, 500 mg

Oral suspension 300 mg/vial

Indications: urinary tract infections; shigellosis.

Cautions: see notes above: avoid in porphyria; liver disease; renal impairment; false positive urinary glucose (if tested for reducing substances); monitor blood counts, renal and liver function if treatment exceeds 2 weeks.

Drug interactions: see notes under ciprofloxacin

Side effects: see notes above; also reported toxic psychosis, weakness, increased intracranial pressure, cranial nerve palsy, and metabolic acidosis.

Dose and Administration: *Urinary tract infections: Oral:*

Adult: 1g every 6 hours for 7 days, reduced in chronic infections to 500 mg every 6 hours; **Child** over 3 months: maximum 50 mg/kg daily in divided doses, reduced in prolonged treatment to 30 mg/Kg daily, or 15 mg/kg twice daily for prophylaxis. *Shigellosis: Oral: Adult:* 1 g every 6 hours for 5 days. **Child over 3 months:** 15 mg/kg every 6 hours for 5 days.

Note: Patient Advice – Take on an empty stomach, preferably one hour before a meal.

Storage: store at room temperature (up to 25°C) in a tight container. Protect from freezing.

Norfloxacin

Table, 400 mg

Indications: uncomplicated urinary tract infections and cystitis caused by susceptible gram-negative and gram-positive bacteria; sexually transmitted disease (eg, uncomplicated urethral and cervical gonorrhea) caused by *N.gonorrhoeae*; prostatitis due to *E. coli*.

Cautions: see notes under ciprofloxacin; renal impairment.

Drug interactions: see notes under ciprofloxacin.

Side effects: see notes above, also reported euphoria, anxiety, tinnitus, polyneuropathy, exfoliative dermatitis, pancreatitis, and vasculitis.

Dose and Administration: *Urinary-tract infections: Adult:* 400 mg twice daily for 7 – 10 days (for 3 days in uncomplicated lower urinary tract infections).

Chronic relapsing urinary tract infections: 400 mg twice daily for up to 12 weeks; may be reduced to 400 mg once daily if adequate suppression within first 4 weeks.

Uncomplicated gonorrhea: 800 mg as a single dose.

Chronic prostatitis: 400 mg twice daily for 28 days.

Storage: at room temperature in a tight container

Sparfloxacin

Tablet, 100 mg, 200 mg

Indications: bacterial exacerbation of chronic bronchitis, community acquired pneumonia.

Cautions: see notes above, renal impairment, cerebral atherosclerosis, epilepsy.

Drug interactions: medications that prolong the QTc, interval and see notes above.

Contraindications: in patients with history of photosensitivity, not recommended for patients with ongoing proarrhythmic conditions; patients younger than 18 years of age, breast-feeding.

Side effects: see notes above and also phototoxicity, QTc interval prolongation (irregular or slow heart rate; recurrent fainting); vaginitis.

Dose and Administrations: *Oral:* **Adult:** 400 mg on the first day, then 200 mg every twenty four hours for a total of ten days of therapy. **Child** up to 18 years of age – use is not recommended in infants, children, or adolescents since fluoroquinolones cause arthropathy in immature animals.

Note: The recommended dose for patients with renal function impairment (creatinine clearance less than 40 ml per minute) is 400 mg on the first day, then 200 mg every forty-eight hours for a total of nine days of therapy.

Storage: at room temperature.

8.1.6 Tetracyclines

Tetracyclines all have a broad spectrum of activity which includes Gram-positive and Gram-negative bacteria. Unlike the penicillins and aminoglycosides they are usually bacteriostatic at the concentrations achieved in the body but act similarly to the aminoglycosides by interfering with protein synthesis in susceptible organisms.

Doxycycline is a tetracycline and is a broad- spectrum antibiotic effective for conditions caused by Chlamydia, rickettsia, brucella and spirochaete, *Borrelia burgdorferi* (Lyme disease). It is a preferred tetracycline since it has a more favourable pharmacokinetic profile than tetracycline.

Doxycycline

Tablet, 100mg

Capsule, 100mg

Indications: respiratory tract infections, including pneumonia and chronic bronchitis, urinary-tract infections, syphilis, chlamydia, mycoplasma, and rickettsia, prostatitis, lymphogranuloma venereum, pelvic inflammatory disease (with metronidazole), Lyme disease; brucellosis (with rifampicin), leptospirosis, scrub typhus and travellers' diarrhoea, psittacosis, cholera, melioidosis, plague, anthrax, Q fever.

Cautions: hepatic function impairment.

Drug interactions: antacids, carbamazepine, ciclosporin, oral contraceptives, ergotamine, ferrous salts, phenobarbital, phenytoin, rifampicin and warfarin.

Contraindications: pregnancy, and breast-feeding, in infants and children up to 8 years of age.

Side effects: nausea, vomiting, diarrhoea, erythema, headache, visual disturbance, hepatotoxicity, pancreatitis,

pseudomembrane colitis, discolouration of infants and children's teeth, photosensitivity.

Dose and Administration:*Infections due to susceptible organisms: Oral: Adult and Child* over 8 years: 200 mg on first day then 100 mg daily; in severe infections, 200 mg daily.*Syphilis: Oral:* 200–300 mg daily in 1–2 divided doses. *Uncomplicated genital chlamydia, non-gonococcal urethritis: Oral:* 100 mg twice daily.

Louse and tick-borne relapsing fevers: Oral: 100 mg or 200 mg as a single dose. *Cholera: Oral: Adult:* 300 mg as a single dose; *Child:* over 8 years, 100 mg as a single dose.

Note: Patient Advice. Capsules should be swallowed whole with plenty of fluid while sitting or standing to prevent oesophageal irritation. May be given with food to counter gastric irritation

Storage: at room temperature in a tight, light-resistant container.

Minocycline hydrochloride

Capsule, 50mg, 100mg

Indications: It is tetracycline derivative and used for treatment of susceptible bacterial infections of both gram-negative and gram-positive organisms; treatment of anthrax (inhalational, cutaneous, and gastrointestinal); acne; meningococcal (asymptomatic) carrier state; Rickettsial diseases (including rockymountain spotted fever,); nongonococcal urethritis, gonorrhoea; acute intestinal amebiasis.

Cautions: Hepatic and renal dysfunction, It may increase muscle weakness in patients with myasthenia gravis, and exacerbate systemic lupus erythematosus; if treatment continued for longer than 6 months, monitor every 3 months for hepatotoxicity, pigmentation and for systemic lupus erythematosus—discontinue if these develop or if pre-existing systemic lupus erythematosus worsens.

Drug interactions: see under tetracycline HCl; also coumarins, dairy products, ergotamine and methysergide, iron, haolin, penicillins, phenindione, quinapril, retinoid, strontium ranelate, sucralfate, sulfonyleureas, zinc, typhoid vaccine(oral), tripotassium dicitratobismuthate.

Contraindications: see under tetracycline HCl

Side-effects: see under tetracycline HCl; also dizziness and vertigo (more common in women); *rarely* anorexia, tinnitus, impaired hearing, hyperaesthesia, paraesthesia, acute renal failure, pigmentation (sometimes irreversible), and alopecia; *very rarely* systemic lupus erythematosus, discoloration of conjunctiva, tears, and sweat.

Dose and administration: 100 mg twice daily prophylaxis of asymptomatic meningococcal carrier state (but no longer recommended), 100 mg twice daily for 5 days usually followed by rifampicin

Note: Capsules should be swallowed whole with plenty of fluid while sitting or standing

Storage: Store at 20⁰c to 25⁰c; protect from light and moisture

Tetracycline hydrochloride

Tablet, 250 mg, 500 mg (coated)

Capsules, 250mg, 500mg

Injection, 100 mg, 250 mg, 500 mg in vial

Indications: exacerbations of chronic bronchitis; brucellosis, chlamydia, mycoplasma, and rickettsia; acne vulgaris, rosacea, typhus, gonorrhoea, chancroid, syphilis, and cholera.

Cautions: caution in patients with renal function impairment.

Drug interactions: aluminium and/or magnesium containing antacids, laxatives, calcium (e.g. milk or other dairy products, eggs) and/or iron supplements, penicillines, or streptomycin.

Contraindications: pregnant or nursing women, infants and children under 8 years of age (it may also depress bone growth and cause permanent discolouration of the teeth).

Side effects: nausea, vomiting, epigastric burning and distress, flatulence and diarrhoea occur most frequently due to gastric irritation. Rarely photosensitivity, skin discoloration, blood dyscrasias may occur.

Dose and Administration: *Orally*, given 1 hour before or 2 hours after meals with adequate amounts of fluid.

Reduce dosage in renal and hepatic function impairment.

Adult: Rickettsial infection (e.g. typhus): 1-2g daily in 2-4 divided doses for 7-10 days. *Gonorrhoea (uncomplicated or disseminated) in penicillin allergies:* 500mg every 6 hours daily for at least 7 days. *Chancroid:* 1-2g daily in 2-4 divided doses for 7 days.

Syphilis (in penicillin allergies): Early syphilis (of not more than 2 years duration) and Late syphilis (2 years and more): 500mg every 6 hours daily for 15 days.

Cholera: 1-2g daily in 2-4 divided doses for 48 – 72 hours. **Child** (8 years and over): usually, *oral*, 25 – 50mg/ml of body weight daily in 2-4 divided doses. *Relapsing fever:* **Adult:** 500mg – 1g every twelve hours. **Child** (8 years and over): 6.25 – 12.5mg/kg of body weight every six hours. **Adult and Child:** *IV or IM:* administration given in two to four divided doses at dose levels of 2.5 to 5 mg/kg/day for patients with normal renal function depending on the severity of the infection.

Storage: at room temperature, in a tight, light-resistant container. *Note: outdated and decomposed tetracycline are toxic and may cause nephrotoxicity and skin lesion.*

8.1.7. Chloramphenicols

Chloramphenicol was the first broad spectrum antibacterial to be discovered; it acts by interfering with bacterial protein synthesis and is mainly bacteriostatic. Its range of activity is similar to that of tetracycline and includes *Gram-positive and Gram-negative bacteria, Rickettsia spp., and Chlamydiaceae*. It is associated with serious haematological adverse effects and should be reserved for the treatment of severe infections, particularly those caused by *Haemophilus influenzae* and typhoid fever.

Chloramphenicol

Capsules, 250mg

Suspension, oral (palmitate), 125mg/5ml; 60ml.

Injection (sodium succinate), 1 g in vial

Indications: severe life-threatening infections, particularly those caused by *Haemophilus influenzae*, and typhoid fever; also, cerebral abscess, mastoiditis, relapsing fever, gangrene, granuloma inguinale, listeriosis, severe melioidosis, plague, psitticosis, tularaemia, Whipple disease, septicaemia, empirical treatment of meningitis

Cautions: it should not be used for the treatment of minor and undefined infections, or as a prophylaxis. Caution in patients with hepatic function impairment, blood disorder, in neonates and infants, in pregnant women, particularly those near term or in labour, and in nursing women.

Drug interactions: phenobarbital, oral contraceptives (estrogen containing), tolbutamide, chlorpropamide, penicillines, or streptomycin.

Contraindications: known hypersensitivity and/or toxic reactions to chloramphenicol.

Side effects: nausea, vomiting diarrhoea, and bone-marrow depression may occur.

Dose and Administration: *Note: A high initial dosage should not be given in the treatment of typhoid fever as sensitivity like reaction occurs. Reduce dose in hepatic and/or renal impairment.***Typhoid Fever:****Adult:** 500mg every 6 hours daily for 14 days. **Child:** 11-30kg, 250mg every 6 hours daily for 14 days. 6-10kg, 125mg every 8 hours daily for 14 days.**Typhus:** **Adult:** 500mg every 6 hours for 10 days. **Child:** 50 – 75 mg/kg of body weight daily in divided doses every 6 hours for 10 days.

Meningitis:*I.V:* infants > 30 days and **Child:** 50 - 100 mg/kg/day divided every 6 hours.**Other infections:** *I.V:*

Adult: 50 - 100 mg/kg/day in divided doses every 6 hours; maximum daily dose: 4 g/day.**Infant** > 30 days and **Child:** 50 - 75 mg/kg/day divided every 6 hours; maximum daily dose: 4 g/day.

Storage: at room temperature, in a tight container.

Thiamphenicol

Capsule, 250 mg

Tablet, 250 mg

Indications, Cautions, Drug interactions and Side effects see under chloramphenicol.

Dose and Administration: *Oral:*

Adult: 1.5g daily; up to 3g daily has been given initially in severe infections.

Child: 30-100mg/kg daily.

Gonorrhoea: oral dose ranged from 2.5g daily for 1 or 2 days through to 2.5g on the first day followed by 2g daily on each of 4 subsequent days.

8.1.8. Miscellaneous

Clindamycin

Capsule, 75 mg, 150 mg

Injection, 150 mg/ml in ampoule

Oral solution, 15 mg/ml

Indications: staphylococcal bone and joint infections; peritonitis, endocarditis prophylaxis; alternate treatment for toxoplasmosis (see section 7.4.5).

Cautions: discontinue immediately if diarrhea or colitis develop; hepatic and renal impairment, neonates and infants; elderly; pregnancy; breastfeeding.

Drug interactions: alcuronium, neostigmine, pyridostigmine, vecuronium.

Contraindications: hypersensitivity to clindamycin.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, antibiotic - associated colitis, rashes, urticaria, and rarely anaphylaxis, erythema multiforme, exfoliative and vesiculobullous dermatitis, jaundice and altered liver function tests; neutropenia, eosinophilia, agranulocytosis, and thrombocytopenia, pain, indurations, and abscess after IM injection; thrombophlebitis after IV injection.

Dose and Administration: *Osteomyelitis or peritonitis:*

Oral: Adult: 150 - 300 mg every 6 hours; up to 450 mg every 6 hours in severe infections. **Child:** 3 - 6 mg/kg every 6 hours. *IM or IV infusion: Adult:* 0.6 - 2.7 g daily in 2 - 4 divided doses, increased up to 4.8 g daily in life-threatening infections; single doses over 600 mg by IV infusion only; single doses by IV infusion not to exceed 1.2 g; **Neonates:** 15 - 20 mg/kg daily. **Child** over 1 month: 15 - 40 mg/kg daily in 3 - 4 divided doses; severe infections, at least 300 mg daily, regardless of weight. *Endocarditis prophylaxis (for procedures under local or no anaesthetic): Oral: Adult:* 600 mg, 1 hour before

procedure. *Endocarditis prophylaxis (for procedures under general anaesthetic): IV infusion: Adult:* 300 mg over at least 10 minutes, at induction or 15 minutes before procedure, then 150 mg 6 hours later by mouth or infusion.

Storage: store at room temperature.

Metronidazole

Tablet, 250mg

Intravenous infusion, 5mg/ml in 100ml

Cream, 0.75%, 1%

Indications: treatment of anaerobic infection, bone and joint infection, meningitis, bacterial endocarditis, prophylaxis of perioperative infection during colorectal surgery, lower respiratory tract infection including pneumonia, empyema and lung abscess, bacterial septicemia, skin and soft tissue infection, inflammatory bowel disease, antibiotic associated colitis, *Helicobacter pylori* associated duodenal ulcer; see also section 1.2.

Cautions: disulfiram like reaction with alcohol; hepatic impairment and hepatic encephalopathy, pregnancy; breastfeeding; clinical and laboratory monitoring in courses lasting longer than 10 days; see also interactions.

Note: Avoid Alcohol use.

Drug interactions: phenytoin, coumatin or indandion derivative anticoagulant, warfarin, disulfiram, alcohol, cimetidine, fluorouracil, lithium, phenobarbitone.

Contraindications: chronic alcohol dependence

Side effects: nausea, vomiting, unpleasant metallic taste, furred tongue and gastrointestinal disturbances; rarely headache, drowsiness, dizziness, ataxia, darkening of urine, erythema multiform, pruritus, urticaria, angioedema, and anaphylaxis; abnormal liver function tests, hepatitis, jaundice, thrombocytopenia, aplastic anaemia, myalgia, arthralgia,

peripheral neuropathy, epileptiform seizures, leucopenia, on prolonged or high dosage regimens

Dose and Administration:Adult: *Antibacterial (systemic), anaerobic infections: Oral:* 7.5mg (base) per kg of body weight up to a maximum of 1 gm, every 6 hours for 7 days or longer; *IV-infusion,* 15mg (base) per kg of body weight initially, then 7.5mg per kg of body weight up to a maximum of 1gm, every six hours for seven days or longer; *Inflammatory bowel disease: Oral:* 500mg (base) four times a day.*Antibiotic associated colitis: Oral:* 500mg (base) three or four times a day.*Helicobacter - pylori associated gastritis or duodenal ulcer: Oral:* 500mg (base) three times a day with amoxicilline for one to two weeks.*Perioperative infections, colonic (prophylaxis):IV infusion:* 15mg (base) per kg of body weight one hour prior to start of surgery and 7.5mg per kg of body weight six and twelve hours after the initial dose.**Child:***Anaerobic infection: Oral:* 7.5mg (base) per kg of body weight every 6 hours, or 10mg per kg of body weight every 8 hours.*Anaerobic infection - for preterm infants: IV infusion:* 15mg per kg of body weight (base) as an initial dose, then 7.5mg per kg of body weight every 12 hours starting 48 hours after the initial dose. Term infants, *IV infusion,* 15mg (base) per kg of body weight as an initial dose, then 7.5mg per kg of body weight every 12 hours starting 24 hours after the initial dose. Infants greater than 7 days of age and children *IV infusion,* 15mg (base) per kg of body weight as an initial dose, then 7.5 mg per kg of body weight every 6 hours.**Storage:** at room temperature, in a well closed, light resistant container. Protect from freezing

Nitrofurantoin

Tablet, 50mg, 100mg

Capsule (macrocrystal), 50mg, 100mg

Oral suspension, 0.5% W/V

Indications: prophylaxis and treatment of urinary tract infection.

Cautions: hypersensitive to nitrofurantoin, diabetes mellitus, electrolyte imbalance, vitamin B and folate deficiency, pulmonary disease, hepatic impairment, peripheral neuropathy.

Drug interactions: hemolytic, neurotoxic medication, probenecid, sulfipyrazone.

Contraindications: impaired renal function, infants less than 3 months, pregnancy, during breastfeeding, glucose 6 phosphate dehydrogenase (G6PD) deficiency, porphyria.

Side effects: pneumonitis (chills, chest pain, cough, fever, troubled breathing, abdominal or stomach pain or upset, diarrhoea, loss of appetite, nausea, vomiting), hematology reactions, specifically granulocytopenia (sore throat and fever) or anemia, neurotoxicity, polyneuropathy, hepatitis, hypersensitivities rust yellow to brown discoloration of urine.

Dose and Administration: *Oral:Adult:* 50 to 100mg every 6 hours. Maximum up to 600 mg daily, or up to 10mg per kg of body weight daily.

Note: Prophylaxis 50 to 100mg once a day at bedtime.

Child: infants and children 1 month of age and over, 0.75 to 1.75mg per kg of body weight every 6 hours.

Note: Prophylaxis - 1mg per kg of body weight once a day at bedtime. Continue medicine for full time of treatment.

Storage: store at room temperature in a tight, light resistant container.

Pentamidine Isothionate

Nebulizer solution, 300mg/vial

Indications: Treatment and prevention of pneumonia by *Pneumocystis carinii* (PCP)

Cautions: Renal and hepatic dysfunction, risk of severe hypotension following administration (monitor blood pressure before starting treatment, during administration, and at regular intervals, until treatment concluded; patient should be lying down when receiving drug parenterally); hypokalaemia, hypomagnesaemia, coronary heart disease, bradycardia, history of ventricular arrhythmias, concomitant use with other drugs which prolong QT-interval; hypertension or hypotension; hyperglycaemia or hypoglycaemia; leucopenia, thrombocytopenia, or anaemia; carry out laboratory monitoring according to product literature; care required to protect personnel during handling and administration.

Drug interactions: Amiodarone, amisulpride, amphotericin, tricyclic antidepressants, droperidol, erythromycin, foscarnet, ivabradine, moxifloxacin, phenothiazines, saquinavir.

Contraindications: Hypersensitivity to pentamidine isethionate or any component of the formulation, pregnancy and breast feeding.

Side effects: severe reactions, sometimes fatal, due to hypotension, hypoglycaemia, pancreatitis, and arrhythmias; also leucopenia, thrombocytopenia, acute renal failure, hypocalcaemia; also reported: azotaemia, abnormal liver-function tests, anaemia, hyperkalaemia, nausea and vomiting, dizziness, syncope, flushing, hyperglycaemia, rash, and taste disturbances; Stevens-Johnson syndrome reported; on inhalation, bronchoconstriction (may be prevented by prior use of bronchodilators), cough, and shortness of breath; discomfort, pain, induration, abscess formation, and muscle necrosis at injection site.

Dose and administration: Prophylaxis of *Pneumocystis jirovecii* (PCP) pneumonia, by inhalation of nebulised solution (using suitable equipment, consult product literature), 300 mg

every 4 weeks *or* 150 mg every 2 weeks [unlicensed for primary prevention].

Storage: Store intact vials at controlled room temperature and protect from light.

Spectinomycin

Injection, 2g in vial

Indications: uncomplicated and disseminated gonorrhoea; adult and neonatal gonococcal conjunctivitis; chancroid. *Note: It is not indicated for pharyngeal gonorrhea.*

Cautions: renal impairment, pregnancy and breastfeeding.

Drug interactions: lithium, botulinum toxin.

Contraindications: hypersensitive to spectinomycin.

Side effects: hypersensitivity (chills, fever, itching or redness of the skin), dizziness, nausea, vomiting, abdominal cramp.

Dose and Administration: *Uncomplicated gonococcal infections and chancroid: deep IM injection: Adult: 2g as a single dose (may be increased to 4g as a single dose divided between 2 injection sites in difficult to treat cases and where there is known antibiotic resistance)*

Disseminated gonococcal infections: deep IM injection: Adult: 2g twice daily for 7 days. Neonatal gonococcal conjunctivitis: deep IM injection: Neonate 25 mg/kg (maximum 75mg) as a single dose.

Storage: at room temperature.

Sulphamethoxazole and Trimethoprim

Tablet (pediatric), 100mg + 20mg; (adult), 400mg + 80mg, 800mg+160mg

Mixture, 200mg + 40mg in each 5ml

Injection, 400mg + 80mg in each 5ml ampoule

Indications: prophylaxis and treatment of *Pneumocystis carinii* infections, toxoplasmosis and *Isospora belli* diarrhea. Treatment of nocardiosis, urinary tract, respiratory tract, typhoid/paratyphoid fevers and prostatic infections caused by susceptible organisms

Cautions: elderly, renal and hepatic function impairment, photosensitivity, Glucose-6-phosphate dehydrogenase (G6PD) deficiency; maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rash – discontinue immediately; predisposition to folate deficiency; asthma; pregnancy; breastfeeding.

Drug interactions: coumarin or indandione derivative anticoagulant, hydantoin, oral hypoglycemics, hemolytics, hepatotoxic medication, methenamine, methotrexate, folate antagonists.

Contraindications: infants up to two months of age, in patients who are allergy to sulfonamide, furosemide, thiazide diuretics, sulfonylureas, carbonic anhydrase inhibitors or trimethoprim.

Side effects: hypersensitivity, photosensitivity, blood disorders unusual bleeding or bruising, unusual tiredness or weakness, hepatitis, Steven's Johnson syndrome, aching joints and muscles, redness, blistering, peeling, or loosening of the skin, unusual tiredness or weakness, toxic epidermal necrosis, dizziness, headache, GIT disturbance, loss of appetite, nausea or vomiting.

Dose and Administration:Adult:Oral: 160mg of trimethoprim and 800mg of sulphamethoxazole every 12 hours may be increased to 320/1600 mg 12 hourly in severe infections.*IV infusion:* 160/800 mg 12 hourly. Each 80/400mg (5ml) to be diluted in 125ml 5% glucose or 0.9% sodium chloride solution

or infused over 1-1.5 hours. *Cerebral toxoplasmosis*: 320/1600mg twice daily for 4 weeks, then 160/800 mg twice daily for 3 months.

Iso spor a belli: 160/800 mg 6 hourly for 10 days.

Primary prophylaxis in HIV-infection: *Oral*: 160/800 mg daily. Lower doses (80/400 mg daily or 160/800 mg 3 times a week) have been shown to be effective for *Pneumocystis pneumonia* and are better tolerated.

Child: *Oral*: 2 months to 5 months, 20/100mg; 6 months to 5 years, 40/200 mg; 6-12 years, 80/400mg, 12 hourly. *IV infusion*: 6/30 mg/kg/day in 2 divided doses, increased to 9/45 mg/kg/day in severe infections.

Pneumocystis carinii pneumonia: *Treatment*: *Oral or IV infusion*: Adult and Child: sulphamethoxazole up to 100mg/kg daily with trimethoprim up to 20mg/kg daily in 2-4 divided doses for 14-21 days.

Prophylaxis: *Oral*: Adult and Child: sulphamethoxazole 25mg/kg with trimethoprim 5 mg/kg in 2 divided doses on alternate days (3 times a week).

Note: For oral, continue medicine for full time of treatment, avoid too much sun or use of sun lamp. Avoid IM administration.

Storage: at room temperature, in a tight, light-resistant container, protect from freezing.

Trimethoprim

Injection, 20 mg/ml

Tablet, 100 mg, 200 mg

Suspension, 50 mg/ml

Indications: acute uncomplicated urinary tract infections, respiratory tract infections and chronic prostatitis and alternative to co-trimoxazole for *Pneumocystis pneumonia*, in combination with dapsone.

Cautions: impaired renal or hepatic function or with possible folate deficiency.

Drug interactions: digoxin, phenytoin or phenobarbital, oral contraceptives, zidovudine and lamivudine.

Contraindications: use in neonates.

Side effects: skin rashes, pruritus, nausea, epigastric pain and glossitis, hyperkalaemia, bone marrow depression (with leukopenia, thrombocytopenia and megaloblastic anaemia).

Dose and Administration: *Oral:* Adult: 100 mg every 12 hours or 200 mg every 24 hours for 10 days; longer treatment periods may be necessary for prostatitis (i.e, 4 - 16 weeks); in the treatment of pneumocystis carinii pneumonia; dose may be as high as 15 - 20 mg/kg/day in 3 - 4 divided doses. **Child:** 4 mg/kg/day in divided doses every 12 hours. *IV:* Acute infection: Adult: 200mg every 12 hours. **Child under 12 years:** 8mg/kg daily in 2-3 divided doses.

Storage: store at room temperature and protect from light

Vancomycin

Injection, 500 mg in vial, 1gm

Indications: generally reserved for the treatment of infections due to cloxacillin - resistant staphylococci and enterococci; also as an alternative agent for prophylaxis and treatment of endocarditis in penicillin allergic patients.

Cautions: renal impairment.

Drug interactions: ototoxic and nephrotoxic agents, e.g. aminoglycosides.

Contraindications: hearing abnormalities.

Side effects: nephrotoxicity including renal failure and interstitial nephritis, ototoxicity, blood disorders, nausea, chills, fever, eosinophilia, anaphylaxis, rashes, including exfoliative dermatitis, Stevens Johnson syndrome, and vasculitis; phlebitis;

on rapid infusion, severe hypotension, wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body, pain and muscle spasm of back and chest.

Dose and Administration: *IV infusion:* Adult: over at least 1 hour, 500 mg 6 hourly or 1 g 12 hourly. **Child:** over at least 1 hour, 10 mg/kg 6 hourly or 20 mg/kg 12 hourly.

Neonates: under 1 week old, initially 15 mg/kg followed by 10 mg/kg 12 hourly; 1 week - 1 month old, 15 mg/kg followed by 10 mg/kg 8 hourly.

Storage: vancomycin reconstituted IV solutions are stable for 14 days at room temperature or refrigeration.

8.1.9. Antituberculous drugs

Tuberculosis is a chronic infectious disease caused primarily by *Mycobacterium tuberculosis* or sometimes *M. bovis*; The closely related form *M. africanum* has occasionally been implicated as a cause of human tuberculosis. Drug treatment for clinical TB Disease always involves multi drug regimens, chosen to provide early bactericidal activity (activity against actively dividing mycobacteria), and sterilizing activity (activity against non-dividing/dormant, semi-dormant organisms), and to prevent resistance. According to the newly revised national TBL and TB/HIV Guideline (2012), tuberculosis cases are classified based on anatomical site of infection as pulmonary tuberculosis (PTB) or extrapulmonary tuberculosis (EPTB) and type of the cases as new case, re-treatment cases (relapsed, treatment failure, return after default) or MDR TB). The complete treatment is divided in two phases as intensive (initial) phase and continuous phase. Intensive phase consists of treatment with combination of 4 drugs for the first 8 weeks for new cases, and with combination of 5 drugs for the first 8 weeks followed by 4 drugs for the next 4 weeks for re-treatment cases. Continuation phase which follows immediately after initial phase requires treatment with a combination of 2 drugs, to be taken for 16 weeks for new cases and

8. Anti-Infectives

treatment with a combination of 3 drugs for re-treatment cases for 20 weeks.

New TB case regimens consist of 8 weeks treatment with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol 2(RHZE) during the intensive phase, followed by 16 weeks with Rifampicin and Isoniazid 4(RH). Re-treatment cases consists of 8 weeks treatment with Streptomycin, Rifampicin, Isoniazid, Pyrazinamide and Ethambutol 2S(RHZE) followed by 4 weeks treatment with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol 1(RHZE) during the intensive phase, followed by 5 months with Rifampicin, Isoniazid and Ethambutol 5(RH)E.

Anti TB drug Dosage for New TB cases

Patient's Weight in Kgs	Treatment Phase, Regimen and Dose	
	Intensive Phase (2 months)	Continuation Phase(4 months)
	number of (RHZE) tablets	number of (RH) tablets
20-29	1 ½	1 ½
30-39	2	2
40-54	3	3
≥55	4	4

Dosage for Previously treated cases regimen:

Patient's Weight in Kgs	Treatment Phase, Regimen and Dose			
	Intensive Phase 3 months		Continuation Phase 5 months	
	Dose of S & number of RHZE tablets	number of RHZE	Number of RHE tablets	Number of RHE tablets
	S*	RHZE	RH	E
20-29	½ (0.5 g)	1 ½	1 ½	1 ^{1/2}
30-39	½(0.5 g)	2	2	1 ^{1/2}
40-54	¾ (0.75g)	3	3	2
≥ 55	1 g	4	4	3

**S in intensive phase will continue for two months only.*

The Programmatic approach to MDRTB treatment in Ethiopia is either standardized individualized or empiric treatment approaches.

The standardized treatment regimen for MDR TB addresses 5 patient categories:

1. *Patients with MDR-TB confirmation, but no full DST results available yet:*

Regimen: E-Z-Km (Am)-Lfx-Eto-Cs

2. *MDR-TB Patients susceptible to both Kanamycin and Quinolone: Regimen is the same as above*

3. *MDR-TB Patients susceptible to Kanamycin, but resistant to Quinolone:*

Regimen: E-Z-Km (Am)-Mfx-Eto-Cs-PAS

4. *MDR-TB Patients susceptible to Quinolone, but resistant to Kanamycin:*

Regimen: E-Z-Cm-Lfx-Eto-Cs

5. *XDR-TB Cases (i.e.: MDR-TB and resistance to Quinolone and Kanamycin)*

Regimen: E-Z-Cm-Mfx-Eto-Cs-PAS

Duration and Phases of MDR TB Treatment

Intensive phase: The injectable agent is used for minimum of 6 months and at least 4 months after culture conversion. The use of an individualized approach which reviews the cultures, smears, x-rays, and the patient's clinical status may also aid in deciding whether or not to continue an injectable agent longer than the above recommendation, particularly in the case of patients for whom the susceptibility pattern is unknown, effectiveness is questionable for an agent(s), or extensive or bilateral pulmonary disease is present. *Continuation phase:* The treatment period following the intensive phase. The total treatment is for minimum duration of 18 months beyond culture conversion (eg. pediatric patients receiving second line treatment with baseline

culture negative result). Thus if the culture is negative at completion of first month of MDR-treatment, intensive phase will be 6 months and continuation phase 13 months. However, if culture conversion(two consecutive negative cultures, from samples collected at least 30 days apart) is at completion of second months, intensive phase will be 6 months and continuation phase 14 months. If culture conversion is at completion of fourth month, intensive phase will be 8 months and continuation phase will be 14 months. Extension of therapy to 24 months may be indicated in chronic cases with extensive pulmonary damage.

Amikacin

Injection, (as sulphate), 50mg/ml, 250mg/ml, 500mg/ml in 2ml vial

Indications: treatment of MDR TB in conjunction with at least two other antituberculosis agent.

Cautions: renal impairment, drug should be discontinued if signs of ototoxicity, nephrotoxicity, during pregnancy and lactation.

Drug interactions:amphotericin, neuromuscular blocking agents.

Contraindications: hypersensitivity to amikacin sulfate

Side effects: neurotoxicity, ototoxicity, nephrotoxicity, allergic reaction, dyspnea, eosinophilia

Dose and Administration:standardized or individually adjusted on the basis of result of sensitivity test.

Storage: stable for 24 hours at room temperature and 2 days at refrigeration when mixed in DW, DNS, NS, LR.

Capreomycin

Powder for injection, 1 g/vial

Indications: treatment of drug resistant tuberculosis in conjunction with at least 2, preferably 3 (new drugs known to be active against the resistant strain) other antituberculosis agents.

Cautions: renal insufficiency or pre-existing auditory impairment, elderly, use with non-antituberculous drugs (i.e., aminoglycoside antibiotics).

Contraindications: hypersensitivity to capreomycin. Renal function test should be monitored weekly and hepatic function should be monitored periodically.

Drug interactions: use of other nephrotoxic and/or ototoxic drugs including aminoglycosides (e.g., Streptomycin), colitsin, polymyxin B, and vancomycin.

Side effects: ototoxicity, tinnitus, nephrotoxicity, eosinophilia, acute tubular necrosis, Bartter's syndrome, hypersensitivity (urticaria, rash, fever), hypokalemia, leukocytosis, hypocalcemia, hypomagnesemia, pain, induration, and bleeding at injection site, vertigo.

Dose and Administration: *IM, I.V.*: Adult: 15 mg/kg per day (maximum dose of 1 g). The dose should be reduced for persons greater than 59 years of age to 10 mg/kg per day (maximum 750 mg). **Children:** 15 to 30 mg/kg per day (maximum dose 1 g) as a single daily dose or given twice-weekly

Storage: store at room temperature.

Cycloserine

Capsule, 250 mg

Indications: in combination with other second- line drugs for treating tuberculosis resistant to first- line agents.

Cautions: epilepsy, depression, severe anxiety, psychosis, severe renal insufficiency, chronic alcoholism.

Drug interactions: alcohol, isoniazid, ethionamide and phenytoin and dosages of anticonvulsants should be reduced if necessary..

Contraindications: hypersensitivity to cycloserine.

Side effects: cardiac arrhythmia, drowsiness, headache, dizziness, vertigo, seizure, confusion, psychosis, hyperirritability, paresthesias,, dysarthria paresis, coma, rash, vitamin B12 deficiency, folate deficiency, liver enzymes increased, tremor.

Dose and Administration:*Oral:***Adult:** Initial: 250 mg every 12 hours for 14 days, then administer 500 mg to 1g/day in 2 divided doses for 18 - 24 months (maximum daily dose: 1 g).**Child:** 10 - 20 mg/kg/day in 2 divided doses up to 1000 mg/day for 18 - 24 months.

Note: The dosage of cycloserine in patients with renal impairment must be adjusted according to the degree of dysfunction and blood cycloserine concentrations.

Storage:store at room temperature

Ethambutol

Tablet, 100mg, 400mg

Indications: tuberculosis, in combination with other drugs (see notes above)

Cautions: visual disturbances,ocular examination recommended before and during treatment; reduce dose and monitor plasma concentration: elderly; pregnancy; breastfeeding.

Contraindications: optic neuritis, poor vision, children under at least 6 years of age, renal impairment

Side effects: optic neuritis, red/green colour blindness, peripheral neuritis, rarely rash, pruritus, urticaria, and thrombocytopenia.

Dose and Administration:Initial phase of combination therapy; see notes above): *Oral:* 15mg/kg (15-20 mg/kg) daily, maximum 1600mg.

Storage: at room temperature, in a well-closed container. Protect from light, moisture, and heat.

Ethambutol + Isoniazid

Tablet, 400mg + 150mg

Indications: tuberculosis, in combination with other drugs (see notes above)

Cautions: see ethambutol and isoniazid

Drug interactions: see ethambutol and isoniazid

Contraindications: preparation not suitable for use in children; see ethambutol and isoniazid.

Side effects: see ethambutol and isoniazid

Dose and Administration:*Tuberculosis, continuation phase of 8 months regimen:* *Oral:* Adult: ethambutol hydrochloride 800mg and isoniazide 300 mg daily.

Storage: at room temperature, in a well closed, light resistant container.

Ethionamide

Tablet, 250 mg

Indications: treatment of drug resistant tuberculosis in conjunction with at least 2, preferably 3 (new drugs known to be active against the resistant strain) other antituberculosis agents.

Cautions: depression, psychiatric illness, chronic alcoholism, epilepsy, hypothyroidism, diabetes.

Drug interactions: isoniazide, cycloserine and terizidone.

Contraindications: hypersensitivity, severe hepatic disease.

Side effects: nausea, vomiting, anorexia, metallic taste, abdominal discomfort, diarrhoea and weight loss, seizures,

pellagra-like encephalopathy responsive to niacin, acute psychosis, anxiety and depression, optic neuritis, and peripheral neuropathy responsive to pyridoxine, hepatotoxicity.

Dose and Administration:*Oral:*Adult: 15 - 20 mg/kg/day as a single dose; Maximum 1 g/day.Child: 10 -20 mg/kg/day in 2 – 3 divided doses after meals or 15mg/kg once daily.

Storage: store at room temperature.

Isoniazid

Tablet, 100mg, 300mg

Injection, 100mg/ml in 10ml ampoule

Oral liquid, 50mg/5ml

Indications: tuberculosis treatment, in combination with other drugs (see notes above); tuberculosis prophylaxis

Cautions: hepatic impairment (need monitoring of liver function); renal impairment; slow acetylator status (increased risk of side effects); epilepsy; history of psychosis; alcohol dependence, malnutrition, diabetes mellitus, HIV infection (risk of peripheral neuritis); pregnancy and breast-feeding; porphyria.

Drug interactions: carbamazepine, ethosuximide, Phenytoin, Serotonergic agents, other drugs (aluminium hydroxide: Isoniazid should be administered at least one hour before the antacid)

Contraindications:Hepatic impairment. Prophylaxis with isoniazid is contraindicated for patients who have active hepatic disease or who have had reactions to the drug. In pregnant women, prophylaxis usually should be delayed until after delivery.

Side effects: nausea, vomiting, constipation, dry mouth; peripheral neuritis with high doses (need pyridoxine prophylaxis), optic neuritis, convulsions, psychotic episodes, vertigo; hypersensitivity reactions including fever,

erythemamultiforme, purpura; blood disorders including agranulocytosis, haemolytic anaemia, aplastic anaemia; hepatitis (especially over age of 35 years); systemic lupus erythematosus-like syndrome, pellagra, hyperreflexia, difficulty with micturation, hyperglycaemia, and gynaecomastia reported.

Dose and Administration: *Tuberculosis, treatment (combination therapy; see also notes above): Oral: 5mg/kg (4-6 mg/kg) daily (maximum, 300 mg daily)*

*Tuberculosis, treatment in critically ill patients unable to take oral therapy (combination therapy): IM: **Adult:** 200 - 300 mg as single daily dose; **Child:** 10 - 20 mg/kg daily.*

Tuberculosis, prophylaxis: Oral: Adult: 300mg daily for at least 6 months; child 5mg/kg daily for at least 6 months. Note: isoniazid should be taken on an empty stomach; if taken with food to reduce gastrointestinal irritation, oral absorption and bioavailability may be impaired. Pyridoxine should be coadministered in individuals susceptible to isoniazid-induced neuropathy.

Storage: at room temperature, in a well closed, light resistant containers.

Kanamycin

Injection, 1g/vial

Indications: in combination with other secondline drugs for treating tuberculosis resistant to first line agents.

Cautions: renal impairment, drug should be discontinued if signs of ototoxicity, nephrotoxicity, pregnancy and lactation.

Drug interactions: amphotericin, neuromuscular blocking agents.

Contraindications: hypersensitivity to kanamycin sulfate.

Dose and Administration: standardized or individually adjusted on the basis of result of sensitivity test, pretreatment body weight and renal status. Adult and child above 15 years: 15mg/kg, daily (up to 1g) given as a single daily dose 5 to 7

times weekly for the 2 to 4 months or until culture conversion where dosage can then be reduced to 15mg/kg daily (up to 1 g) 2 or 3 times weekly, in older age of more than 59 years 10 mg/kg is recommended up to 750mg daily dose recommended. Pediatric dosage (younger than 15 years): 15 to 30mg/kg daily (up to 1 g) given once daily or twice weekly.

Storage: at 20-25⁰c

Levofloxacin

Tablet, 250mg, 500mg and 750mg

Infusion, 5mg/ml

Indications: in combination with other secondline drugs for treating tuberculosis resistant to first line agents.

Cautions: not recommended in children < 18 years of age. CNS disorders or renal dysfunction, history of prolongation QT interval, peripheral neuropathy.

Drug interactions: warfarin, class IA and class III antiarrhythmics, erythromycin, cisapride, antacids, oral electrolyte supplements, quinapril, sucralfate and some didanosine formulations, cimetidine, corticosteroids, digoxin, (iron, multivitamins, mineral supplements: administer levofloxacin at least two hours before or two hours after), antidepressants and antidiabetic agents, NSAIDs, probenecid, theophylline.

Contraindications: hypersensitivity reactions to levofloxacin or other quinolones.

Side effects: dizziness, fever, headache, insomnia, abdominal pain, dyspepsia, nausea, vomiting, diarrhea, constipation, decreased vision, pharyngitis, dyspnea.

Dose and Administration: standardized or individually adjusted on the basis of result of sensitivity test

Storage: store at room temperature.

Moxifloxacin Hydrochloride

Tablet, 200mg, 400mg

Injection, 200mg/100ml

Indications: in combination with other second line drugs for treating tuberculosis resistant to first line agents

Cautions: Safety and efficacy not established in children or adolescent younger than 18 years of age or in pregnant or lactating woman. CNS disorders, prolongation of QT interval, peripheral neuropathy.

Drug interactions: class IA and class III antiarrhythmics, antacids (at least four hours before or eight hours after antacids that contain aluminium or magnesium), quinapril, sucralfate, didanosine (at least four hours before or eight hours after buffered didanosine), cimetidine, corticosteroids, (iron, multivitamins, mineral supplements: administer moxifloxacin at least four hours before or eight hours after this preparation except calcium supplements), corticosteroids (increase the risk of febrile tendon disorder).

Contraindications: known hypersensitivity to moxifloxacin or other quinolones, or any ingredient in the formulation.

Side effects: Tendinopathy and tendon rupture, dizziness, seizure, confusion, tremor, hallucination, clostridium difficile associated diarrhea (pseudomembranous colitis).

Dose and Administration: Adult and children 15 years of age or older receive 400 mg once daily. Intermittent regimen of moxifloxacin 400mg once daily (5 days per week) or 400 mg 3 times weekly is also used.

Storage: follow manufacturers advice

Para-Amino Salicylic Acid (PAS)

Sachet, 4mg

Indications: is a second-line Anti-TB agent. Its importance in the management of pulmonary and other forms of tuberculosis has markedly decreased since more active and better-tolerated drugs have been developed.

Side effects: Gastrointestinal problems including anorexia, nausea, epigastric pain, abdominal distress, and diarrhea are predominant and often limit patient adherence. Patients with peptic ulcers tolerate the drug especially poorly. Hypersensitivity reactions to aminosalicylic acid are seen in 5% to 10% of patients. High fever may develop abruptly, with intermittent spiking, or it may appear gradually and be low-grade. Generalized malaise, joint pains, and sore throat may be present at the same time. Skin eruptions of various types appear as isolated reactions or accompany the fever. Among the hematological abnormalities that have been observed are leukopenia, agranulocytosis, eosinophilia, lymphocytosis, an atypical mononucleosis syndrome, and thrombocytopenia. Acute hemolytic anemia may appear in some instances.

Dosage and administration: It is administered orally in a daily Adult dose of 10 to 12 g with the daily dose being divided into 2 to 4 equal portions. Children should receive 150 to 300 mg/kg per day in 3 to 4 divided doses. *Note: it is a gastric irritant; the drug is best administered after meals.*

Prothionamide

Tablet, 250 mg

Indication: Treatment of multibacillary leprosy (in combination with dapsone and rifampicin), to prevent emergence of drug resistance.

Cautions: Liver function tests must be performed at the start of treatment and repeated periodically throughout.

Contraindications: - Known hypersensitivity, Hepatic dysfunction, Pregnancy.

Side effects: Gastrointestinal disturbances, allergic reactions, alopecia, convulsions, dermatitis, diplopia, dizziness, headache, hypotension, peripheral neuropathy and rheumatic pains. Liver dysfunction and toxic hepatitis may occur.

Dosage and administration: Adults and children: 5.0 mg/kg daily (usual adult dose 250-375 mg).

Storage: Protonamide tablets should be kept in tightly closed containers protected from light.

Pyrazinamide

Tablet, 400mg, 500mg, 750mg

Indication: tuberculosis, in combination with other drugs (see notes above)

Cautions: hepatic impairment (dose related: need monitoring of hepatic function); renal impairment; diabetes mellitus (monitor blood glucose - may change suddenly); increased uric acid level in urine; breast-feeding.

Note: Patients or their carers should be told how to recognize signs of liver disorders and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, Vomiting, malaise or jaundice develop.

Drug interactions: uricosurics (probenecid, sulfinpyrazone)

Side effects: hepatotoxicity including fever, anorexia, hepatomegaly, jaundice, liver failure; nausea, vomiting; arthralgia; gout; thrombocytopenia, sideroblastic anaemia; urticaria; skin flushing.

Contraindications: severe hepatic impairment; porphyria, acute gout, hypersensitivity to pyrazinamide.

Dose and Administration: *Tuberculosis (initial phase of combination therapy):* Oral: 25-mg/kg (20-30mg/kg) daily, maximum 2000mg per day

Storage: at room temperature, in a well closed container.

Rifabutin

Capsule, 150 mg

Indications: treatment of pulmonary tuberculosis in combination with other agents. Prophylaxis of *M. avium-intracellulare* complex (MAC); treatment of non-tuberculous mycobacteria

Cautions: severe hepatic or renal dysfunction.

Drug interactions: clarithromycin, azithromycin, ciprofloxacin, fluconazole, isoniazid, protease inhibitors (PIs), non nucleoside reverse transcriptase inhibitors (NNRTIs). Hematologic status should be monitored periodically during therapy with this drug. Contraindications: hypersensitivity to rifamycins, neutropenia or other hematologic effects (thrombocytopenia).

Side effects: rash, gastrointestinal intolerance (nausea, vomiting, anorexia, abdominal pain and diarrhea), headache, insomnia, seizure, parasthesia, aphasia, confusion, and hematological effects (leucopenia, neutropenia, thrombocytopenia and anemia), hepatotoxicity. Hypersensitivity reactions (flu-like syndrome, chest pain, eosinophilia, bronchospasm, shock) are reported rarely, oveitis (may be unilateral or bilateral).

Dose and Administration: *Oral:* Adult 15 years of age or older: *Tuberculosis, in combination with other antituberculosis agent:* 5mg/kg (up to 300mg) given once daily or 5mg/kg 2 or 3 times weekly daily.

Pediatrics: 10-20mg/kg (up to 300mg) can be given daily or twice weekly. *Non- tuberculous mycobacteria treatment:* 450 -

600 mg daily. *Non-tuberculous mycobacteria prophylaxis*: 300 mg daily.

Storage: store at room temperature.

Rifampicin

Capsule, 150mg, 300mg, 600mg

Syrup, 20mg/5ml

Powder for injection (sodium) 300mg, 600mg in vial

Indications: tuberculosis, in combination with other drugs (see notes above), leprosy.

Cautions: reduce dose in hepatic impairment, liver function tests and blood counts required in liver disorders, elderly, and on prolonged therapy; renal impairment (if dose above 600 mg daily), pregnancy, breastfeeding, porphyria, discolour soft contact lenses.

Note: Advise patients on oral contraceptives to use additional means. Resumption of rifampicin treatment after a long interval may cause serious immunological reactions, resulting in renal impairment, haemolysis, or thrombocytopenia. Discontinue permanently if serious adverse effects occur.

Drug Interactions: clarithromycin, aminoslyclic acid, ciprofloxacin, chloramphenicol, atovaquone, clofazimine, elalapril, PIs, NNRTIs, anticonvulsants, antifungals, .azathioprine, ciclosporin, contraceptives, dexamethasone, fluconazole, fludrocortisone, glibenclamide, haloperidol, hydrocortisone,, levonorgestrel, , medroxyprogesterone, nelfinavir, nifedipine, norethisterone, phenytoin, prednisolone, guanidine, , verapamil, warfarin

Contraindications: hypersensitivity to rifamycins, jaundice, pregnancy, fertility and lactation.

Side effects: severe gastrointestinal disturbances including anorexia, nausea, vomiting, diarrhea, rashes, fever, influenza-

like syndrome and respiratory symptoms, collapse, shock, haemolytic anaemia, leucopenia, acute renal failure, and thrombocytopenic purpura-more frequent with intermittent therapy, alterations of liver function jaundice and potentially fatal hepatitis (dose related; do not exceed maximum dose of 600 mg daily); stains body fluid, local sensitivity and dermatologic reactions (pruritis, urticarial, pemphigoid reactions, Steven Jhonson Syndrome, toxic epidermal necrolysis, vasculitis), adrenocortical insufficiency.

Dose and Administration:*Tuberculosis (combination therapy; see notes above):* Oral: Adult and children 15 years of age or older: 10mg/kg (8 to 12mg/kg) daily (maximum dose, 600mg daily). Pediatric: 10 to 20mg/kg (up to 600mg) daily.

Note: take dose at least 30 minutes before a meal, as absorption is reduced when taken with food.

Storage: should be stored at a temperature of 30⁰c (preferably between 15-30⁰c) or less, in a tight, light - resistant container

Rifampicin + Isoniazid

Tablet, 60mg+30mg, 150mg + 100mg, 300mg + 150mg, 150mg+75mg; Capsule, 150mg + 100mg

Indications: Tuberculosis, continous phase for 4 month regimn

Cautions: preparation not suitable for use in children; see under rifampicin, and isoniazid

Drug interactions, Contraindications, Side effects; see under rifampicin, and isoniazid

Dose and Administration:*Tuberculosis, 6-month regimen (combination therapy: Oral: 10mg/kg (rifampicin) and 10mg/kg (isoniazid) 3 times a week.*

Rifampicin + Isoniazid + Pyrazinamide

Tablet, 60mg +30mg+150mg, 150mg + 75mg + 400mg

Indications: tuberculosis, in combination with other drugs.

Cautions; Side effects, Drug interactions; see Rifampicin, Isoniazid, and Pyrazinamide

Contraindications: preparations not suitable for use in children; see rifampicin, isoniazid, and Pyrazinamide.

Dose and Administration:*Tuberculosis, initial phase of 6 - month treatment regimens:* Oral: Adult: rifampicin 10mg/kg, isoniazid 5mg/kg, and Pyrazinamide 25 mg/kg daily or rifampicin 10mg/kg, isoniazid 10mg/kg and Pyrazinamide 35mg/kg 3 times a week.

Rifampicin + Isoniazid + Pyrazinamide + Ethambutol

Tablet, 150mg + 75mg + 400mg + 275mg

Indications: tuberculosis (see notes above)

Cautions, Side effects, Drug interactions, Contraindications; see rifampicin, isoniazid,

Pyrazinamide and Ethambutol.

Dose and Administration:*Tuberculosis, induction phase of 6-month regimen (see notes above):* Oral: rifampicin 10mg/kg, isoniazid 5mg/kg, Pyrazinamide 25mg/kg, and Ethambutol hydrochloride 15mg/kg daily

Streptomycin Sulphate

Powder for injection, 1g, 0.5g bases in vial

Indications: tuberculosis, in combination with other drugs (see notes above)

Cautions: children - painful injection, avoid use if possible, infants, and elderly (dosage adjustment), and monitor renal, auditory, and vestibular function, and plasma streptomycin concentrations.

Drug interactions: alcuronium, ciclosporin, cisplatin, furosemide, neostigmine, pyridostigmine, suxamethonium, and vecuronium

Contraindications: hearing disorders; renal impairment, myasthenia gravis, pregnancy

Side effects: vestibular and auditory damage; nephrotoxicity; hypersensitivity reactions - withdraw treatment; paraesthesia of mouth, rarely, hypomagnesaemia on prolonged therapy; antibiotic associated colitis; also nausea, vomiting, rash; rarely, haemolytic anaemia, aplastic anaemia, agranulocytosis, thrombocytopenia; pain and abscess at injection site.

Dose and Administration: *Tuberculosis (initial phase of combination therapy; see notes above): deep IM injection or IV: Adult: 15mg/kg (12-18mg/kg) daily as a single dose, maximum 1000mg (patients over 60 years may not tolerate doses above 500 to 750mg daily)*

Pediatric younger than 15 years of age or weighing 40kg or less: 20-40mg/kg daily (up to 1g).

Storage: at room temperature protect from light.

Note: Reconstituted solutions of streptomycin sulphate are stable for one week when stored at room temperature and protected from light, however streptomycin sulfate powder for injection contains no preservatives and the possibility of microbial contamination of reconstituted solutions must be considered.

Terizidone

Capsule 250mg

Indication: tuberculosis both pulmonary and extra pulmonary by resistant strains of mycobacterium TB or avium

Cautions: epilepsy, mental illness especially depression, severe anxiety, psychosis, severe renal insufficiency, chronic alcoholism.

Drug interactions: alcohol, isoniazid, ethionamide and phenytoin, fluoroquinolones, oral anticoagulants.

Contraindications: hypersensitivity to terizidone.

Side effects: Dizziness, slurred speech, convulsions, headache, tremor, insomnia, confusion, depression and altered behavior.

Dosage and administration: It is available as hard gelatine capsule of 250 mg each. The usual adult dose is 15 to 20 mg/kg per day in three to four divided doses. Maximum recommended dose is 4 capsules a day i.e 1 gm daily. The maximum daily dose is 15 to 20 mg/kg, the maximum dose being 750 mg. The daily dose can be divided into 250 mg in the morning and 500 mg in the evening.

8.1.10. Antileprotics

Leprosy (Hansen's disease) is a chronic disease caused by *Mycobacterium leprae*; it affects the peripheral nervous system, the skin, and some other tissues. It is transmitted from person to person when bacilli are shed from the nose and skin lesions of infected patients, but most individuals are naturally immune, and symptoms are suppressed. For treatment purposes patients may be classified as having paucibacillary (PB) or multibacillary (MB) leprosy. The 2 forms may be distinguished by skin smears, but facilities are not always available to process them and their reliability is often doubtful.

Drugs recommended are dapson, rifampicin and clofazimine.

A three drug regimen is recommended for multibacillary leprosy and a two drug regimen for paucibacillary leprosy. Any patient with a positive skin smear should be treated with the multidrug therapy regimen for MB leprosy. The regimen for PB leprosy should never be given to a patient with MB leprosy. If diagnosis in a particular patient is not possible the multi drug therapy regimen for MB leprosy must be used.

Multibacillary leprosy (3 drug regimen): Rifampicin: 600mg once-monthly, supervised (450mg for adults weighing less than 35kg).

Dapsone: 100mg daily, self administered (50mg daily or 1 - 2 mg/kg daily for adults weighing less than 35kg)

Clofazimine: 300mg once - monthly, supervised, and 50mg daily (or 100mg on alternate days), self-administered.

Multibacillary leprosy should be treated for at least one year. Treatment should be continued unchanged during both type I (reversal) and type II (erythema nodosum leprosum) reactions. During reversal reactions neuritic pain or weakness can herald the rapid onset of permanent nerve damage. Treatment with prednisolone (initially 40 to 60mg daily) should be instituted at once. Mild type II reactions may respond to aspirin or chloroquine. Severe type II reactions may require corticosteroids; thalidomide is also useful in men and post menopausal women who have become corticosteroid dependent, but it would be used under specialist supervision and it should never be used in women of child bearing potential (significant teratogenic risk). Increase doses of clofazimine 100mg 3 times daily for the first month with subsequent reductions, are also useful but may take 4 - 6 weeks to attain full effect.

Paucibacillary leprosy (2 - drug regimen):

Rifampicin: 600mg once - monthly, supervised (450mg for those weighing less than 35kg)

Dapsone: 100mg daily, self-administered (50mg daily or 1-2 mg/kg daily for adults weighing less than 35kg)

Paucibacillary leprosy should be treated for 6 months. If treatment is interrupted the regimen should be recommended where it was left off to complete the full course. *Neither the multibacillary nor the paucibacillary antileprosy regimen is sufficient to treat tuberculosis.*

Clofazimine

Capsule, 50mg, 100mg

Indications: multibacillary (MB) leprosy; type II lepra reactions.

Cautions: pre-existing gastrointestinal symptoms (reduce dose, increase dose interval or discontinue if symptoms develop during treatment); liver and renal impairment; pregnancy and breast-feeding; may discolour soft contact lenses.

Note: Patients should be warned that Clofazimine might cause a reddish - brown discolouration of skin, conjunctiva, tears, sputum, sweat, urine, and faces.

Side effects: reversible discoloration of skin, hair, cornea, conjunctiva, tears, sweat, sputum; symptoms including pain, nausea, vomiting and diarrhoea; severe mucosal and submucosal oedema with prolonged treatment with high doses - may be severe enough to cause sub acute small bowel obstruction.

Dose and Administration: Leprosy, see notes above

Lepromatous lepra reactions, dosage increased to 300mg daily for maximum of 3 months.

Dapsone

Tablet, 25mg, 50mg, 100mg

Injection, 20% in 50ml ampoule

Indications: paucibacillary (PB) and multibacillary (MB) leprosy (see notes above)

Cautions: cardiac or pulmonary disease; anaemia (treat severe anaemia before starting); G6PD deficiency (including breastfeeding affected infants); pregnancy; breast-feeding; porphyria.

Note: on long term treatment patients and their carers should be told how to recognize blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.

Drug interactions: rifamycins, amprenavir, and probenecid.

Contraindications: hypersensitivity to sulfones; severe anaemia.

Side effects: (dose-related and uncommon at doses used for leprosy), haemolysis, methaemoglobinaemia, neuropathy, allergic dermatitis (rarely including toxic epidermal necrolysis and Stevens-Johnson syndrome), anorexia, nausea, vomiting, tachycardia, headache, insomnia, psychosis, hepatitis, agranulocytosis; dapsone syndrome (rash with fever and eosinophilia)-discontinue immediately (may progress to exfoliative dermatitis, hepatitis, hypoalbuminaemia, psychosis and death)

Dose and Administration: *Leprosy:* 1 - 2mg/kg daily, see notes above

Storage: at room temperature, in a well - closed, light - resistant containers.

Rifampicin

Capsule, 150mg, 300mg, and 600mg

Indications: Paucibacillary leprosy; multibacillary leprosy; tuberculosis (section 7.1.3)

Cautions, Drug interactions, Side effects, Contraindications; see under section 7.1.3

Dose and Administrations: see notes above.

8.2. Antifungals

Fungal infections may be classified as superficial, affecting only the skin, hair, nail, or mucous membranes, or systemic, affecting the body as a whole; systemic infections tend to occur more frequently in immunocompromised individuals such as those with AIDS.

Drugs used in fungal infections:*Polyene antifungals:* The polyene antifungals include amphotericin and Nystatin; neither drug is absorbed when given by mouth. They are used for oral, oropharyngeal, and perioral infections by local application in the mouth. Nystatin is used principally for candida albicans infections of the skin and mucous membranes, including esophageal and intestinal candidiasis. Amphotericin B is active against most fungi and yeasts. It is the drug of choice for most serious systemic mycotic infections.

Imidazole Antifungals: among the imidazole antifungal, Ketoconazole is better absorbed by mouth than other imidazoles. It has been associated with fatal hepatotoxicity; prescribers should weigh the potential benefits of ketoconazole treatment against the risk of liver damage and should carefully monitor patients both clinically and biochemically. It should not be used for superficial fungal infections. Miconazole is grouped in imidazole antifungals. Miconazole can be used locally for oral infections; it is also effective in intestinal infections. Systemic absorption may follow use of miconazole oral gel and may result in significant drug interactions.

Triazole Antifungals: Fluconazole is very well absorbed after oral administration. It also achieves good penetration into the cerebrospinal fluid to treat fungal meningitis. Itraconazole is indicated for mucocutaneous candidiasis and in dermatomycoses unresponsive to conventional therapy. It is also used in the treatment of histoplasmosis, blastomycosis and invasive aspergillosis.

Other Antifungals: Griseofulvin is effective for widespread or intractable dermatophyte infections but has been superseded by newer antifungals, particularly for nail infections. It is usually well tolerated and is licensed for use in children. Duration of therapy is dependent on the site of the infection and may be

required for a number of months. Flucytosine is a synthetic fluorinated pyrimidine with a narrow spectrum of antifungal activity, particularly against *Cryptococcus* and *Candida* spp. In susceptible fungi, it is converted to fluorouracil by cytosine deaminase. Flucytosine is myelosuppressive and plasma concentrations above 75mcg/ml are associated with myelotoxicity.

Amphotericin B

Powder for injection, 10mg, 50mg in vial

Lozenges, 10mg

Indications: the drug of choice for most severe systemic mycoses such as disseminated candidiasis, cryptococcosis, mucormycosis, histoplasmosis, extracutaneous sporotrichosis and blastomycosis. Also used in leishmaniasis (see section 7.4.3)

Cautions: when given parenterally, toxicity common (*close supervision necessary and test dose required*); renal impairment; hepatic and renal function test, blood counts, and plasma electrolyte monitoring required; corticosteroids (avoid except to control reactions); pregnancy and breast-feeding; avoid rapid infusion (risk of arrhythmias).

Drug interactions: cardiac glycosides, ciclosporin, corticosteroids, tacrolimus.

Contraindications: hypersensitivity to amphotericin.

Side effects: when given parenterally, anorexia, nausea and vomiting, diarrhea, epigastric joint pain, anaemia; disturbances in renal function (including arrhythmias), blood disorders, neurological disorders (including hearing loss, diplopia, convulsions, peripheral neuropathy), abnormal liver function (discontinue treatment), rash, anaphylactoid reactions; pain and thrombophlebitis at injection site.

Dose and Administration: Adult:The dose and duration of therapy depend on the infecting organism. The daily dose must not exceed 1.5mg/kg. The following have been suggested.*Extrapulmonary cryptococcosis:IV infusion:* 0.7 mg/kg/day for 4-8 weeks.*Invasive candidiasis:IV infusion:* 0.6 mg/kg/day; duration of therapy should be 2 weeks after resolution of clinical features and candidaemia, but longer courses are recommended for neutropenic patients and endocarditis.

Candidaemia (in patients without neutropenia):IV infusion: 0.5-0.6mg/kg/day until at least 14 days after resolution of signs/last positive deep-site culture.

Mucormycosis or invasive aspergillosis: IV infusion: 1 to 1.5 mg/kg/day; total dose 2.5-3g.

Lozenges: Suck 1, slowly, 4 times daily; up to 8 times daily in severe conditions.

Clotrimazole

Powder, 1%

Mouth paint, 1%

Indications: fungal skin infections; vaginal candidiasis; otitis externa

Cautions: Pregnancy, contact with eyes and mucous membranes should be avoided.

Drug interactions: Benzodiazepines,calcium channel blockers, cisapride, cyclosporine, ergot derivatives, selected HMG-CoA reductase inhibitors, mesoridazole, mirtazapine, nateglinide, nefazodone, pimozone, quinidine, sildenafil, tacrolimus, thioridazine, venlafaxine,and other CYP3A4 substrates.

Contraindications: Hypersensitivity to clotrimazole or any component of the formulation.

Side-effects: Occasional local irritation and hypersensitivity reactions include mild burning sensation, erythema, and itching. Treatment should be discontinued if these are severe.

Dose and administration: Apply 2–3 times daily

Fluconazole

Capsule/tablet, 50mg, 100mg, and 200mg

Oral Suspension, 50mg /5ml, 200mg /5ml

Indications: vaginal and oropharyngeal candidiasis not responding to topical therapy; oesophageal and systemic candidiasis; cryptococcal meningitis and maintenance therapy to prevent relapse of cryptococcal disease in patients with AIDS.

Cautions: renal or hepatic impairment.

Drug interactions: enzyme-inducing agents (e.g rifampicin), hydrochlorthiazide, phenytoin, sulphonylureas, hypoglycemic agents, cyclosporin, nortriptyline, and zidovudine, terfenadine, oral anticoagulants and theophylline.

Contraindications:hypersensitivity to other azole antifungals.

Side effects: nausea, abdominal discomfort, diarrhoea, flatulence, headache, rash (discontinue treatment or monitor closely if infection invasive or systemic); less frequently dyspepsia, vomiting, taste disturbance, abnormalities of liver enzymes, angioedema, dizziness, seizures, alopecia, pruritus, toxic epidermal necrolysis, and Stevens Johnson syndrome reported, severe cutaneous reactions in AIDS patients also reported.

Dose and Administration: Adult: *Vaginal candidiasis:Oral:* 150mg as a single dose.*Oropharyngeal candidiasis:Oral:* 50-100mg daily for 7-14 days.

Oesophageal candidiasis:Oral: 100-200mg daily for 14-28 days.*Systemic candidiasis:Oral or IV:* 400mg daily.*Cryptococcal meningitis:Oral or IV:* 400mg daily for 8-10

weeks, prevention of relapse in patients with AIDS, 200mg daily. Child: *Oropharyngeal candidiasis*: Oral or IV: 3-6 mg/kg on the first day, then 3 mg/kg/day. *Systemic candidiasis, cryptococcal meningitis*: Oral or IV: 6-12mg/kg/day daily. *Prevention of fungal infections in immunocompromised patients following cytotoxic chemotherapy or radiotherapy*; 3 to 12 mg/kg/day, depending on extent and duration of neutropenia
Storage: store tablets and powder for oral suspension below 30°C. *Reconstituted suspension and fluconazole injection should be stored at 5°C - 30°C. Do not freeze reconstituted suspension or intravenous infusion.*

Fluconazole in Sodium Chloride

IV infusion 2mg+9mg/ml

See fluconazole above

Flucytosine

Capsule, 250mg, 500mg

IV infusion, 10 mg/ml

Solution for Injection, 2.5 g/250 ml

Indications: adjunct to amphotericin B (or fluconazole) in cryptococcal meningitis and in systemic candidosis.

Cautions: elderly, renal impairment, pregnancy and breast-feeding.

Drug interactions: amphotericin, cytarabine.

Contraindications: hypersensitivity to flucytosine.

Side effects: rash, nausea, vomiting, diarrhea, alterations in liver function tests; less frequently, confusion, hallucinations, convulsions, headache, sedation, vertigo, blood disorders including leukopenia, potentially fatal thrombocytopenia and aplastic anemia.

Dose and Administration: Adult and Child: *Systemic candidosis and cryptococcosis:* IV infusion: (over 20 - 40 minutes), 200 mg/kg daily in 4 divided doses, for usually no more than 7 days (at least 4 months in cryptococcal meningitis); extremely sensitive organisms, 100 - 150 mg/kg daily in 4 divided doses.

Systemic candidosis: initial treatment or after IV therapy, *Oral:* 50 - 150 mg/kg daily in 4 divided doses.

Storage: store in airtight containers and protect from light. I.V infusion should be stored between 18°C and 25°C.

Griseofulvin

Tablet, 125mg, 250mg, 500mg

Suspension, 125mg / 5ml

Indications: dermatophyte infections of the skin, scalp, hair and nail where topical therapy has failed or is inappropriate.

Cautions: rarely aggravation or precipitation of systemic lupus erythematosus; breast-feeding; griseofulvin may impaired the ability to drive or operate machinery, see also drug interaction.

Drug interactions: phenobarbitone, coumarin anticoagulants and oral contraceptives, aspirin.

Contraindications: patients with porphyria and liver failure, lupus erythematosus and related conditions, pregnancy (avoid pregnancy during and for 1 month after treatment, men should not father children with in 6 months of treatment).

Side effects: side effects are usually mild and transient and consist of headache, skin rashes, dryness of the mouth an altered sensation of taste, and gastro-intestinal disturbances; angioedema, erythemamultiforme, toxic epidermal necrolysis, proteinuria, leucopenia and other blood dyscrasias, candidaisis, paraesthesia, photosensitization, and severe headache have been reported occasionally. Depression, confusion, dizziness,

insomnia, and fatigue. Griseofulvin may precipitate or aggravate systemic lupus erythematosus.

Dose and Administration: Adult: *Oral:* 500mg daily, in divided doses or as a single dose, in severe infection dose may be doubled reducing when response occurs;

Child: 10mg/kg daily in divided doses or as a single dose.

Storage: at room temperature, in a tight container.

Itraconazole

Capsule, 100 mg, 200 mg

Oral solution, 10 mg/ml.

Indications: vulvovaginal, oropharangeal or oesophageal candidiasis and dermatomycoses, not responding to conventional therapy. Useful for endemic mycoses, e.g. histoplasmosis, and may be an effective alternative to amphotericin B for aspergillosis.

Cautions: hepatic disease.

Drug interactions: antacids, sucralfate, H₂-receptor antagonists (cimetidine), didanosine, carbamazepine, phenytoin, rifampicin, ciclosporin, cisapride, terfenadine, digoxin, indinavir, ritonavir, midazolam, triazolam, warfarin.

Contraindications: hypersensitivity to any azole antifungal.

Side effects: skin rash, gastrointestinal disturbances (nausea, diarrhea, abdominal pain, dyspepsia, vomiting, constipation, anorexia) and headache; transient increase in liver enzymes and rarely, hepatitis.

Dose and Administration: *Oral:* Adult: *Vulvovaginal candidiasis:* 200 mg morning and evening for 1 day.

Oropharyngeal candidiasis: 100 mg (200 mg in AIDS or neutropenia) daily for 15 days.

Oropharyngeal and Oesophageal candidiasis in HIV infection: solution: 200 mg daily (given as 1 or 2 doses) for 1 to 2 weeks;

solution held in the mouth before swallowing. Dose may be doubled in resistant cases.

Systemic mycoses: 200 - 400 mg daily in single or 2 divided doses.

Tinea Corporis, tinea cruris: 100 mg daily for 15 days.

Tinea pedis, tinea manuum: 100 mg daily for 30 days.

Storage: Capsule: store at room temperature; protect from light and moisture. Oral solution: store at $\leq 25^{\circ}\text{C}$; do not freeze.

Ketoconazole

Tablet, 200mg

Syrup, 20mg /5ml

Indications: in chronic mucocutaneous candidiasis, fungal infections of the gastro intestinal tract, and dermatophyte infections of the skin and fingernails. It is also used for the treatment of systemic blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, & aracoccidioidomycosis.

Cautions: during breast-feeding, in pediatrics and geriatrics, alchlorhydria, hypochlorhydria, alcoholism, renal function impairment

Drug interactions: antimuscarinic agents, antacids H_2 - receptors antagonists (*note: patients should be advised to take these medications at least 2 hours after taking ketoconazole*); rifampicin, isoniazid, phenytoin, astemizole, terfenadine, cisapride, corticosteroids, cyclosporin, oral anticoagulants, alcohol, oral contraceptives, tolbutamide, sucralfate, midazolam and triazolam, didanosin, digoxin and indinavir.

Contra indications: pre-existing liver disease, pregnancy; concurrent use of astemizole, cisapride and terfenadine with ketoconazole is contra indicated; hypersensitivity to azole antifungals

Side effects: gastro intestinal disturbance, gynaecomastia, impotence, menstrual irregularities, oligospermia, azoospermia, decreased male libido, liver toxicity, and adrenal cortex suppression.

Dose and Administration: *Oral:* Adult: Candidiasis, vulvovaginal: 200 to 400mg once a day for five days.

Carcinoma, prostatic: 400mg three times a day.

Cushing's syndrome: 600 mg to 1.2 grams a day.

Paronychia: 200 to 400 mg once a day.

Pityriasis versicolor: 200 mg once a day for five to ten days.

Pneumonia, fungal or septicemia, fungal: 400 mg to 1 gram once a day. For all other antifungal indications: 200 to 400 mg once a day.

Child: Candidiasis, vulvovaginal: Child 2 years of age and older: 5 to 10 mg per kg of body weight once a day for five days. Infants and Child up to 2 years of age: Dosage has not been established.

Paronychia or Penicillin marneffeii infection or pneumonia, fungal or septicemia, fungal: children 2 years of age and older: 5 to 10 mg per kg of bodyweight once a day.

Infants and Child up to 2 years of age: Dosage has not been established. For all antifungal indications: Child 2 years of age and older: 3.3 to 6.6 mg per kg of body weight once a day.

Note: Advise the patient to take the medication with food to increase absorption, and to avoid alcoholic beverages.

Storage: in a well-closed container at room temperature.

Miconazole

Tablet, 250 mg

Oral Gel, 25mg /ml

Intravenous infusion, 10 mg/ml in 20 ml

Indications: in the treatment of mucocutaneous candidiasis, dermatophytosis, and pityriasis versicolor.

Cautions: pregnancy and breast feeding; avoid in porphyria, haematocrit, haemoglobin and serum electrolytes and lipids should be monitored regularly; see also interactions.

Drug interactions: oral anticoagulants, sulphonylurea hypoglycaemic drugs, or phenytoin (miconazole enhance the activity of these drugs); amphotericin

Contraindications: hepatic impairment

Side effects: nausea, vomiting and diarrhea (usually on long-term treatment); rarely allergic reactions; isolated reports of hepatitis.

Dose and Administration:*Prevention and treatment of oral and intestinal fungal infections* 125 to 250 mg as tablet or 5 - 10 ml oral gel in the mouth after food 4 times daily, keep in oral cavity near lesions before swallowing; child under 2 years, 62.5mg as tablet or 2.5ml twice daily; 2 - 6 years 125mg of tablet or 5ml oral gel twice daily; over 6 years, 125mg of tablet or 5ml oral gel 4 times daily.*Systemic fungal infections:* Adult: *IV:* range from 0.2 to 1.2 g three times daily. Each dose must be diluted in at least 200 mL of sodium chloride 0.9% or glucose 5% and infused slowly over 30 to 60 minutes. Child: *IV:* 20 to 40 mg/kg body-weight daily (intravenously) but not more than 15 mg/kg of miconazole should be given at each infusion.

Storage: at room temperature.

Nystatin

Tablet, 500,000IU

Oral suspension, 100,000 units/ml

Indications: prophylaxis and treatment of candidiasis of skin and mucous membranes.

Side effects: nausea, vomiting, and diarrhea; Steven Johnson syndrome, irritation.

Dose and Administration: *Oral: Adult: intestinal candidiasis:* 500, 000 unit every 6 hours, doubled in severe infections;
Child: 100,000 units 4 times daily prophylaxis, 1 million units once daily Neonate: 100,000 units once daily.
Storage: at room temperature in a tight light resistant container.

Sertaconazole Nitrate

Skin cream, 2%

Indication: tinea pedis, tinea corporis, tinea cruris, tinea manuum, pityriasis (tinea) versicolor.

Cautions: elderly, breast feeding, children younger than 12 years of age.

Contraindications: hypersensitivity to sertaconazole nitrate, other imidazole derivatives, or any ingredient in the formulation

Side effects: contact dermatitis, dry skin, burning skin, application site reaction and skin tenderness.

Dose and Administration: Apply twice daily for 4 weeks, for topical use only.

Storage: store at room temperature

Terbinafine HCL

Tablet 125mg, 150mg, 250 mg

Indications: dermatophyte infections of the nails, ringworm infections (including tinea pedis, cruris, and corporis) where oral therapy appropriate (due to site, severity or extent)

Cautions: pregnancy; psoriasis (risk of exacerbation); autoimmune disease (risk of lupus-erythematosus-like effects)

Contraindications: hepatic impairment; breast feeding

Renal impairment: use half normal dose if eGFR less than 50 mL/minute/1.73 m² and no suitable alternative available.

Side effects: abdominal discomfort, anorexia, nausea, diarrhoea; headache; rash and urticaria occasionally with

arthralgia or myalgia; *less commonly* taste disturbance; *rarely* liver toxicity (including jaundice, cholestasis and hepatitis)—discontinue treatment, angioedema, dizziness, malaise, paraesthesia, hypoaesthesia, photosensitivity; *very rarely* psychiatric disturbances, blood disorders (including leucopenia and thrombocytopenia), lupus erythematosus-like effect, exacerbation of psoriasis, serious skin reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis)—discontinue treatment if progressive skin rash; also reported, pancreatitis, vasculitis, influenza-like symptoms, rhabdomyolysis, disturbances in smell.

Dose and administration: *By mouth:* 250 mg daily usually for 2–6 weeks in tinea pedis, 2–4 weeks in tinea cruris, 4 weeks in tinea corporis, 6 weeks–3 months in nail infections (occasionally longer in toenail infections); *child:* usually for 4 weeks, tinea capitis, over 1 year, body-weight 10–20 kg, 62.5 mg once daily; body-weight 20–40 kg, 125 mg once daily; body-weight over 40 kg, 250 mg once daily

8.3. Antivirals

8.3.1. Anti-Retroviral (ARV) Agents

Currently there are six categories of ARVs. Namely, nucleoside analogue reverse transcriptase inhibitors (NRTIs), non nucleoside analogue reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors (IIs), chemokine receptor 5 (CCR5) inhibitors and fusion inhibitors (FIs). Highly active antiretroviral therapy (HAART) is the use of a combination of three or more antiretrovirals to achieve durable suppression of replication.

As HIV mutates rapidly and there is a high viral turnover; inappropriate drug prescribing may cause rapid development of drug resistance.

Response to therapy may be measured virologically (by serial monitoring of viral load), immunological (by serial monitoring of CD4 or total lymphocyte count) or clinically. Viral load monitoring is the only way to detect the emergence of resistance.

The Ethiopian national ARV guideline (*see the latest guideline*) suggests that treatment should be commenced in a symptomatic HIV-positive patient (WHO stage 3 or 4) or in patients with a CD4 count of < 300 cells/mm³. It can be also initiated in stage II when the total lymphocyte count drops below 1200/mm³ in settings where there is no CD4 count.

In Ethiopia, HIV regimens are classified as first line (preferred and alternative) and second line regimens. The first line regimens consist of either the loose ARVs or fixed dose combinations (FDCs) of two NRTIs and an NNRTI (either NVP or EFV). The second line regimens are used in circumstances when there is treatment failure which consisted use of either loose compounds or FDCs of two or three NRTIs and a protease inhibitor (PI).

Post Exposure prophylaxis (PEP): To be effective treatment has to commence as soon as possible (within 1 to 2 hours, post-exposure). However, the maximum delay for initiation of treatment, which would prevent infection, is not known in humans. Do not consider PEP beyond 72 hours post exposure. Prophylaxis is to be given for 28 days.

Mother to Child Transmission (MTCT): ARVs prevent transmission of HIV from mother to infant. Several antiretroviral regimens using zidovudine, zidovudine plus lamivudine, nevirapine, or HAART showed to reduce perinatal transmission. There are three circumstances for ARV drugs during pregnancy. These include Women who become pregnant while on ART, Pregnant women eligible for ART and Pregnant

women not eligible for ART. The first scenario the mother should continue the regimens unless there is a need for substituting EVZ with NVP, in case of second scenario the mother should put on ART according to clinical setting and in case of the third scenario the mother should put on PMTCT according to the national PMTCT guideline. In all the three clinical scenarios for the use of ARVs in pregnant mothers, ARV prophylaxis should be administered to the newborn, based on the national PMTCT guidelines.

Nucleoside Reverse Transcriptase Inhibitors

Nucleoside reverse transcriptase inhibitors (NRTIs) are nucleoside analogues, which act as false substrates for reverse transcriptase and terminate the DNA chain. Currently available NRTIs are abacavir (ABC), didanosine (ddI), lamivudine (3TC), zalcitabine (ddc) and zidovudine (AZT or ZDV), emtricitabine (FTC) and tenofovir (TDF).

Regimens: Dual NRTI is the conventional backbone of triple therapy. Selection of a dual NRTI combination must avoid cross-resistance and antagonism. According to national ARV guideline combinations.

Start one of the following regimens in ART-naive individuals eligible for treatment. AZT + 3TC + EFV; AZT + 3TC + NVP; TDF + 3TC (or FTC) + EFV; TDF + 3TC (or FTC) + NVP (*Strong recommendation, moderate quality of evidence*). Certain dual NRTI backbone combinations should not be used in three-drug therapy. These are d4T + AZT (proven antagonism), d4T + ddI (overlapping toxicities) and 3TC + FTC (interchangeable, but should not be used together).

Preferred first-line ART in treatment-naive adults and adolescents: Adults and adolescents: AZT or TDF + 3TC or FTC + EFV or NVP. Pregnant women: AZT + 3TC + EFV or NVP.

8. Anti-Infectives

HIV/TB coinfection: AZT or TDF + 3TC or FTC + EFV.

HIV/HBV coinfection: TDF + 3TC or FTC + EFV or NVP.

Alternatives: TDF+3TC+NVP, d4T+3TC+EFV,

ABC+3TC+NVP, ABC+3TC+EFV and ABC+3TC+ZDV i.e combination of two NRTI and an NNRTI;

Preferred second-line ART options Preferred options

Adults and adolescents (including pregnant women): If d4T or AZT used in first-line therapy TDF + 3TC or FTC + ATV/r or LPVr. If TDF used in first-line therapy AZT + 3TC + ATV/r or LPVr.

Hepatitis B coinfection: AZT + TDF + 3TC or FTC + ATV/r or LPVr.

Abacavir (ABC)

Tablets, 60mg, 300mg (as sulphate)

Oral liquid 20mg/ml

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: hepatic and renal impairment, pregnancy, breastfeeding.

Drug interactions: the potential for clinically significant drug interactions is low.

Contraindications: prior hypersensitivity to the drug

Side effects: hypersensitivity reactions, nausea, vomiting, diarrhoea, anorexia, lethargy, fatigue, fever, headache, pancreatitis, lactic acidosis

Dose and Administration: *Oral:* Adult: 300mg 12 hourly; Child: 3 months - 16 years, 8mg/kg twice daily

Storage: store at room temperature.

Didanosine (DDI, ddI)

Tablet, 25mg, 150mg

Chewable / dispersible tablet, 100mg,

capsule (delayed release) 125mg, 200mg, 250mg, 400mg

Indications: treatment of HIV infection, in combination with at least two other antiretroviral drugs

Cautions: peripheral neuropathy or hyperuricaemia; renal and hepatic impairment; pregnancy and breast-feeding; dilated retinal examinations recommended every 6 months, or if visual changes occur.

Drug interactions: drugs in which absorption is impaired by increased gastric pH, e.g. fluoroquinolones, some protease inhibitors, dapson: take at least 2 hours before or 2 hours after didanosine.

Contraindications: history of pancreatitis, alcoholism; conditions requiring sodium restriction.

Side effects: pancreatitis, peripheral neuropathy especially in advanced HIV infection suspend (reduced dose may be tolerated when symptoms resolve), lactic acidosis hyperuricaemia (suspend treatment if significant elevation), diarrhea; nausea, vomiting, dry mouth, asthenia, headache, hypersensitivity reactions, retinal and optic nerve changes (especially in children), diabetes mellitus, raised liver enzymes, liver failure.

Dose and Administration: Adult: *Oral:* ≥ 60 kg, 200 mg 12 hourly or 400 mg daily; < 60 kg, 125 mg 12 hourly or 250 mg daily. **Child:** *Oral:* 240 mg/m² daily or 120 mg/m² 12 hourly. *Note: Half hour pre-meals or 1 hour after meal.*

Storage: store at room temperature

Emtricitabine (FTC)

Capsule, 200mg

Indications: Treatment of HIV infection in combination with at least two other antiretroviral agents.

Cautions: lactic acidosis, severe hepatomegaly, hepatic failure, renal impairment.

Drug interactions: concomitant use of nucleoside analogues.

Contraindications: hypersensitivity to emitricitabine.

Side effects: headache, dizziness, insomnia, rash, diarrhea, nausea, abdominal pain, skeletal weakness, cough, rhinitis.

Dose and Administration:*Oral:* Adult: 200mg once daily.

Storage: store at room temperature.

Lamivudine (3TC)

Tablet, 150mg

Oral solution, 10mg/ml

Indications: HIV infection; reduction of perinatal transmission of HIV; post - exposure prophylaxis; only in combination with other antiretrovirals. Chronic hepatitis B infection (*off-label use*).

Cautions: renal impairment, hepatic disease, pregnancy and breastfeeding.

Drug interactions: co-trimoxazole, trimethoprim component of co- trimoxazole.

Contraindications:significant anaemia or neutropenia, known hypersensitivity to the drug.

Side effects: nausea, vomiting, diarrhoea, abdominal pain, cough; headache, insomnia, malaise, fever, rash, alopecia, muscle disorders, nasal symptoms; peripheral neuropathy; rarely pancreatitis (discontinue); neutropenia, anaemia and thrombocytopenia; lactic acidosis; raised liver enzymes and serum amylase reported.

Dose and Administration: *Oral:* Adult: 150 mg 12 hourly; < 50 kg, 2 mg/kg 12 hourly.*Chronic hepatitis B infection:* 100-150mg once daily. In patients with concomitant HIV infection, use the dose for HIV treatment.**Child:** 3 months-12 years: 4 mg/kg (maximum 150mg) twice daily. Neonates < 30 days old: 2 mg/kg twice daily.

Storage: store at 2 - 25 °C temperature

Stavudine (d4T)

Capsules, 15mg, 20mg, 30mg

Powder for oral solution, 1mg/mL

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: peripheral neuropathy and pancreatitis or concomitant use with other drugs associated with pancreatitis; hepatic disease, renal impairment, pregnancy and breastfeeding.

Drug interactions: zidovudine, didanosine, zalcitabine, dapson, ethambutol, ethionamide and isoniazid, pentamidine, valproate.

Side effects: Cumulative exposure to d4T has the potential to cause disfiguring, painful and lifethreatening side-effects, such as lipodystrophy, peripheral neuropathy and lactic acidosis., pancreatitis, headache, gastrointestinal intolerance (diarrhoea, nausea, anorexia), neutropenia, thrombocytopenia, myalgia, elevated liver enzymes.

Dose and Administration: *Oral:* Adult: >60kg, 40mg 12 hourly; <60kg, 30mg 12 hourly. Renal impairment: creatinine clearance 26-50ml/min, half dose 12 hourly; creatinine clearance <25 ml/min, half dose 24 hourly. **Child:** > 3 months and ≤ 30kg, 1mg/kg 12 hourly; > 30 kg, as for adults.

Storage: store capsules and powder for oral solution at room temperature. Following reconstitution, oral solution should be stored at 2-8°C for up to 30 days.

Zalcitabine (ddC, DDC)

Tablet, 375 mcg, 750mcg

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: peripheral neuropathy, history of pancreatitis; known hypersensitivity to the drug.

Drug interactions: aminoglycosides, amphotericin B and foscarnet; antacids, cimetidine, didanosine, drugs associated with peripheral neuropathy (e.g. stavudine, chloramphenicol); drugs associated with pancreatitis (e.g. alcohol), metoclopramide, probenecid.

Side effects: these tend to be dose related and may be difficult to distinguish from the underlying disease. They tend to be more frequent and severe in advanced disease. Dose-related peripheral neuropathy, oral ulcers, pancreatitis, hepatitis, arthralgia and gastrointestinal disturbances. Pharyngitis, headache, dizziness, rash, pruritus, weight loss, fatigue, chest pain, leucopenia, thrombocytopenia, rigors and sweating
Oesophageal ulcers, hypersensitivity reactions

Dose and Administration: Adult: *Oral:* 0.75mg 8 hourly.

Storage: store at room temperature.

Zidovudine / Azidothymidine (ZDV, AZT,)

Tablets, 300 mg

Capsules, 100 mg, 250 mg

Syrup, 50 mg/5ml

IV infusion, 10 mg/ml

Indications: HIV infection; reduction of perinatal transmission of HIV; Post-exposure prophylaxis. Usually in combination with other antiretrovirals.

Cautions: haematological toxicity; vitamin B12 deficiency (increased risk of neutropenia); reduce dose or interrupt treatment according to product literature if anaemia or myelosuppression, renal impairment; hepatic impairment; risk of lactic acidosis.

Drug interactions: ganciclovir, myelosuppressive agents, probenecid.

Contraindications: abnormally low neutrophile counts or haemoglobin; neonates either with hyperbilirubinaemia

requiring treatment other than phototherapy or with raised transaminase.

Side effects: haematological effects include anaemia and leucopenia or neutropenia. Platelet count may rise initially after starting therapy. Nausea, headache, myalgia, insomnia, and rarely, myopathy, lactic acidosis, seizures, confusion, mania, and hepatotoxicity.

Dose and Administration:Adult:Oral: 300 mg 12 hourly, Dose may be reduced to 250 mg 12 hourly if needed.*IV infusion:* over 1 hour, 1-2 mg/kg 4 hourly, in 5% glucose to give a zidovudine concentration 2 or 4 mg/ml. The IV route is used only until oral therapy can be given.*PMTCT:*

Adult: Oral: 300mg 12 hourly for at least the last 4 weeks of pregnancy; from onset of labour to delivery, 300 mg 3 hourly.

Child:Oral: 3 months - 12years, 180 mg/m² 12 hourly; maximum800mg/day

Neonates: for prevention of MTCT, initiated within 12 hours of birth and given for the first 6 week of life: *Oral:* 2 mg/kg 6 hourly,*IV:* 1-5 mg/kg 8 hourly

Premature infants: *Oral:* 1.5 mg/kg 12 hourly for 2 weeks, then mg/kg 6 hourly. IV, as for term infants

Storage: store at room temperature.

Tenofovir (TDF)

Tablet, 300mg

Indications:treatment of HIV infection, in combination with other antiretrovirals.

Cautions:co-infection with hepatitis B (severe acute exacerbation of hepatitis reported on discontinuation); renal impairment, porphyria.

Drug interactions: didanosine, drugs that reduce renal function or compete for active tubular secretion (aciclovir, valaciclovir, ganciclovir), lopinavir-ritonavir, other nephrotoxic agents.

Side effects: mild to moderate gastrointestinal effects, such as nausea, diarrhoea, vomiting and flatulence. Tenofovir is nephrotoxic and cause renal impairment (including acute renal failure), proteinuria and Fanconi syndrome (renal tubular injury with severe hypophosphataemia). Reduction in bone mineral density may occur. Rare – hypersensitivity reactions; hyperlactataemia and hepatic steatosis.

Dose and Administration: Adult: *Oral:* 300 mg once daily. Renal impairment: Increase dose interval. Creatinine clearance 30 – 50 ml/min, 48 hours; 10 – 30 ml/min, twice weekly; < 10 ml/min, not recommended

Non - Nucleoside Reverse Transcriptase Inhibitors

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) inhibit reverse transcriptase enzyme activity directly. They potently suppress HIV replication. High-level resistance develops rapidly and they must always be used in combination, usually with 2NRTIs. Cross-resistance within the class occurs. Hypersensitivity rashes are common. Currently available NNRTIs include nevirapine and efavirenz.

Efavirenz (EFV, EFZ)

Tablet, 50mg, 200mg, 600mg

Capsules, 50mg, 100mg, 200mg

Tablet for oral suspension, 100mg

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: hepatic and renal impairment, breast feeding, elderly; history of mental illness or substance abuse.

Drug interactions: efavirenz may either induce or inhibit metabolism of other hepatically metabolised drugs. Cisapride, midazolam, triazolam, ergot alkaloids, terfenadine, rifampicin, phenytoin, carbamazepine, phenobarbitol, warfarin, protease inhibitors, oral contraceptives.

Contraindications: pregnancy (teratogenic); substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured.

Side effects: rash including Stevens Johnson Syndrome, dizziness, headache, insomnia, somnolence, abnormal dreams, fatigue, impaired concentration (administration at bed time in the first 2 - 4 weeks reduces CNS effects); nausea; less frequently vomiting, diarrhoea, hepatitis, depression, anxiety, psychosis, amnesia, ataxia, stupor, vertigo; raised serum cholesterol, elevated liver enzymes (especially if seropositive for hepatitis B or C), pancreatitis.

Dose and Administration:*Oral: Adult:* 600mg once daily as a single dose at night.**Child:** administered once daily, preferably at bedtime: over 40kg, 600mg; 32.5 - 40kg, 400mg; 25-32.5kg, 350mg; 20 - 25kg, 300mg; 15-20kg, 250mg; 13-15kg, 200mg.*Not recommended for children under 3 years or under 13kg.*

Storage: store at room temperature.

Nevirapine (NVP)

Tablet, 200 mg

Suspension, 50 mg/5ml

Indications: treatment of HIV infection, in combination with other antiretrovirals; reduction of perinatal transmission of HIV in combination with other ARVs.

Cautions: hepatic and renal impairment.

Drug interactions: oral contraceptives; rifampicin and rifabutin; protease inhibitors.

Contraindications: hypersensitivity to the drug.

Side effects: rash including Stevens-Johnson syndrome and rarely, toxic epidermal necrolysis, hepatitis or jaundice reported; nausea, vomiting, abdominal pain, diarrhoea, headache, drowsiness, fatigue, fever; hypersensitivity reactions; anaphylaxis, angioedema, urticaria also reported.

Dose and Administration:*Oral:* Adult: 200 mg daily for 14 days followed by 200 mg 12 hourly.

PMTCT: 200 mg to the mother at the onset of labour; 2 mg/kg to the infant within 72 hours.**Child:** 2 months - 8 years, 4mg/kg once daily for 2 weeks, then 7mg/kg twice daily; \geq 8 years, 4mg/kg once daily for 2 weeks, then 4mg/kg twice daily. Maximum 400mg/day.

Storage: store at room temperature.

Protease Inhibitors

Protease inhibitors inhibit the HIV protease enzyme. Inhibition of this enzyme prevents cleavage of viral polyproteins, and results in immature, non-infectious HIV viral particles.

Protease inhibitors cause potent suppression of HIV replication. They must always be used in combination, and they are reserved for second-line therapy if the initial treatment regimen of 2 NRTIs + 1NNRTI fails. Currently available protease inhibitors include amprenavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir. There is cross-resistance between some of these. They undergo hepatic cytochrome P450 metabolism and some, especially ritonavir, are potent hepatic enzyme inhibitors. This is exploited therapeutically by using subtherapeutic doses of ritonavir to reduce metabolism of other protease inhibitors, allowing the use of lower doses and/or increased dosing intervals. Drug interactions are common.

Lipodystrophy and metabolic disorders

Abnormal fat distribution, with increased abdominal girth, dorsocervical fat deposition, breast enlargement and peripheral fat wasting (lipo-atrophy) has been associated with HAART. The protease inhibitors are most strongly associated with fat accumulation. Protease inhibitors may also cause metabolic abnormalities, such as hypercholesterolaemia, hypertriglyceridaemia and insulin resistance. These may occur with or without lipodystrophy.

Atazanavir

Tablet/capsule, 100mg, 150mg, 200mg, 300mg

Indications: treatment of HIV-1 infections in combination with at least two other antiretroviral agents.

Note: In patients with prior virologic failure, coadministration with ritonavir is recommended.

Cautions: patients with pre-existing conduction abnormalities or with medications which prolong AV conduction; hepatic dysfunction.

Drug interactions: cisapride, ergot derivatives, sildenafil, antiarrhythmics, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, protease inhibitors, quinidine, verapamil.

Contraindications: do not use in children <3 months of age due to potential for kernicterus; hypersensitivity to atazanavir.

Side effects: hyperglycemia, facial atrophy, breast enlargement, rash, nausea, depression, dizziness, fatigue, fever, headache, insomnia, pain, peripheral neuropathy, lipodystrophy, vomiting, diarrhea, jaundice, myalgia.

Dose and Administration: *Oral:* Adult: *Antiretroviral-naïve patients:* 400mg once daily; administer with food

Antiretroviral-experienced patients: 300mg once daily plus ritonavir 100mg once daily; administer with food

Coadministration with efavirenz: Antiretroviral-naïve patients: it is recommended that atazanavir 300mg plus ritonavir 100mg be given with efavirenz 600mg (all as a single daily dose); administer with food. *Antiretroviral-experienced patients:* recommendations have not been established.

Indinavir (IDV)

Capsule, 200mg, 400mg

Indications: treatment of HIV infection, in combination with two Nucleoside reverse transcriptase inhibitors and usually with low-dose ritonavir booster.

Cautions: hepatic impairment; ensure adequate hydration to reduce risk of nephrolithiasis; diabetes mellitus; haemophilia; pregnancy; breast feeding, metabolism of many drugs inhibited if administered concomitantly.

Drug interactions: carbamazepine, dexamethasone, efavirenz, ergotamine, nelfinavir, nevirapine, Phenobarbital, phenytoin, rifampicin, ritonavir, saquinavir.

Side effects: nephrolithiasis, unconjugated hyperbilirubinaemia, lipodystrophy, hypercholesterolaemia, hypertriglyceridaemia and insulin resistance. Nausea, vomiting, diarrhoea, hair loss, dry skin and skin rashes may occur. Allergic reactions include anaphylaxis, erythema multiforme and Stevens – Johnson syndrome. Acute haemolytic anemia and decreased neutrophil counts have been reported.

Dose and Administration: *Oral:* Adult: 800 mg 8 hourly, 1 hour before or 2 hours after a meal; alternatively indinavir 800 mg plus ritonavir 100 -200 mg 12 hourly (independent of meals). Child: 4-17 years, 500 mg/m² (maximum 800 mg) 8 hourly.

Note. Administer 1 hour before or 2 hours after a meal; may be administered with low-fat, light meal; when given with didanosine

tablets, allow 1 hour between the drugs (antacids in didanosine reduce absorption of indinavir)

Storage: store at room temperature and in a tight container.

Nelfinavir (NFV)

Tablet, 250 mg

Oral powder, 50 mg/g

Indications: HIV infection in combination with two other antiretroviral drugs.

Cautions: hepatic and renal impairment; diabetes mellitus; haemophilia.

Drug interactions: carbamazepin, contraceptives, ergotamine, phenobarbital, quinidine, ritonavir, saquinavir.

Side effects: diarrhoea, nausea, vomiting, flatulence, abdominal pain; rash, reports of elevated creatine kinase, hepatitis, pancreatitis, neutropenia, hypersensitivity reactions including bronchospasm, fever, pruritus and facial oedema, lipodystrophy and metabolic effects.

Dose and Administration: *Oral:* Adult: 1.25g twice daily or 750mg 3 times daily. **Child:** under 1 year, 40 - 50mg/kg 3 times daily or 65 - 75mg/kg twice daily; 1-13 years, 55 - 65 mg/kg twice daily.

Note: Administer with or after food, powder may be mixed with water, milk, formula feeds or pudding; it should not be mixed with acidic foods or juices owing to its taste.

Storage: store at room temperature and in tight containers.

Ritonavir (RTV)

Capsule, 100 mg

Oral Solution, 80 mg/ml

Indications: treatment of HIV infection and as a booster to increase effect of indinavir, lopinavir or saquinavir and in combination with two other antiretroviral drugs.

Cautions: hepatic impairment; diabetes mellitus; haemophilia.

Drug interactions: amiodarone, cisapride, clozapine, dextro-propoxyphene, pethidine, pimoziide, quinidine and terfenadine; ergot alkaloids and derivatives; sedatives and hypnotics; HMG CoA reductase inhibitors; rifabutin; anticonvulsants; ketoconazole, macrolides; oral contraceptives; protease inhibitors.

Contraindications: severe hepatic impairment.

Side effects: gastrointestinal intolerance (nausea, vomiting and diarrhoea), vasodilation, orthostatic hypotension and syncope, hypertriglyceridaemia, pancreatitis, lipodystrophy, dyspepsia, oral ulceration, dry mouth, hyperaesthesia, hypersensitivity reactions, including anaphylaxis.

Dose and Administration:*Oral:* Adult: 600 mg 12 hourly. Gradual dose escalation may provide relief if nausea occurs or initiation: 300mg 12 hourly for 1 day, 400mg 12 hourly for 2 days, 500mg 12 hourly for 1 day, then 600mg 12 hourly. **Child:** Over 2 years, initially (to minimise nausea) 250mg/m² 12 hourly, increased gradually over a week to 350mg/m² 12 hourly upto a maximum of 600mg 12 hourly. As a booster with other antiretroviral drugs: Adult: 100 mg twice daily.

Child 6 months: 13 years: 57.5 mg/m² twice daily (or 3 to 5 mg/kg twice daily) (maximum 100 mg twice daily).

Storage: liquid-filled capsules should be stored at 2 - 8 °C but may be stored at a temperature lower than 25 °C for up to 30 days. Store oral solution at room temperature

Saquinavir (SQV)

Tablet, 500 mg

Capsule, 200 mg

Oral solution, 80mg/ml

Indications: HIV infection in combination with two other antiretroviral drugs and usually with low - dose ritonavir booster.

Cautions: hepatic and renal impairment; diabetes mellitus, haemophilia, pregnancy and breastfeeding.

Drug interactions: indinavir, nevirapine, phenobarbital, phenytoin, rifampicin, ritonavir.

Contraindications: hypersensitivity to the drug.

Side effects: diarrhoea, buccal and mucosal ulceration, abdominal discomfort, nausea, vomiting; headache, peripheral neuropathy, paraesthesia, dizziness, insomnia, mood changes, ataxia, musculoskeletal pain, asthenia; fever, pruritus, rash and other skin eruptions, rarely Stevens - Johnson syndrome; other rare adverse effects include thrombocytopenia and other blood disorders, seizures, liver damage, pancreatitis and nephrolithiasis; reports of elevated creatine kinase, raised liver enzymes and neutropenia when used in combination therapy; lipodystrophy and metabolic effects.

Dose and Administration: Adult: Oral: in combination with nucleoside reverse transcriptase inhibitors and low-dose ritonavir booster: saquinavir 1g and ritonavir 100 mg twice daily. In combination with other antiretroviral drugs but without ritonavir booster): 1.2g every 8 hours after a meal. **Child under 16 years**, safety and efficacy not established.

Note: Administer with or after food.

Storage: saquinavir liquid-filled capsules should be stored at 2 - 8 °C in airtight container but may be stored at a temperature lower than 25 °C for upto 3 months. For tablets store at room temperature

Darunavir

Tablet (f/c), 300mg

Indications: co-administered with ritonavir, and with other antiretroviral agents, is indicated for the treatment of HIV infection in antiretroviral treatment-experienced adult patients, such as those with HIV-1 strains resistant to more than one protease inhibitor.

Cautions: sulfonamide sensitivity; monitor liver function before and during treatment, hepatic impairment, pregnancy, breast-feeding.

Drug interactions: Abacavir, bromazepam, clarithromycin, dantrolene, lidocaine, lopinavir, lovastatin, saquinavir, tacrolimus, tadalafil, tamoxifen, tamsulosin, telithromycin, temsirolimus, teniposide, tiagabine, tolterodine, topotecan, tramadol, trazodone, trimipramine, vardenafil, venlafaxine, verapamil, vinblastine, vincristine, voriconazole, zolpidem, zonisamide, zopiclone.

Contraindications: Allergy to darunavir, ritonavir, sulfa medications, or any of the ingredients in darunavir.

Side effects: haematemesis, myocardial infarction, angina, QT interval prolongation, syncope, bradycardia, tachycardia, palpitation, hypertension, flushing, peripheral oedema, dyspnoea, cough, peripheral neuropathy, anxiety, confusion, memory impairment, depression, abnormal dreams, convulsions, increased appetite, weight changes, pyrexia, hypothyroidism, osteoporosis, gynaecomastia, erectile dysfunction, reduced libido, dysuria, polyuria, nephrolithiasis, renal failure, arthralgia, visual disturbances, dry eyes, conjunctival hyperaemia, rhinorrhoea, throat irritation, dry mouth, stomatitis, nail discoloration, acne, seborrhoeic dermatitis, eczema, increased sweating, alopecia

Dose and Administration: With low-dose ritonavir, adult and child over 6 years, body-weight over 40 kg, previously treated with antiretroviral therapy, 600 mg twice daily; child over 6 years, previously treated with antiretroviral therapy, body-weight 20–30 kg, 375 mg twice daily; body-weight 30–40 kg, 450 mg twice daily

With low-dose ritonavir, adult over 18 years not previously treated with antiretroviral therapy, 800 mg once daily. *Missed dose: If a dose is more than 6 hours late on the twice daily regimen (or more than 12 hours late on the once daily regimen), the missed dose should not be taken and the next dose should be taken at the normal time*

Storage: store at room temperature and in a tight container.

Integrase Inhibitor

Raltegravir

Tablet, 400mg

Indications: in combination with other antiretroviral drugs for HIV infection resistant to multiple antiretrovirals

Cautions: risk factors for myopathy or rhabdomyolysis; chronic hepatitis B or C (greater risk of hepatic side effects); hepatic impairment; pregnancy;

Drug Interactions: histamine H₂-antagonists, proton pump inhibitors, rifampicin

Contraindications: breast-feeding

Side effects: abdominal pain, flatulence, constipation, lipodystrophy; dizziness, asthenia; arthralgia; pruritus, hyperhidrosis; less commonly vomiting, gastritis, hepatitis, myocardial infarction, hypertriglyceridaemia, allodynia, headache, renal failure, anaemia, neutropenia, and muscle spasm

Dose and administration: adult and child over 16 years, 400 mg twice daily

Combination ARVs:

Lamivudine + Nevirapine +Stavudine

Tablet, 150mg +200mg + 30mg; 30mg+50mg+6mg; 60mg+100mg+12mg

Indications: for the treatment of HIV infection, once patients have been stabilized on the maintenance regimen of nevirapine 200 mg bid, and have demonstrated adequate tolerability to nevirapine.

Cautions: it should not be administered to patients who have just initiated therapy with nevirapine. This is because an initial lead-in dosing of 200 mg nevirapine once daily for 2 weeks is recommended. Following this lead-in dose, a dose escalation (maintenance dose) to 200 mg nevirapine bid may be carried out in the absence of any hypersensitivity reactions.

Dose and Administration: Adult:200mg+150mg+30mg:1 tablet twice daily for patients weighing <60 kg; 200mg + 150mg + 40mg: 1 tablet twice daily for patients weighing >60 kg

Lamivudine +Zidovudine + Nevirapine

Tablet, 150mg +300mg +200mg; 30mg +60mg +50mg

Indications: treatment of HIV infection, once patients have been stabilized on the maintenance regimen of nevirapine 200mg bid, and have demonstrated adequate tolerability to nevirapine.

Cautions, Drug Interactions, Contraindications and side effects: see under Lamivudine, Zidovudine and Nevirapine

Dose and Administration: Adult: Tablet, 150mg +300mg +200mg (one tablet twice daily)

Note:Lamivudine +Zidovudine + Nevirapine Tablets, 150mg +300mg +200mg should not be administered to patients who have

just initiated therapy with nevirapine. This is because an initial lead-in dosing of 200mg nevirapine once daily for 2 weeks, along with the standard doses of lamivudine + zidovudine twice daily is recommended. Following this lead-in dose, a dose escalation (maintenance dose) to Lamivudine + Zidovudine + Nevirapine Tablets, 150mg +300mg +200mg twice daily may be carried out in the absence of any hypersensitivity reactions. Patients who interrupt nevirapine dosing for more than 7 days should restart the recommended dosing, using one 200mg nevirapine tablet daily for the first 14 days (lead-in) in combination with the other lamivudine + zidovudine, followed by Lamivudine + Zidovudine + Nevirapine Tablets, 150mg +300mg +200mg twice daily in the absence of any signs of hypersensitivity.

Abacavir sulphate + Lamivudine + Zidovudine

Tablet, 60mg+30mg+60mg

Indications: It is indicated in combination with other antiretrovirals or alone for the treatment of HIV-1 infection.

Contraindications: Previously hypersensitivity to abacavir or any other component of the product.

Dose and Administration: Children 6 weeks of age and above: Children weighing 25 kg or more, adolescents and adults: For these patient groups other fixed-dose formulations with higher amounts of the active substances are available.

Number of tablets by weight to be taken twice daily (12 hourly)				
3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg
1	1.5 ⁺	2	2.5 [*]	3

⁺ *This dose can be delivered as one and a half tablets twice daily, or by giving 2 tablets in the morning and one tablet in the evening. This dose can be delivered as two and a half tablets twice daily, or by giving 3 tablets in the morning and 2 tablets in the evening.*

Tenofovir +Lamivudine

Tablet, 300mg +300mg

Indications: in combination with other antiretrovirals for the treatment of HIV-1 infection,

Cautions, Drug Interactions, Contraindications and side effects: see under Tenofovir and Lamivudine

Dose and Administration: one tablet once daily taken orally with or without food.

Storage: Store in cool dry place

Lamivudine+ Zidovudine (Combivir)

Tablets, 150mg+ 300mg, 30mg+60mg

Cautions, contraindications and side effects: see individual drugs

Dose and Administration:Adult and Child >12 years: *Oral:* one tablet twice daily.

Lamivudine +Stavudine

Tablet, 150mg +30mg

Indications: treatment of HIV infection as a component of combination antiretroviral therapy.

Cautions, Drug Interactions, Contraindications and side effects: see under lamivudine and stavudine

Dose and Administration: Adult: 1 tablet two times a day

Efavirenz +Emitricitabine + Tenofovir

Tablet, 600mg +200mg +300mg

Indications: alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

Cautions, Drug Interactions, Contraindications and side effects: see under Efavirenz, Emitricitabine and Tenofovir

Dose and Administration: Adult: one tablet on an empty stomach, preferably at bed time

Emtricitabine + Tenofovir

Tablet, 200mg + 300mg

Indications: Treatment of HIV infection in combination with other antiretroviral agents.

Cautions, contraindications and side effects see individual drugs

Dose and Administration:*Oral:* Adult: one tablet (emtricitabine 200mg and tenofovir 300mg) once daily.

Abacavir sulphate +Lamivudine

Tablet, 600mg+300mg,

Indications: Treatment of HIV infection in combination with other antiretroviral agents.

Caution: pregnancy

Contraindications: because dosage of abacavir and lamivudine cannot be adjusted individually, the fixed-combination preparation should not be used in pediatric patients.

Dose and Administration:*Oral:* 600mg/300mg once daily

Storage: store at room temperature.

Lopinavir +Ritonavir

Capsule, 133.33mg +33.33mg

Oral suspension, 80mg +20mg/ml

Tablet, 200mg +50mg; 100mg +25mg

Indications: treatment of HIV-1 infection in combination with other antiretroviral agents.

Cautions, Drug Interactions, Contraindications and side effects: see under lopinavir and ritonavir.

8. Anti-Infectives

Dose and Administration: Adult: two 200/50 mg tablets twice daily taken with or without food or 800mg + 200mg once daily.

Note: once daily dosing is recommended only for treatment-naive adults. Lopinavir/ritonavir should not be administered once-daily in regimens that include efavirenz, nevirapine, amprenavir, fosamprenavir, or nelfinavir

Age or Weight	Oral Solution (80 mg lopinavir/ 20 mg ritonavir per ml)	Tablets (100mg lopinavir/25mg ritonavir)
Age 14 days to 6 months	16/4 mg/kg BID, or 300/75 mg/m ² BID	Use oral solution
Age 6 months to 18 years		
7-15 kg	(12/3 mg/kg BID)	
7 to 10 kg	1.25 ml BID	Tablets are not recommended; use oral solution
>10 to <15 kg	1.75 ml BID	Tablets are not recommended; use oral solution
15-40 kg	(10/2.5 mg/kg BID)	
15 to 20 kg	2.25 mL BID	2 tablets BID (100/25 mg formulation) or 1 tablet BID (200/50 mg formulation)
>20 to 25 kg	2.75 mL BID	2 tablets BID or 1 tablet BID (200/50 mg formulation)
>25 to 30 kg	3.5 mL BID	3 tablets BID (100/25 mg formulation)
>30 to 35 kg	4 mL BID	3 tablets BID (100/25 mg formulation)
>35 to 40 kg	4.75 mL BID	4 tablets BID (100/25 mg formulation) or 2 tablets BID (200/50 mg formulation)
>40 kg	400/100 mg BID (same as adult dosage)	
>40kg	5 ml BID	4 tablets BID (100/25 mg formulation) or 2 tablets BID (200/50 mg formulation)

8.3.2 Anti-Hepatitis

Adefovir dipivoxil

Tablet, 10mg

Indications: chronic hepatitis B infection with *either* compensated liver disease with evidence of viral replication, and histologically documented active liver inflammation and fibrosis *or* decompensated liver disease

Cautions: monitor liver function tests every 3 months, and viral markers for hepatitis B every 3–6 months during treatment (continue monitoring for at least 1 year after discontinuation—recurrent hepatitis may occur on discontinuation); monitor renal function before treatment then every 3 months, more frequently in renal impairment or in patients receiving nephrotoxic drugs; elderly; discontinue if deterioration in liver function, hepatic steatosis, progressive hepatomegaly or unexplained lactic acidosis
Renal impairment: 10 mg every 48 hours if eGFR 30–50 mL/minute/1.73 m²; 10 mg every 72 hours if eGFR 10–30 mL/minute/1.73 m²; no information available if eGFR less than 10 mL/minute/1.73 m²; see also Cautions above

Side-effects: nausea, vomiting, dyspepsia, abdominal pain, flatulence, diarrhoea; asthenia, headache; renal failure; hypophosphataemia; rash and pruritus; also reported pancreatitis

Dose and administration: adult over 18 years, 10 mg once daily

Entacavir

Tablet, 0.5mg, 1mg

Oral solution, 0.05mg/ml

Indications: chronic hepatitis B infection *either* with compensated liver disease (with evidence of viral replication,

and histologically documented active liver inflammation or fibrosis) *or* decompensated liver disease

Cautions: monitor liver function tests every 3 months, and viral markers for hepatitis B every 3–6 months during treatment (continue monitoring for at least 1 year after discontinuation—recurrent hepatitis may occur on discontinuation); HIV infection—risk of HIV resistance in patients not receiving ‘highly active antiretroviral therapy’; lamivudine-resistant chronic hepatitis B—risk of entecavir resistance; discontinue if deterioration in liver function, hepatic steatosis, progressive hepatomegaly or unexplained lactic acidosis

Renal impairment: reduce dose if eGFR less than 50 mL/minute/1.73 m²; consult product literature

Pregnancy: toxicity in *animal* studies—manufacturer advises use only if potential benefit outweighs risk; effective contraception required during treatment.

Breast-feeding: manufacturer advises avoid—present in milk in *animal* studies.

Side-effects: nausea, vomiting, dyspepsia, diarrhoea, raised serum amylase and lipase, headache, fatigue, dizziness, sleep disturbances; *lesscommonly* thrombocytopenia, rash, alopecia

Dose and administration: Compensated liver disease not previously treated with nucleoside analogues, adult over 18 years, 500 micrograms once daily. Compensated liver disease with lamivudine-resistant chronic hepatitis B adult over 18 years, 1 mg once daily; consider other treatment if inadequate response after 6 months. Decompensated liver disease, adult over 18 years, 1 mg once daily.

Note: To be taken at least 2 hours before or 2 hours after food

Ribavirin

Tablet, 200mg

Indications: severe respiratory syncytial virus bronchiolitis in infants and children; in combination with peginterferon alfa or interferon alfa for chronic hepatitis C in patients without liver decompensation

Cautions: Exclude pregnancy before treatment, cardiac disease, gout, eye examination recommended before treatment, thyroid function test recommended before treatment

Interactions: Abacavir, Azathioprine, Didanosine, Stavudine, Zidovudine

Contraindications: Pregnancy, breast-feeding, renal impairment, severe cardiac disease, including unstable or uncontrolled cardiac disease in previous 6 months; haemoglobinopathies, severe debilitating medical conditions; autoimmune disease, uncontrolled severe psychiatric condition; history of severe psychiatric condition in children

Side-effects: Haemolytic anaemia, nausea, vomiting, dyspepsia, abdominal pain, flatulence, constipation, diarrhoea, colitis, chest pain, palpitation, tachycardia, peripheral oedema, changes in blood pressure, syncope, flushing, cough, dyspnoea, headache, dizziness, asthenia, impaired concentration and memory, sleep disturbances, abnormal dreams, anxiety, depression, suicidal ideation, psychoses, dysphagia, weight loss, dysphonia, paraesthesia, hypoaesthesia, ataxia, hypertonia, influenza-like symptoms, thyroid disorders, hyperglycaemia, menstrual disturbances, breast pain, prostatitis, sexual dysfunction, micturition disorders, dehydration, hypocalcaemia, myalgia, arthralgia, hyperuricaemia, visual disturbances, eye pain, dry eyes, hearing impairment, tinnitus, earache, dry mouth, taste disturbances, mouth ulcers, stomatitis, glossitis, tooth disorder, gingivitis, alopecia, pruritus, dry skin, rash, increased sweating, psoriasis, photosensitivity, and acne;

Dose and administration: *Oral:Adult:* Chronic hepatitis C, genotype 1,4 (in combination with peginterferon alfa-2a): <75kg: 1000mg/day in 2 divided doses for 48 weeks; ≥75kg: 1200 mg/day in 2 divided doses for 48 weeks. *Chronic hepatitis C, genotype 2,3 (in combination with peginterferon alfa-2a):* 800mg/day in 2 divided doses for 24 weeks.

Note: Tablet: Should be administered with food.

Telbivudine

Tablet, 600mg

Indications: chronic hepatitis B infection with compensated liver disease, evidence of viral replication, and histologically documented active liver inflammation or fibrosis

Cautions: pregnancy, breast feeding, hepatic impairment, renal impairment

Interactions: Interferon Alfa

Counselling: Patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, or numbness, tingling or burning sensations

Side effects: nausea, diarrhoea, abdominal pain, raised serum amylase and lipase; cough; dizziness, headache, fatigue; rash; less commonly; taste disturbance, arthralgia, myalgia, myopathy (discontinue treatment), and peripheral neuropathy; also reported, lactic acidosis and rhabdomyolysis

Dose and Administration: Adult and child over 16 years, 600 mg once daily

8.3.3. Other Antivirals

Acyclovir

Tablet, 200mg, 400mg

Powder for injection, 250mg, 500mg in vial

Cream, 5% 2mg

Ointment, 5%

Indications: treatment of primary genital herpes; disseminated varicella-zoster (chickenpox) in immunocompromised patients; herpes simplex encephalitis and herpes zoster.

Cautions: renal impairment, maintain adequate hydration; pregnancy and breast-feeding.

Drug interactions: probenecid, any nephrotoxic drugs.

Contraindications: hypersensitivity to acyclovir.

Side effects: nausea, vomiting, abdominal pain, diarrhea, headache, fatigue, rash urticaria, pruritus, photosensitivity; rarely hepatitis, jaundice, dyspnoea, angioedema, anaphylaxis, neurological reactions (including dizziness, confusion, hallucinations and drowsiness); acute renal failure, decreases in hematological indices; on intravenous infusion, severe local inflammation (sometimes leading to ulceration), fever, and rarely agitation, tremors, psychosis and convulsions.

Dose and Administration: Adult: *Treatment of primary genital herpes:* Oral: 200mg 5 times daily for 7-10 days or 400 mg 3 times daily for 7-10 days.

Prevention of recurrence of genital herpes: Oral: 400 mg twice daily. *Disseminated varicella-zoster (chickenpox) in immunocompromised patients:* IV infusion: 10 mg/kg 3 times daily for 7 days. *Herpes simplex encephalitis:* IV infusion: 10 mg/kg 3 times daily for 10 days. *Herpes zoster:* 800mg every 4 hours (5 times/day) for 7-10 days. Child: For up to 12 years, IV infusion (over at least 1 hour), 250 mg/m² 8 hourly for 5-7 days. This may be doubled in herpes encephalitis and in varicella-zoster in immunocompromised patients.

Varicella (chickenpox): 20mg/kg (maximum 800mg/dose) 4 times daily for 5 days, initiated within 24 hours of appearance of the rash.

Storage: store at controlled room temperature.

Adenine Arabinoside

Injection, 500 mg in vial

Vidarabine was formerly used intravenously in the treatment of severe and disseminated herpes simplex infections and herpeszoster but aciclovir is preferred.

Amantadine hydrochloride

Capsule, 100mg.

Syrup, 50mg/5ml

Indications: Parkinson's disease (not for drug induced parkinson - like syndromes) (See section 4.5); influenza prophylaxis.

Cautions: epilepsy, serious mental disorders, a history of eczematoid rashes, congestive heart failure and/ or peripheral oedema, or orthostatic hypotension.

Drug interactions: agents with anticholinergic effects, alcohol, CNS stimulants, hydrochlorothiazide and triamterene, levodopa.

Contraindications: hypersensitivity to amantadine.

Side effects: livedo reticularis (skin discolouration) mainly of the legs; oedema of the legs. CNS reactions like psychotic episodes, convulsions and nausea. Headache, constipation, insomnia and nervousness, urinary retention, dry mouth, blurred vision as well as neutropenia and skin rashes have occurred.

Dose and Administration:*Oral:* Adult: *Influenza A viral infection:* 100mg twice daily; initiate within 24-48 hours after onset of symptoms; discontinue as soon as possible based on clinical response (generally within 3-5 days or within 24-48 hours after symptoms disappear).

Influenza A prophylaxis: 100mg twice daily.

Parkinson's disease: 100mg twice daily as sole therapy; may increase to 400mg/day if needed with close monitoring. Child:

Influenza A treatment: 1-9 years: 5mg/kg/day in 2 divided doses. ≥ 10 years and < 40 kg: 5mg/kg/day; maximum dose: 150 mg/day. 10-12 years and ≥ 40 kg: 100 mg twice daily
Storage: store at 15-30 °C; protect from freezing.

Famciclovir

Tablet, 125mg, 250mg, 500mg

Indications: treatment of herpes zoster, acute genital herpes simplex and suppression of recurrent genital herpes.

Cautions: renal impairment; pregnancy and breastfeeding.

Drug interactions: see under acyclovir

Side effects: nausea, vomiting, headache, rarely dizziness, confusion, hallucinations, rash, abdominal pain and fever have been reported in immunocompromised patients.

Dose and Administration: Adult: *Oral: herpes zoster:* 250mg 3 times daily for 7 days or 750mg once daily for 7 days (in immunocompromised, 500mg 3 times daily for 10 days). *Genital herpes, first episode,* 250mg 3 times daily for 5 days; recurrent infection, 125mg twice daily for 5 days (in immunocompromised, all episodes, 500mg twice daily for 7 days). *Genital herpes, suppression,* 250mg twice daily (in HIV patients, 500mg twice daily) interrupted every 6-12 months. Child: not recommended.

Foscarnet

IV, 24 mg/ml

Indications: treatment of cytomegalovirus retinitis in AIDS patients when ganciclovir fails or is contraindicated, also for aciclovir resistant herpes simplex virus infection.

Cautions: renal impairment.

Drug interactions: ciprofloxacin, cyclosporin, amphotericin B, I.V pentamidine, aminoglycosides, ritonavir, and saquinavir.

Contraindications: hypersensitivity to foscarnet.

Side effects: fever, headache, seizure, nausea, diarrhea, vomiting, anemia, nephrotoxicity, fatigue, dizziness, depression, confusion, rash, anorexia, granulocytopenia, leukopenia, vision abnormalities, coughing, dyspnea.

Dose and Administration: Adult: *CMV retinitis: I.V.:*

Induction treatment: 60 mg/kg/dose every 8 hours or 100 mg/kg every 12 hours for 14-21 days. Maintenance therapy: 90-120 mg/kg/day as a single infusion.

Acyclovir-resistant HSV induction treatment: I.V.: 40 mg/kg/dose every 8-12 hours for 14-21 days.

Storage: store injection at room temperature.

Ganciclovir

Capsules, 250mg, 500mg

Powder for IV infusion, 500 mg/vial

Indications: treatment of slight or life threatening cytomegalovirus (CMV) infections in immuno-compromised patients, and for the prevention of CMV disease in transplant recipients.

Cautions: thrombocytopenia, impaired renal function.

Drug interactions: zidovudine; agents that inhibit renal tubular secretion; antineoplastic agents, co-trimoxazole.

Contraindications: hypersensitivity to ganciclovir.

Side effects: myelosuppression, neutropenia, thrombocytopenia, CNS effects, fever, skin rash, GI disturbances; liver function abnormalities; phlebitis. Fertility may be impaired.

Dose and Administration: Adult: *CMV retinitis:*

IV infusion: initially 5mg/kg 12 hourly infused at a constant rate over 1 hour (10mg/kg/day) for 14 - 21 days. Maintenance: IV infusion 6mg/kg/day for 5 days /week; or 5mg/kg/day for 7 days/week. *Oral:* maintenance therapy (in HIV - infected

patients, when retinitis is stable): 1g 3 times daily, or 500mg 6 times daily, with food.

Storage: store intact vials at room temperature and capsules at 5-25°C.

Oseltamivir Phosphate

Capsule, 30mg, 45mg

Powder to reconstitute as suspension, 12mg/ml

Indications: treatment of uncomplicated acute illness due to influenza (A or B) infection in children ≥ 1 year of age and adults who have been symptomatic for no more than 2 days; prophylaxis against influenza (A or B) infection in children \geq year of age and adults.

Cautions: Renal impairment, primary or concomitant bacterial infections, pregnancy, breastfeeding, oseltamivir is not a substitute for the influenza virus vaccine. Safety and efficacy for use in hepatic impairment, treatment or prophylaxis in immunocompromised patients, patients with chronic cardiac and/or respiratory disease and in children < 1 year of age have not been established

Contraindications: Hypersensitivity to oseltamivir or any component of the formulation.

Side effects: nausea, vomiting, abdominal pain, diarrhoea; headache; conjunctivitis; *less commonly* eczema; also reported hepatitis, gastro-intestinal bleeding, arrhythmias, neuropsychiatric disorders (more frequent in children and adolescents), visual disturbances, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Dose and Administration: Dosage: Oral Treatment: Initiate treatment within 2 days of onset of symptoms; duration of treatment: 5 days: Children: 1-12 years: ≤ 15 kg: 30mg twice daily

8. Anti-Infectives

>15kg to ≤ 23kg: 45mg twice daily

>23 kg to ≤ 40kg: 60mg twice daily

>40kg: 75mg twice daily

Adolescents ≥13 years and Adults: 75mg twice daily

Prophylaxis: Initiate treatment within 2 days of contact with an infected individual; duration of treatment: 10 days, Children: 1-12 years

≤15kg: 30mg twice daily

>15kg to ≤ 23kg: 45mg twice daily

>23 kg to ≤ 40kg: 60mg twice daily

>40kg: 75mg twice daily

Adolescents ≥13 years and Adults: 75mg once daily. During community outbreaks, dosing is 75mg once daily. May be used for up to 6 weeks; duration of protection lasts for length of dosing period.

Dosage adjustment in renal impairment: Adults: CrCl 10-30 mL/minute:

Treatment: Reduce dose to 75mg once daily for 5 days

Prophylaxis: 75mg mg every other day or 30mg once daiy

Storage: Capsules: Store at 25⁰c.Oral suspension: Store at 25⁰c and reconstitute with water. Once reconstituted, store suspension under refrigeration at 2⁰c to 8⁰c; do not freeze. Use within 10days of preparation.

Ribavirin

Tablet, 200mg

Indications: in combination with peginterferon alfa-2a injection for the treatment of chronic hepatitis C in patients with compensated liver disease that were previously untreated with alpha interferons.

Cautions: monitor for anemia 1-2 weeks after initiation; cardiac, pulmonary, and elderly patients; paediatric patients < 3 years of age.

Drug interactions: nucleoside analogues (didanosine, lamivudine, stavudine, zidovudine).

Contraindications: hypersensitivity to ribavirin; women of childbearing age who will not use contraception reliably; pregnancy; male partners of pregnant women; hemoglobinopathies; as monotherapy for treatment of chronic hepatitis C; patients with autoimmune hepatitis; anemia, severe heart disease.

Side effects: dizziness, headache, fatigue, fever, insomnia, irritability, depression, emotional lability, impaired concentration, alopecia, rash, pruritus, nausea, anorexia, vomiting, dyspepsia, decreased hemoglobin, myalgia, dyspnea, flu-like syndrome.

Dose and Administration:*Oral:* Adult: *Chronic hepatitis C, genotype 1, 4 (in combination with peginterferon alfa-2a):* <75kg: 1000mg/day in 2 divided doses for 48 weeks; ≥75kg: 1200 mg/day in 2 divided doses for 48 weeks. *Chronic hepatitis C, genotype 2,3 (in combination with peginterferon alfa-2a):* 800mg/day in 2 divided doses for 24 weeks. *Tablet: Should be administered with food.*

Storage: store at room temperature.

Valaciclovir

Tablet, 500mg

Indications: treatment of herpes zoster and of herpes simplex infections of the skin and mucous membranes including initial and recurrent genital herpes.

Cautions: maintain adequate hydration; renal impairment; pregnancy and breast-feeding.

Drug interactions: see acyclovir.

Side effects: as a prodrug of acyclovir it is anticipated that side effects will be comparable; nausea and headache reported.

Dose and Administration:*herpes zoster:* 1g 3 times daily for 7 days. *Herpes simplex*, first episode, 500mg twice daily for 5 days (up to 10 days if severe); recurrent infection, 500mg twice daily for 5 days.*Child: not recommended.*

8.4. Antiprotozoals

8.4.1 Antimalarials

Malaria is one of the most serious protozoal infections, which is transmitted by anopheline mosquitoes and rarely by congenital transmission, transfusion of infected blood or use of contaminated syringes among drug addicts. It is caused by infection by any of four species of plasmodium. *Plasmodium vivax* is the most extensively distributed and cause much debilitating disease. *P. falciparum* is also widespread, and causes the most severe infections, which are responsible for nearly all malarial - related deaths. *P. Ovale* is mainly confined to Africa and is less prevalent, while *P.malariae*, which causes the least severe but most persistent infections also occur widely.

Certain tissue forms of *P. vivax* and *P. ovale* which persist in the liver for many months and even years are responsible for the relapses characteristic of malaria such latent forms are not generated by *P. falciparum* or *P. malariae*. Recrudescence of these infections results from persistent blood forms in inadequately treated or untreated patients.

Treatment of Malaria

Blood Schizontocides are the mainstay of the treatment of acute malaria and some are used for prophylaxis. They include the 4-aminoquinolines (chloroquine), the related arylaminoalcohols

(quinine and mefloquine), and artemisinin and its derivatives (artemether, artemether + lumefantrone (AL) and artesunate). They suppress malaria by destroying the asexual blood forms of the parasites but, because they are not active against intrahepatic forms, they do not eliminate infections by *P.vivax* and *P.ovale*.

Chloroquine, a rapidly acting schizontocide, is well tolerated, safe and inexpensive. It should be used to treat malaria wherever the parasites remain susceptible. *P.malaria* and *P.ovale* remain fully sensitive to chloroquine where as wide spread chloroquine resistance strains of *P. falciparum* have been reported in many countries. Resistance in *P. vivax* has also become established in several parts of the world. Infections acquired in areas of known or unknown chloroquine resistance are treated now with quinine followed. Parenteral administration of chloroquine may be used when there is no expectation of resistance in cases of severe and complicated malaria, when the patient is unable to take oral medication and when neither quinine nor quinidine is available.

If subsequent relapse occurs in *P.ovale* and *P.vivax* infections primaquine should be administered, after a second course of chloroquine, to eliminate the intrahepatic infection. Because sulfonamides can induce hypersensitivity in pregnant women and possible kernicterus in the newborn; AL should be used whenever possible to treat chloroquine resistant malaria except during the 1st trimester of pregnancy during which quinine should be used. If AL is not available oral Quinine is used.

Quinine, given orally, should be reserved for *p - falciparum* infections likely to be unresponsive to other drugs. It is used as the first-line treatment for pregnant women during the first trimester and for children of less than 5 kg.

Rectal Artesunate or intramuscular [IM] artemether are used as pre-referral treatment for severe malaria cases (*Patients arriving at a health post with severe malaria are given rectal artesunate (or intramuscular artemether when rectal artesunate is unavailable)*).

Intravenous) artesunate infusion or IM injection (or, alternatively, quinine IV infusion when artesunate is not available) is the first-line anti-malarial drug for management of severe malaria and should be replaced by a full dose of AL for artesunate infusion or IM injection and quinine oral for quinine infusion or IM injection once the patient is able to swallow.

First Line Treatment for Severe Malaria

IV or IM artesunate (preferred) or, IM artemether or IV quinine infusion (artesunate not available) or IM quinine (artesunate not available) can be used for severe malaria case mangmnet due to *P. falciparum*.

The recommended treatment for severe malaria in all patients including pregnant women is artesunate infusion, or alternatively quinine infusion or alternatively artemether IM if both of these are unavailable. Pre-referral therapy for severe malaria in pregnant women is with rectal artesunate, or rectal artemether or alternatively IM quinine if both of these are unavailable. Special precaution should be taken to prevent hypoglycaemia in pregnancy. *Primaquine and mefloquine are contraindicated during pregnancy. Intermittent preventive treatment with sulfadoxine-pyrimethamine (SP) is not recommended in Ethiopia.*

Mefloquine remains effective except in certain areas of resistance.No parenteral preparations are currently available, and is thus suitable only for patients who can take drugs by mouth. It is generally well tolerated, although, some adverse effects have been reported. However, because of the danger of

the emergence of mefloquine-resistant strains of *P. falciparum* and because of its potential toxicity, it should be used only following either microscopic or careful clinical diagnosis of *P. falciparum* infections that are known or strongly suspected to be resistant to chloroquine. Mefloquine and atovaquone-proguanil are the recommended chemoprophylactic anti-malaria drugs in Ethiopia.

In multi-drug resistant malaria, preparations of artemisinin or its derivatives (artemether or artesunate) offer the only prospect of cure. They should not be used in the first trimester of pregnancy. For the treatment of multiresistant falciparum malaria oral artesunate may be an effective antimalarial.

A fixed-dose of oral formulation of artemether with lumefantrine is recommended for the treatment of uncomplicated falciparum malaria. The combination is not for use in first trimester pregnancy. AL is used for mixed infections due to both *P. falciparum* and *P. vivax*.

Primaquine is recommended as a radical cure for 14 days for patients who are not living in malaria endemic areas. In the otherhand Primaquine is not currently recommended at the health post level, because the prevalence of glucose-phosphate-dehydrogenase (G6PD) deficiency is not known in Ethiopia. As a result, it is difficult to detect and manage complications of primaquine at this level.

Pregnancy: malaria is especially dangerous during pregnancy and the seriousness of the disease usually outweighs any potential risk from treatment.

For falciparum malaria, the adult treatment doses of oral and intravenous quinine can safely be given to pregnant women.

In the case of *P. vivax* or *P. ovale*, however, the radical cure with primaquine should be postponed until the pregnancy

is over; instead chloroquine should be continued at a dose of 600mg each week during the pregnancy.

AL is not recommended for infants under 5 kg and pregnant women in first trimester with uncomplicated malaria. Use oral quinine in such cases.

First line of treatment of uncomplicated malaria *P. falciparum* positive by multi-species RDT: AL is the recommended first-line drug for treatment of uncomplicated *P. falciparum* malaria. AL tablets are given according to body weight in six doses over three days.

Second line treatment of uncomplicated malaria

AL may be used to treat *P. vivax* infection when chloroquine is unavailable. If AL is not available for *P. falciparum* or mixed malaria infections, use oral quinine. If both chloroquine and AL are not available for *P. vivax* infection, use quinine.

Prophylaxis against malaria

No drug regimen gives assured protection to everybody, and indiscriminate use of existing antimalarials increases the risk of inducing resistance.

Mefloquine may be used for prophylaxis in areas of high risk. Where possible prophylaxis should be started 2-3 weeks before travel to enable any adverse reactions to be identified before exposure (over three-quarters of adverse reactions occur by the third dose) and should be continued for 4 weeks after the second and third trimesters. It should be used in early pregnancy only if alternative drugs are either not available or unlikely to be effective and when it is impracticable for the woman to leave the endemic area.

Proguanil, a predominantly tissue schizontocide with little blood schizontocidal activity, is a causal prophylactic agent since it is active against pre-erythrocytic intrahepatic forms, particularly of *P.falciparum*. The latent persistent liver

forms of *P.ovale* and *P.vivax* are unresponsive. However, there is evidence that it may be effective against *P.vivax* only immediately after the initial infection. *P.falciparum* resistance to proguanil and related compounds may occur in malaria endemic areas and particularly where it has been employed in mass prophylaxis. Proguanil is used for prophylaxis with chloroquine in areas where there is resistance to chloroquine but a low risk of infection as it may give some protection against *P.falciparum* and may alleviate symptoms if an attack occurs. **Pregnancy:** travel to malarious areas should be avoided during pregnancy; if travel is unavoidable, effective prophylaxis must be used. Chloroquine and proguanil may be given in usual doses in areas where *P.falciparum* strains are sensitive; in the case of proguanil, folic acid 5mg daily should be given.

Alpha, Beta Arteether

Injection, 150mg/2ml

Indications: Chloroquine resistant malaria, complicated falciparum malaria and cerebral malaria.

Cautions: Pregnancy, breastfeeding.

Contraindications: Contraindicated in patients with hypersensitive to artemisinin derivatives.

Dose and Administration: Alpha, Beta arteether is for intramuscular use only. Adult: 150mg/ml once daily for 3 consecutive days. Children: 3mg/Kg per day administered by intramuscular injection over a 3-day period.

Storage: Store in cool dark room.

Artemether

Injection, 80 mg/ml, 40 mg /ml, 20 mg/ml

Suppository, 40 mg

Oral suspension, 40 mg/0.5ml, 80mg/ml

Indications: is an alternative treatment for malaria pre-referral therapy or alternate severe malaria treatment.

Contraindications: first trimester of pregnancy. IM Artemether should only be used during the first trimester of pregnancy when IV/IM artesunate (preferred) and IV/IM quinine are both unavailable.

Side effects: headache, nausea, vomiting, abdominal pain, diarrhoea; dizziness, tinnitus, neutropenia, elevated liver enzyme values; cardiotoxicity; neurotoxicity – in animal studies.

Dose and Administration: Adult and Child over 6 months: *IM*: loading dose of 3.2 mg/kg, then 1.6 mg/kg daily until patient can tolerate oral medication or to maximum of 7 days. Artemether seems to be as effective as IV quinine when given rectally to infants in coma from cerebral malaria. The initial dose for babies weighing less than 9 kg was 40 mg (one suppository). For those weighing more than this it was 80 mg. All then received a 40 mg suppository once a day for 6 days.

Artesunate

Tablet, 100mg, 200mg, injection, 60mg/ml, Suppository 50mg, 100mg.

Indications: Rectal artesunate treatment for emergency pre-referral therapy for severe malaria and treatment of severe malaria due to *P. falciparum*.

Cautions: risk of recurrence if used alone in non-immune patients.

Contraindications: first trimester of pregnancy.

Side effects: headache, nausea, vomiting, abdominal pain, diarrhoea, dizziness, tinnitus, neutropenia, elevated liver enzyme values; ECG abnormalities, including prolongation of QT interval; temporary suppression of reticulocyte response and induction of blackwater fever, reported.

Dose and Administration: Rectal artesunate treatment for emergency pre-referral therapy for severe malaria dosed at 10mg/kg body weight. Once able to tolerate oral medicines, complete Artemether-lumefantrine (AL) treatment.

Artemether + Lumfantrine

Tablet (dispersible), 20mg + 120mg

Indications: treatment of uncomplicated malaria due to *P.falciparum* and mixed infections. AL may be used to treat *P. vivax* infection when chloroquine is unavailable.

Cautions: electrolyte disturbances, concomitant administration of drugs that prolong QT interval; severe renal or hepatic impairment.

Drug interactions: amiloride, amitriptyline, azithromycin, chloroquine, chlorpromazine, ciprofloxacin, clomipramine, erythromycin, fluconazole, fluphenazine, furosemide, grapefruit juice, hydrochlorothiazide, mefloquine, naldixic acid, ofloxacin, procainamide, pyrimethamine, quinidine, quinine, spironolactone, sulfadoxine + pyrimethamine.

Contraindications: pregnancy (first trimester) and infants less than 5 kg, breastfeeding, history of arrhythmias, of clinically relevant bradycardia, and congestive heart failure accompanied by reduced left ventricular ejection fraction.

Side effects: abdominal pain, anorexia, diarrhoea, nausea and vomiting; headache, dizziness, sleep disorders; palpitations; arthralgia, myalgia; cough; asthenia; fatigue; pruritus, rash.

Dose and Administration: *Oral:* Adult: 35-65kg, 4 tablets as a single dose repeated after 8 hours, then twice daily on the following 2 days (i.e. 3-day course of 6 doses). Over 65 kg, as for 35-65 kg, but with closer monitoring for treatment failure / recrudescence

Child: 5 - < 15kg, 1 tablet; 15 - < 25kg, 2 tablets; 25 - < 35kg, 3 tablets; 35 - 65 kg, 4 tablets, repeated after 8 hours, then twice daily on the following 2 days (i.e. a 3-day course of 6 doses).

Storage: At room temperature.

Chloroquine Phosphate

Tablets, 250mg, 500mg (equivalent to 150mg, 300mg chloroquine base)

Syrup, 50mg/5ml

Injection, 50mg/ml;(equivalent to 40 mg chloroquine base)

Indications: treatment of *P. vivax* malaria.

Cautions: patients should avoid alcoholic beverages while taking chloroquine.

Side effects: gastro-intestinal disturbances, headache, also convulsions, visual disturbances, depigmentation or loss of hair, skin reactions (rashes, pruritus); rarely, bone-marrow suppression; other side effects (not usually associated with malaria prophylaxis or treatment).

Drug interactions: carbamazepine, ciclosporin, digoxin, ethosuximide, mefloquine, phenytoin and valproic acid.

Dose and administration: Orally with meals or milk and intramuscularly. Where chloroquine syrup is not available the tablets can be given to children by crushing and mixing with sweetened milk on spoon.

8. Anti-Infectives

Oral treatment of cases with chloroquine dose table for 150mg base/tablet or 50mg base/5ml syrup:

Age group in year	Chloroquine Dosage (Expressed in mg base and in tablets)	
Under 1 year	75mg ½ tab 40 mg ¼ tab 75mg ½ tab 75mg ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
1 -5 years	150mg 1 tab 75mg ½ tab 75mg ½ tab 75mg ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
6 – 9 years	300mg 2 tab 150mg 1 tab 150mg 1 tab 150mg 1 tab	STAT 6 hours later 2 nd . Day 3 rd . day
10 -15 years	450mg 3 tab 225 mg 1 ½ tab 225 mg 1 ½ tab 225 mg 1 ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
ADULT (16 years and over)	600mg 4 tab 300 mg 2 tab 300 mg 2 tab 300 mg 2 tab	STAT 6 hours later 2 nd Day 3 rd day

Storage: at room temperature.

Dihydroartemisinin

Tablet, 60mg

Dihydroartemisinin appears to offer no advantage over artesunate or artemether for the treatment of uncomplicated or severe malaria. However, it may be used in the absence of micro-scopic diagnosis if the compound is the recommended first-line treatment.

Dose and Administration: 4 mg/kg in divided loading dose on the first day followed by 2 mg/kg daily for 6 days.

Mefloquine hydrochloride

Tablet, 250mg

Indications: prophylaxis of malaria for travelers to areas where high risk of malaria

Cautions: pregnancy, cardiac conduction disorders; avoid for prophylaxis in severe hepatic impairment and in epilepsy; breastfeeding, infants under 3 months.

Drug interactions: artemether + lumfantrine, atenolol, carbamazepine, chloroquine, digoxin, ethosuximide, nifedipine, phenytoin, propranolol, quinidine, quinine, timolol, valproic acid, verapamil.

Contraindications: neuropsychiatric disorders including depression or convulsions; hypersensitivity to quinine.

Side effects: nausea, vomiting, diarrhoea, abdominal pain, anorexia, headache, dizziness, loss of balance, somnolence, insomnia and abnormal dreams; neurological and psychiatric disturbances including sensory and motor neuropathies, tremor, ataxia, visual disturbances, tinnitus, vestibular disorders; convulsions, anxiety, depression, confusion, hallucinations, panic attacks, emotional instability, aggression, agitation and psychoses; circulatory disorders, tachycardia, bradycardia, cardiac conduction disorders; muscle weakness, myalgia, arthralgia; rash, urticaria, pruritus, alopecia; disturbances in liver function tests, leukopenia, leucocytosis, thrombocytopenia; rarely, Stevens-Johnson syndrome, atrioventricular block and encephalopathy.

Dose and Administration: prophylaxis should start 1-3 weeks departure and continue for 4 weeks after last exposure, 5 mg /kg mefloquine salt once weekly

8. Anti-Infectives

Weight (Kg)	Age (approx.)	Number of tablets per week
<9	< 3 months	Not Recommended
9 – 19	3 – 23 months	¼
20 – 30	2 – 7 year	½
31 – 45	8 – 10 year	¾
36 – 50+	11 – 14+	1

Atovaquone-proguanil

Tablet 250mg atovaquone and 100mg proguanil hydrochloride

Indication: Prophylaxis of *Plasmodium falciparum* malaria

Dosage and administration: Start prophylaxis 1 or 2 days before entering a malaria-endemic area and continue during the stay and for 7 days after return.

Contraindication: Prophylaxis of *P. falciparum* in patients with severe renal function impairment (Ccr less than 30 mL/min); hypersensitivity to any component of the product. Weight and dosage schedule:

Weight (kg)	Atovaquone/Proguanil HCl Total Daily Dose	Dosage Regimen
11-20	62.5 mg/25 mg	1 Pediatric Tablet daily
21-30	125 mg/50 mg	2 Pediatric Tablets as a single dose daily
31-40	187.5 mg/75 mg	3 Pediatric Tablets as a single dose daily
>40	250 mg/100 mg	1 Tablet (adult strength) as a single dose daily

Primaquine phosphate

Tablet, 7.5mg base, 15mg base

Indications: For the prevention of relapses (radical cure) of malaria caused by *Plasmodium vivax* and *Plasmodium ovale*.

Cautions: G6PD deficiency, history of acute hemolytic anemia, systemic disease associated with agranulocytopenia (e.g. rheumatoid arthritis), and in those patients who are hypersensitive to Primaquine. Caution is also required during breast-feeding.

Drug interactions: bone marrow depressants, and other drugs that cause hemolysis (e.g dapsone).

Contraindications: during pregnancy and in patients with Glucose 6 phosphate dehydrogenase (G6PD) deficiency.

Side effects: haemolytic anemia especially in G6PD deficiency, leucopenia, abdominal pain or cramps, nausea, vomiting, methemoglobinemia (cyanosis - bluish fingernails, lips, or skin, dizziness or light headedness, difficult breathing, unusual tiredness or weakness).

Dose and Administration:Adult: : *Oral:* 26.3mg (15mg base) once a day for 14 days or 45 mg base once weekly for 8 weeks. Child:*Oral:* 0.68mg (0.39mg base) per kg of body weight once a day for 14 days.

Storage: at room temperature in a well closed, light-resistant container.

Quinine Dihydrochloride

Tablet, (Dihydrochloride or sulphate), 300mg, 600mg

Injection, 300mg/ml in 1ml ampoule

Indications: quinine is indicated an alternate drug for the treatment of severe and complicated malaria, and may be used when the preferred drug, intravenous artesunate, and the alternate drug IM artemether, is unavailable. Oral quinine is used as the first-line treatment of uncomplicated *p. falciparum malaria* for pregnant women during the first trimester and for children of less than 5 kg.

Cautions: during pregnancy and breast feeding, in patients with atrial fibrillation, conduction defects, heart block and glucose 6 phosphate dehydrogenase (G6DP) deficiency.

Drug interactions: mefloquine, quinidine, cimetidine, halofantrine, digoxin, antacids, other hemolytics.

Contraindications: haemoglobinuria, optic neuritis and in patients hypersensitive to quinine or quinidine.

Side effects: cinchonism (blurred vision or change in colour vision, severe headache, nausea or vomiting, ringing or buzzing in ears or transient loss of hearing), GIT disturbances (abdominal or stomach cramps or pain, nausea, vomiting, diarrhoea), confusion, hypersensitivity reaction (fever, angioedema, blood disorder including thrombocytopenia and intravascular coagulation), acute renal failure, hypoglycemia.

Resistant *Plasmodium falciparum* malaria:

Dose and Administration: *Oral:* Adult: 600 mg (quinine sulfate) every 8 hours for 3, 7, or 10 days; Child: 10 mg/kg (quinine sulfate) every 8 hours for 3, 7, or 10 days; duration of treatment depends on local susceptibility of *P. falciparum* and whether or not additional antimalarials also used. *Note: Patient Advice: If all or part of a dose is vomited within one hour, the same amount must be readministered immediately.* Treatment of multiple-drug resistant *Plasmodium falciparum* malaria (in patients unable to take quinine by mouth): Slow IV infusion (over 4 hours): Adult: 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 8 hours; Child: 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 12 hours; Initial dose should be halved in patients who have received quinine, quinidine or mefloquine during the previous 12 – 24 hours.

Storage: at room temperature in a well closed container (for tablet).

8.4.2. Amoebicides and Antigiardial Agents

Metronidazole is a 5-nitroimidazole derivative with activity against protozoa and anaerobic bacteria. In amoebiasis, metronidazole acts as an amoebicide at all sites of infection with *Entamoeba histolytica*. Because of its rapid absorption it is probably less effective against parasites in the bowel lumen and is therefore used in conjunction with a luminal amoebicide such as diloxanide furoate or di-iodohydroxyquinoline in the treatment of amoebic dysentery and in extra-interstitial amoebiasis, including hepatic amoebiasis. Tinidazole has the antimicrobial actions of metronidazole and usually administered as a single dose by mouth with or without food. Dehydroemetine, a synthetic derivative of emetine, is a tissue amoebicide with similar actions and uses, although probably of lower toxicity.

Chloroquine Phosphate

Tablet, 150mg base

Syrup, 50mg base /5ml

Injection, 150mg base in 5ml ampoule

Indications: treatment of extraintestinal amebiasis, usually in combination with an effective intestinal amebicide. However, it is not considered a primary drug. See also under section 7.4.1.

Cautions: pregnancy and breast-feeding, severe blood disorders, hepatic function impairment; severe neurological disorders, retinal or visual field changes. See also under section 7.4.1.

Drug interactions: mefloquine, antiepileptics, cardiac glycosides, and cyclosporin.

Side effects: see under section 7.4.1.

Dose and Administration: Extraintestinal amebiasis:

Adult: 1g/day (600mg base) for 2 days followed by 500 mg/day (300 mg base) for at least 2 – 3 weeks

Child: 10 mg/kg (base) once daily for 2 – 3 weeks (up to 300 mg base/day)

Storage: Store in a well-closed container and at room temperature.

Dehydroemetine

Injection, 30 mg/ml in 1 and 2 ml ampoules

Indications: treatment of intestinal amoebiasis.

Cautions: breast-feeding, pregnancy, severe disease of any organ.

Contraindications: cardiac, renal, or neuromuscular disease.

Side effects: nausea, vomiting, diarrhoea, weakness, low blood pressure, irregular heartbeats, pain at the injection site

Dose and Administration: Adult: *IM*: 1mg/kg daily (maximum daily dose of 60 mg), generally for up to 4 – 6 day, but no more than 5 days in children. Elderly or severely ill patients, 0.5 mg/kg

Storage: store at room temperature.

Diloxanide Furoate

Tablet, 500mg

Indications: chronic amoebiasis, intestinal amoebiasis. It is a drug of choice for asymptomatic patients with *E.histolytica* cysts in the faces.

Side effects: flatulence, vomiting, urticaria, pruritus

Dose and Administration: *Oral*: Adult: 500mg 3 times daily for 10 days. Child over 25 kg, 20mg/kg daily in 3 divided doses for 10 days; course may be repeated if necessary.

Metronidazole

Table/Capsule, 250mg

Syrup 4% w/v, 250mg/5ml, 200mg/5ml, 250mg/5ml

Suspension (oral), 125mg/5ml

Intravenous infusion, 5mg / ml in 100ml

Suppositories, 500mg

Indications: invasive amoebiasis and giardiasis, trichomoniasis, tissue nematode infections, bacterial infections (section 7.1.2); *Helicobacter pylori* eradication.

Cautions, Drug interactions, Contraindications, Side effects
-see section 7.1.2 under metronidazole.

Dose and Administration: Invasive amoebiasis: Oral: Adult and Child: 30mg/kg daily in 3 divided doses for 8 - 10 days; subsequent course of luminal amoebicide.

Invasive amoebiasis (if oral administration not possible): IV infusion: Adult and Child: 30 mg/kg daily in 3 divided doses (until patient able to complete course with oral drugs), subsequent course of luminal amoebicide.

Giardiasis: Oral: Adult: 2g once daily for 3 days,

Child: 15mg/kg daily in divided doses for 5 - 10 days.

Urogenital trichomoniasis: Oral: Adult: 2g as a single dose or 400 – 500 mg twice daily for 7 days; sexual partners should be treated concomitantly.

Note 1: In amoebiasis and giardiasis, various dosage regimens are used and definitive recommendations should be based on local experience.

Note 2: Patient Advice: Metronidazole tablets should be swallowed whole with water, during or after a meal; metronidazole suspension should be taken one hour before a meal.

Storage: at room temperature, in a well closed, light resistant container.

Tinidazole

Tablet, 250mg, 500mg

Indications: in the treatment of susceptible protozoal infections and in the treatment and prophylaxis of anaerobic bacterial infections.

Cautions: see under metronidazole; avoid porphyria

Drug interactions: alcohol

Side effects: see under metronidazole

Dose and Administration: Intestinal amoebiasis, 2gm daily for 2 - 3 days; Child: 50 - 60 mg/kg daily for 3 days. Amoebic involvement of liver, 1.5 - 2gm daily for 3 - 6 days, Child: 50 - 60mg/kg daily for 5 days.

Urogenital trichomoniasis and giardiasis, single 2gm dose (repeated once if necessary); Child: single dose of 50 - 75 mg/kg.

Ornidazole

Tablet, 500mg

Indication: treatment of susceptible protozoal infections (amoebiasis, giardiasis, and trichomoniasis) and also in treatment and prophylaxis of anaerobic bacterial infections

Cautions: use of ornidazole should be avoided during pregnancy and breast feeding mothers, do not take alcohol while taking ornidazole

Contraindications: contraindicated in patients who are hypersensitive to the ornidazole

Side effects: dose related side effects such as gastrointestinal disturbances, nausea and vomiting, weakness, dizziness, drowsiness, insomnia, changes in mood and peripheral neuropathy

Drug interactions: alcohol, disulfiram

Dose and administration: adults oral: amoebiasis 500 mg twice daily for 5 to 10 days, for amoebic dysentery or amoebic liver abscess 1.5 g as a single dose for 3 days

Children: 25 mg per kg body weight as a single dose for 5 to 10 days, amoebic dysentery 40 mg per kg as a single dose for 3 days. Trichomoniasis: adults: a single dose of 1.5 g or a 5 day course of 500 mg twice daily, children: 25 mg per kg as a single dose

8.4.3. Leshmaniacydes

Leishmaniasis is caused by the protozoa leishmania. It can be categorized as visceral, cutaneous or mucocutaneous. It may be a self-limiting localized skin lesion but may range from this to disseminated progressive disease. In endemic areas there is usually a reservoir of disease in a mammalian host and the usual vectors are sand flies.

Sodium Stibogluconate, an organic pentavalent antimony compound, is the treatment of choice for visceral leishmaniasis. The dose is 20mg/kg daily (max. 850 mg) for at least 20 days by intramuscular or intravenous injection; the dosage varies with different geographical regions and expert advice should be obtained. Skin lesions are treated for 10 days.

Amphotericin is used with or after an antimony compound for visceral leishmaniasis unresponsive to the antimonial alone; side effects may be reduced by using liposomal amphotericin at a dose of 1-3mg/kg daily for 10 - 21 days to a cumulative dose of 21- 30mg/kg.

Pentamidine Isethionate has been used in antimony resistant visceral leishmaniasis, but although the initial response is often good, the relapse rate is high; it is associated with serious side effects.

Amphotericin B

Powder for injection, 50mg / vial

Liposomal injection, 10mg, 50mg / vial,

Logenzegs, 10mg

Oral suspension, 100mg/ml

Indications: leishmaniasis

Cautions, Drug interactions, and Side effects (see section 7.2).

Dose and Administration: Adult: *IV infusion:* 0.25 mg/kg/day, increased gradually to 0.5-1mg/kg/day; total dose 1-3g. *Liposomal injection: treatment of visceral leishmaniasis: Immunocompetent patients:* 3 mg/kg/day on days 1-5, and 3 mg/kg/day on days 14 and 21; a repeat course may be given in patients who do not achieve parasitic clearance. *Immunocompromised patients:* 4 mg/kg/day on days 1-5, and 4 mg/kg/day on days 10, 17, 24, 31, and 38.

Paramomycine

Injection 375mg/ml

Indication: Paromomycin sulfate is indicated for intestinal amebiasis—acute and chronic (Note- It is not effective in extraintestinal amebiasis); management of hepatic coma—as adjunctive therapy.

Note: this medicine is aminoglycoside antibiotic, prescribed for certain types of intestinal infections such as amebiasis, cryptosporidiosis and leishmaniasis.

Cautions: in patients with history of hearing problems, ulcer, myasthenia gravis, Parkinson disease or kidney problems, dehydration, any allergy, who are taking other medications, elderly, children, during pregnancy and breastfeeding.

Contra indications: Hypersensitivity to the medicine or any component of the formulation. It is also contraindicated in intestinal obstruction.

Side-effects: Nausea, vomiting, abdominal cramps and diarrhea.

Dose and Administration: Intestinal amebiasis: Adults and Pediatric Patients: Usual dose—25 to 35 mg/kg body weight daily, administered in three doses with meals, for five to ten days. Management of hepatic coma: Adults: Usual dose—4 g daily in divided doses, given at regular intervals for five to six days.

Storage: Store it at controlled room temperature (20°-25°C) and in an airtight container.

Pentamidine Isethionate

Powder for injection, 200mg, 300mg/ vial

Indications: pentamidine is used parenterally in the treatment of early African Trypanosomiasis, of various forms of leishmaniasis, and of pneumonia due to pneumocystis carinii.

Cautions: avoid rapid intravenous administration of pentamidine. Patients should remain supine during administration and their blood pressure should be monitored. Pentamidine should be used under close supervision and great care. Caution should be taken during pregnancy, breastfeeding (breast-feeding is not recommended during pentamidine therapy because of the potential risks to the new born), and in geriatric patients. Patients should be instructed in proper oral hygiene during treatment, including caution in use of regular toothbrushes, dental floss, and toothpicks. Pentamidine Isethionate should be used with caution when the following medical problems exist: bleeding disorder; bone marrow depression, cardiac disease or arrhythmias, dehydration, renal function impairment, diabetes mellitus, hypoglycemia, & hypotension.

Drug interactions: bone marrow depressants, radiation therapy, and didanosine, foscarnet, nephrotoxic medications.

Contraindications: previous allergic reaction to pentamidine.

Side effects: nephrotoxicity, leucopenia, anaemia, thrombocytopenia, raised liver enzyme, hypoglycaemia followed by hyperglycaemia and insulin dependent diabetes mellitus, hypotension, the IM administration often causes pain, swelling, sterile abscess formation, and muscle necrosis at the site of injection.

Dose and Administrations:*Note: Pentamidine is toxic when given by injection and can affect the kidney, liver, blood and pancreas but systemic effects are rare following inhalation.* **Adult:** Leishmaniasis visceral: Intravenous infusion, 2 to 4 mg per Kg of body weight, administered over one to two hours, once a day for up to fifteen days. Administration may be repeated in one to two weeks if required. Leishmaniasis, cutaneous: Intravenous infusion, 2 to 4 mg per kg of body weight, administered over one to two hours, once or twice a week until the lesions heal. Trypanosomiasis, African (without CNS involvement): Intravenous infusion, 4 mg per Kg of body weight, administered over one to two hours, once a day for ten days. Pneumonia, Pneumocystis carinii: Intravenous infusion, 4 mg per Kg of body weight, administered over one to two hours. Once a day for fourteen to twenty-one days, depending on clinical response. Usual adult prescribing limits: Trypanosomiasis, African –3 to 5 mg per Kg of body weight a day. Child: See adult dose

Storage: Prior to reconstitution, store between 2°C and 8°C (36°F and 80°F), unless otherwise specified by manufacturer. Protect dry powder and reconstituted solution from light.

Sodium Stibogluconate

Injection, 100mg/ml

Indications: a primary agent in the treatment of Leishmaniasis. It is treatment of choice for visceral leishmaniasis.

Cautions: hepatic impairment, pregnancy, IV injection must be given slowly over 5 minutes (to reduce risk of local thrombosis) and stopped if coughing and substernal pain, mucocutaneous disease, heart-disease occur. Treat intercurrent infections (e.g. Pneumonia)

Contraindications: significant renal impairment, breast-feeding.

Side effects: anorexia, nausea, vomiting, abdominal pain, headache, lethargy, myalgia, raised liver enzyme, coughing and substernal pain, rarely anaphylaxis, fever, sweating, flushing, vertigo, bleeding from nose and gum, jaundice, rash, pain and thrombosis on IV administration, IM injections is also painful.

Dose and Administration: See notes above.

8.4.4. Trypanocides

African trypanosomiasis, or sleeping sickness, is a protozoan infection transmitted by *Glossina Spp.* (tsetse flies). Two subspecies of *Trypanosoma brucei*- *T. brucei gambiense* and *T. brucei rhodesiense* - produce distinctive clinical forms of the diseases. The early stage of African Trypanosomiasis results from infection of the blood stream and lymph nodes. The late meningoencephalitic stage results from infection of the central nervous system.

The drugs used for treatment are pentamidine, suramin and melarsoprol. Treatment of early-stage infections of *T. b. rhodesiense* with suramin sodium and *T. b. gambiense* with Pentamidine Isethionate can be curative if started before the central nervous system has become involved. In areas where pentamidine resistance occurs, suramin sodium may be used for *T. b. gambiense* infection. Melarsoprol is used for confirmed cases of *T. b. rhodesiense* and *T. b. gambiense* with meningoencephalitic involvement.

Melarsoprol

Powder for injection, 36 mg/ml

Indications: treatment of meningoencephalitic stage of *T.b. gambiense* or *T.b. rhodesiense* infections.

Cautions: episodes of reactive encephalopathy, pneumonia and malaria, malnutrition; G6PD deficiency, leprosy.

Contraindications: pregnancy, influenza epidemics.

Side effects: fatal reactive encephalopathy characterized by headache, tremor, slurred speech, convulsions and ultimately coma, myocardial damage, albuminuria, hypertension, hypersensitivity reactions, agranulocytosis, dose-related renal and hepatic impairment, hyperthermia, urticaria, headache, diarrhoea and vomiting - in late stage of treatment.

Dose and Administration: Adult and Child: *Slow IV injection:* gradually increased from 1.2 mg/kg to maximum of 3.6 mg/kg daily in courses of 3 - 4 days with intervals of 7 - 10 days between courses or 2.2 mg/kg daily for 10 days.

Storage: store at room temperature.

Melarsonyl potassium

Powder for injection, 200mg

Melarsonyl potassium is a water-soluble derivative of melarsoprol which was formerly used as an alternative to melarsoprol but was probably more toxic and less effective.

Pentamidine Isethionate

Powder for injection, 200mg, 300mg/ vial

Indications, Cautions, Drug interactions, Contraindications, Side effects, see under leishmaniacides (section 7.4.3)

Dose and Administration: Treatment of haemolympathic stage of *T.b. gambiense* infection: IM injection: Adult and Child: 4 mg/kg daily or on alternative days for a total of 7 - 10 doses.

Treatment of meningoencephalitic stage of *T.b.gambiense* (prior to melarsoprol): IM injection: Adult and Child: 4mg/kg daily on days one and two. *Note: Reconstitution and Administration. According to manufacturer's directions, Pentamidine Isethionate is toxic; care is required to protect personnel during handling and administration.*

Suramin Sodium

Powder for injection 1gm / vial

Indications: Suramin is a trypanocide used in the treatment of the early stages of African trypanosomiasis.

Cautions, Contraindications, Side effects; see under suramin sodium, section 7.5.1

Dose and Administration: Suramin is not used as a sole therapy for late stage infection with central nervous involvement. Because of the danger of severe reaction, a test dose of 100 - 200mg should be given before initial treatment.

Adult: *IV* if test dose tolerated - 20mg per kg of body weight of suramin up to maximum of 1gm in adults given every 5 or 7 days, usually to a total of 5 injections and not exceeding of injections.

8.4.5. Medicines for Toxoplasmosis

Toxoplasmosis is caused by infection with the protozoan parasite *Toxoplasma gondii*. Toxoplasmosis in immunocompetent individuals is usually asymptomatic. Patients with impaired immunity may develop serious complications such as encephalitis, myocarditis, and pneumonitis.

The treatment of choice is a combination of pyrimethamine and sulfadiazine. Calcium folinate should also be given every third day during treatment to counteract

megaloblastic anaemia. Treatment is ideally continued for several weeks after clinical cure. Prolonged even life long, maintenance therapy should be considered for AIDS patients since the tissue cyst forms of *T.gondii* will not have been affected by the initial treatment.

Congenital toxoplasmosis is not a problem in women who have toxoplasma antibody before conception but primary toxoplasmosis during early pregnancy is serious because of the risk of transplacental transmission, which may result in foetal death or congenital toxoplasmosis.

Clindamycin has some antiprotozoal actions, and has been used, usually with other antiprotozoals, in various infections including toxoplasmosis. Clindamycin with pyrimethamine has been used for treatment of toxoplasmosis instead of the more usual treatment with pyrimethamine plus sulfadiazine, in patients unable to tolerate sulfonamides.

Clindamycin

Capsule, 75 mg, 150 mg

Injection, 150 mg/ml in ampoule

Oral solution, 15 mg/ml

Indications: treatment for toxoplasmosis.

Cautions, Drug interactions, Contraindications, Side effects and Storage see section 7.1.2.

Dose and Administrations:*patients with AIDS and toxoplasmic encephalitis: Oral:* Clindamycin 600mg every 6 hours for at least 3 weeks, maintenance, 1200mg daily; patients also received pyrimethamine or Clindamycin 600mg four times daily together with pyrimethamine 75mg daily for 6 weeks. Acute therapy with pyrimethamine and clindamycin 600mg four times daily by mouth or 1200mg every 6 hours intravenously.

Primaquine Phosphate *see above*

Tablet, 15 mg

Pyrimethamine

Tablet, 25mg

Indications: in combination with sulfapyrimidine - type sulfonamide in the treatment of toxoplasmosis.

Cautions: pregnancy and breast-feeding, hepatic function impairment and in those patients hypersensitive to pyrimethamine.

Drug interactions: bone marrow depressants, folate antagonists.

Contraindications: pregnancy (14 or 16 weeks), hypersensitivity, history of seizures disorders, anaemia and bone marrow depression.

Side effects: Atrophic glossitis (pain, burning, or inflammation of the tongue, change in or loss of taste), blood dyscrasias, specifically agranulocytosis (fever, sore throat), megaloblastic anaemia (unusual tiredness, or weakness), or thrombocytopenia (unusual bleeding or bruising), GIT disturbance (anorexia, Nausea, vomiting, diarrhoea), Hypersensitivity (skin rash).

Dose and Administration: Toxoplasmosis (in second and third trimesters of pregnancy): Oral: Adult: 25mg daily for 3-4 weeks. Toxoplasmosis in neonates: Oral: 1 mg/kg daily; duration of treatment depends on whether neonate has overt disease-continue for 6 months, or is without overt disease but, born to mother infected during pregnancy-treat for 4 weeks, followed by further courses if infection confirmed. Toxoplasmosis in immunodeficiency: Oral: Adult: 200mg in divided doses on first day, then 75-100mg daily for at least 6 weeks, followed by a suppressive dose of 25-50mg daily.

Chorioretinitis: Oral: Adult: 75mg daily for 3 days then 25mg daily for 4 weeks; in unresponsive patients, 50 mg daily for a further 4 weeks.

Note: for the treatment of toxoplasmosis, pyrimethamine must always be taken with sulfadiazine. Take with meals and continue medicine with full time of treatment.

Storage: at room temperature in a tight, light-resistant container.

Spiramycin

Tablet, 3 mega unit

Indications: for treatment of toxoplasmosis.

Caution, Drug interactions and Side effects see erythromycin (section 7.1.2).

Dose and Administration: *Oral:* Adult: 6-9 million units daily, in 2 or 3 divided doses. Doses of up to 15 million units have been given daily in divided doses for severe infections.

Storage: store at room temperature.

Sulfadiazine

Tablet, 500mg

Indications: toxoplasmosis (with pyrimethamine); rheumatic fever

Cautions: hepatic and renal impairment; maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rashes - discontinue immediately; elderly; asthma, G6PD deficiency; pregnancy - avoid in first trimester, but may be given thereafter if danger of congenital transmission; breast feeding; see also interactions.

Drug interactions: ciclosporin, glibenclamide, pyrimethamine & co-trimoxazole (increased risk of antifolate effect), Warfarin

Contraindications: hypersensitivity to sulfonamides, severe renal failure or severe hepatic impairment, porphyria.

Side effects: nausea, vomiting, diarrhea, headache, hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum; rarely, erythemamultiforme and toxic epidermal necrolysis; crystalluria resulting in haematuria, oliguria, anuria, blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura - discontinue immediately, liver damage, pancreatitis, antibiotic - associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, and electrolyte disturbances .

Dose and Administrations:Toxoplasmosis (in second and third trimesters of pregnancy): Oral: Adult: 3g daily in 4 divided doses.Toxoplasmosis in neonates: Oral: 85mg/kg daily in 2 divided doses; duration of treatment depends on whether the neonate has overt disease continue for 6 months, or is without overt disease but born to mother infected during pregnancy - treat for 4 weeks, followed by further courses, if infection confirmed.Toxoplasmosis in immunodeficiency: Oral: Adult: 4 - 6g daily in 4 divided doses for at least 6 weeks, followed by a suppressive dose of 2 - 4g daily.

Note: For the treatment of toxoplasmosis, Sulfadiazine must always be taken with pyrimethamine.

Storage: below 30°C in a tight container, protect from light.

Sulfadoxine +Pyrimethamine

Tablet, 500mg +25mg

Injection, 500mg +25mg in2.5ml ampoule

Indication: Toxoplasmosis

Contraindications: should not be given to pregnant women whose gestational age is less than 16 weeks (4 months)

Dose and Administration: two tablets (1000mg+ 50mg) twice daily for two days then two tablets daily for six weeks.

8.5. Anthelmintics

8.5.1. Filaricides

Filarial nematode infections are endemic in large areas of the tropics and produce considerable morbidity. These are loiasis (arises from infections with *loa loa*), lymphatic filariasis (by *wuchereria bancrofti*, *brugia malayi*, or *B.timori*), onchocerciasis (river blindness, is caused by infection with the filarial nematode *onchocerca volculus*), mansonella infections.

Diethylcarbamazine is effective against microfilariae and adults of *loa loa*, *Wuchereria bancrofti*, and *Brugia malayi*. To minimise reactions, treatment is commenced with a dose of diethylcarbamazine citrate 1 mg/kg on the first day and increased gradually over 3 days to 6mg/kg daily in divided doses; this dosage is maintained for 21 days and usually gives a radical cure for these infections. Close medical supervision is necessary particularly in the early phase of treatment. In heavy infections there may be a febrile reaction, and in heavy *loa loa* infection there is a small risk of encephalopathy. In such cases treatment must be given under careful in-patient supervision and stopped at the first sign of cerebral involvement. (And specialist advice sought).

Ivermectin is very effective in onchocerciasis and it is now the drug of choice. A single dose of 150 micrograms/kg by mouth produces a prolonged reduction in microfilarial levels. Retreatment at intervals of 6 to 12 months depending on symptoms must be given until the adult worms die out.

Reactions are usually slight and most commonly take the form of temporally aggravation of itching and rash.

Suramin is the only macrofilaricide that is currently available for use against *Onchocera volvulus*. Administered intravenously over a period of several weeks suramin also kills microfilariae. It is, however, one of the most toxic substances used in clinical medicine and should always be given under medical supervision in a hospital. A careful assessment must always be made of the patient's capacity to withstand the effects of suramin treatment both before and during administration.

Diethyl Carbamazine Citrate

Tablet, 50 mg

Indications: in the treatment of lymphatic filariasis due to *Wuchereria bancrofti* (bancroftian filariasis), *Brugia malayi*, or *B. timori*. It is also used in loiasis due to *Loa loa* and also for toxocariasis.

Cautions: treatment with diethyl carbamazine should be closely supervised since hypersensitivity reactions are common and may be severe, especially in patients with onchocerciasis or loiasis. Avoid mass treatment schedules for infants, pregnant women, the elderly and debilitated patients, especially those with cardiac or renal disease. Caution if dizziness, loss of vision, night blindness, or tunnel vision occurs. Diethyl carbamazine should be administered with caution (eg. Gradually increasing doses) to prevent or minimize allergic reactions.

Side effects: itching and sweating of face, especially eyes; fever, lymphadenopathy; skin rash and visual disturbances; nausea; vomiting; headache; dizziness, drowsiness.

Dose and Administration: Oral: Lymphatic filariasis (bancroftian): Adult and Child over 10 years: 6mg/kg daily, preferably in divided doses after meals, for 21 days; Child under

10 years, half the adult dose; mass treatment program, Adult and Child over 10 years, 6mg/kg in divided doses over 24 hours, once a year; Child under 10 years, half the adult dose. Lymphatic filariasis (brugian): Adult and Child over 10 years, 3-6mg/kg, preferably in divided doses after meals, for 6-12 days; Child under 10 years, half the adult dose; mass treatment control program, Adult and Child over 10 years, 3-6mg/kg in divided doses over 24 hours, 6 times at weekly or monthly intervals; Child under 10 years, half the adult dose. Occult filariasis: Adult: 8mg/kg daily for 14 days, repeated as necessary if symptoms return.

Loiasis, treatment: Adult: 1mg/kg as a single dose on the first day, doubled on two successive days, then adjusted to 2-3mg/kg 3 times daily for a further 18 days. Loiasis, prophylaxis: Adult: 300mg weekly for as long as exposure occurs

Note: Diethyl Carbamazine should be taken immediately after meals.

Storage: in airtight containers at room temperature.

Ivermectin

Tablet, 3mg, 6mg (scored)

Indications: suppressive treatment of onchocerciasis; as a secondary agent in the treatment of bancroftian filariasis caused by wucheria bancrofti.

Cautions: breast-feeding (avoid treating mother until infant is 1 week old).

Contraindications: pregnancy (delay treatment until after delivery), hypersensitivity to ivermectin.

Side effects: Mazotti like reaction, specifically arthralgia or myalgia (joint or muscle pain), dizziness, fever, headache, lymphadenopathy (painful and tender nodes in necks, armpits, or groin), skin rash or itching - due to death of microflaria in

skin; or unusual tiredness or weakness; postural hypotension (light headedness while standing).

Dose and Administration: Bancroftian filariasis: Oral: Adult: 200mcg (0.2mg) per kg of body weight as a single dose. Suppression of microfilariae: Oral: Adult and Child over 5 years (and weighing over 15kg), 150mcg/kg as a single dose once a year.

Note: avoid food or alcohol for at least 2 hours before and after a dose.

Storage: at room temperature in a well-closed container.

Primaquine *see above*

Tablet, 15 mg

Suramin Sodium

Powder for injection, 1gm in vial

Indications: curative treatment of onchocerciasis; trypanosomiasis (sec. 7.4.4)

Cautions: administer only under close medical supervision in hospital and with general condition of patient improved as far as possible before treatment (see notes above); first dose - possible loss of consciousness (see under dosage, below); maintain satisfactory food and fluid intake during treatment; urine tests before and weekly during treatment - reduce dose if moderate albuminuria, discontinue immediately if severe albuminuria or casts in urine.

Contraindications: previous anaphylaxis or suramin sensitivity, pregnancy (delay treatment until after delivery); severe liver or renal function impairment; elderly or debilitated; total blindness (unless required for relief from intensely itchy lesions).

Side effects: nausea, vomiting, shock, loss of consciousness reaction such as urticaria and pruritis, and later paraesthesia,

hyperaesthesia of the palms and soles, skin eruptions, fever, photophobia and lachrymation, albuminuria, haematuria.

Dose and Administration: *Curative treatment of onchocerciasis: slow IV injection:* Adult 3.3mg/kg as a single dose (see first (test) dose administration, below), followed at weekly intervals by incremental doses of 6.7 mg/kg, 10.0mg/kg, 13.3 mg/kg, 16.7 mg/kg, and 16.7mg/kg on weeks 2 to 6 respectively (total dose 66.7 mg/kg over 6 weeks). Reconstitute in water for injections to produce a final concentration of 10%. First (test) dose: Administer first dose with particular caution; wait at least 1 minute after injecting the first few microlitres; inject the next 0.5ml over 30 seconds and wait 1 minute; inject the remainder over several minutes.

8.5.2. Schistosomicides

Schistosomiasis, a waterborne parasitic infection, is caused by several species of trematode worms (blood flukes).

Intestinal schistosomiasis is caused principally by *Schistosoma mansoni* as well as *S.japonicum*, *S.mekongi*, and *S.intercalatum*. Urinary schistosomiasis is caused by *S.haematobium*. The latter is an important predisposing cause of squamous cell cancer of the bladder.

Praziquantel is used for the treatment of chronic schistosomiasis and is effective against all species of schistosomes.

Metrifonate and oxamniquine are also used but are only effective against *S.haematobium* and *S.mansoni* respectively. Antischistosomal drugs may cause clinical deterioration if used during the acute phase of infection; treatment is either delayed or given in conjunction with a corticosteroid.

Metrifonate

Tablet, 100mg

Indications: urinary schistosomiasis due to *S.haematobium*.

Cautions: avoid for those recently exposed to insecticides or other agricultural chemicals with anticholinesterase activity; pregnancy.

Drug interactions: depolarizing muscle relaxants such as suxamethonium (avoid for at least 48 hours), organophosphorus insecticides.

Side effects: cholinergic side effects, nausea, vomiting, abdominal pain, diarrhea, headache, dizziness, and weakness.

Dose and Administration:*Oral:* 7.5mg/kg in three doses at intervals of 2 weeks.

Storage:Store at a temperature not exceeding 25°C.

Oxamniquine

Capsule, 250mg

Suspension, 250mg/5ml

Indications: intestinal schistosomiasis due to *Schistosoma mansoni* (acute stage and chronic hepatosplenic disease)

Cautions: epilepsy, pregnancy, breast-feeding. May impair ability to perform skilled tasks, for example operating machinery, driving.

Side effects: dizziness and drowsiness, headache, vomiting, diarrhea, intense reddish discoloration of urine occur commonly; rarely, urticaria, hallucinations, epileptiform convulsions; raised liver enzyme values; transient fever, eosinophilia.

Dose and Administration:Intestinal Schistosomiasis due to *S.mansoni* (East and central Africa, Arabian peninsula):*Oral:* Adult and Child 30mg/kg in 2 divided doses.

Storage: at room temperature in a tight container.

Praziquantel

Tablet, 600mg

Indication: treatment of schistosomiasis; intestinal tapeworm infections (*T. solium*, *T. saginata*, *D. latum* and *H. nana*); *cysticercosis* caused by *T. solium*.

Cautions: moderate to severe liver disease and in those hypersensitive to praziquantel; pregnancy and breast-feeding, nursing mothers (discontinue breast-feeding on the day of therapy and for 72 hours thereafter). The drug causes drowsiness that patients are to be advised not to drive vehicles or operate machineries.

Side effects:CNS effects (dizziness, drowsiness, headache, malaise), fever, GIT effects (abdominal cramps or pain, loss of appetite, nausea or vomiting, bloody diarrhoea), increased sweating, skin rash, hives or itching.

Dose and Administration:*Oral:* Adult and Child (above 4):*S. haematobium*, *S.mansoni:**Oral:* 20mg per kg of body weight two times a day for 1 day. *S.Japonium*, *S. mekongi:**Oral:* 20mg per kg of body weight 3 times a day for 1 day.*T. solium*, *T. saginata*, infections: 5-10mg/kg as a single dose.*H. nana* infection: 15-25 mg/kg as a single dose. *D. latum* infection: 10-25mg/kg as a single dose. *Cysticercosis:* 50mg/kg daily in 3 divided doses for 14 days with prednisolone (or similar corticosteroid) given 2-3 days before and throughout treatment period.

Storage: store below 30°C

8.5.3. Other Anthelmintics

Albendazole

Tablet, 200mg, 400mg

Oral Suspension, 100mg/5ml

Indications: for the treatment of single or mixed intestinal nematode infection such as ascariasis, enterbiasis, hookworm

infection, or trichuriasis and strongyloidiasis. Also for treatment of hydatid disease caused by *Echinococcus granulosus*

Cautions: breast-feeding. Exclude pregnancy before starting treatment.

Contraindications: pregnancy.

Side effects: GIT disturbances, headache, dizziness, changes in liver enzyme, rarely reversible alopecia (loss of hair), rash, fever, blood disorders, including leucopenia and pancytopenia.

Dose and Administration: Adult and Child over 2 years: *Oral: Single or mixed intestinal parasites:* *Oral:* 400 mg as a single dose (given for 3 days in heavy mixed infestations involving *Trichuris* or *Taenia* spp.). Repeated after 3 weeks if required.

Strongyloidiasis: 400mg given once or twice daily for 3 consecutive days. May be repeated after 3 weeks.

Giardiasis: 400 mg once daily for 5 days

Hydatid: <60 kg: 15mg/kg/day in 2 divided doses (maximum: 800mg/day); ≥ 60 kg body weight: 400mg twice daily. Administer dose for three 28-day cycles with a 14-day drug-free interval in between.

Storage: at room temperature.

Levamisole

Tablet, 40mg

Indications: treatment of ascariasis, hookworm and mixed ascariasis with hookworm infections; with fluorouracil for the treatment of colorectal carcinoma after complete resection of primary tumour.

Cautions: sensitive to levamisole

Drug interactions: anticoagulants (cumarine and indandione), bone marrow depressants.

Contraindications: advanced liver or kidney disease, pre-existing blood disorders.

Side effects: nausea, vomiting, abdominal pain, dizziness and headache.

Dose and Administration:*Oral:* Adult: 120mg (3 tablets) as a single dose. Child: 3mg per kg of body weight as a single dose.

Mebendazole

Tablets, 100mg, 500mg

Oral suspension, 100mg/5ml

Indications: For the treatment of whipworm (*trichuris trichuria*), pinworm (*Enterobius Vermicularis*), roundworm (*Ascaris Lumbricoids*), hookworm (*Ancylostoma duodenale, Nectar americanus*), and capillariasis in single or mixed infections.

Cautions: ulcerative colitis, liver diseases, hypersensitivity, treatment of intestinal worm is recommended in children over 1 year of age, there is limited data to assess the risk-benefit in those under one year. During pregnancy and in nursing women. In hookworm and whipworm infections iron supplements may be required as anemia may occur. To prevent reinfection all other infected member of the family should be treated. Personal hygiene and sanitation should be observed and all bedding and nightclothes washed after treatment, especially in pinworm infection.

Side effects: transient abdominal pain or upset, nausea, vomiting, diarrhoea, dizziness, headache, skin rash and itching may occur occasionally in cases of massive infection and expulsion of worms.

Dose and Administration:*Oral:* Adult and Child over 1 year: *Ascariasis:* 500mg as a single dose or 100mg twice daily for 3 days.

Hookworm infections, trichuriasis: 100mg twice daily for 3 days; if eggs persist in the faeces, second course after 3-4 weeks; alternatively 500mg as a single dose.

Adult and Child over 2 years:*Enterobiasis*: 100mg as a single dose, repeated after interval of 2-3 weeks; all household members over 2 years should be treated at the same time.*Capillariasis*: 200mg daily for 20-30 days; for mass treatment control programmes, 500mg as a single dose 4 times a year.Roundworm, Whipworm, Hookworm mixed infection: 100mg twice daily, morning and evening, for 3 consecutive days. May be repeated in 2- 3 weeks if required.Tapeworm (*Taenia* spp.): 100 mg twice daily for 6 days. There are reports of high success rates with higher doses for shorter periods (200mg twice daily for 4 days or 300mg twice daily for 3 days). Repeat after 3 weeks if necessary.

Storage: at room temperature, in well-closed containers.

Niclosamide

Tablet (chewable), 500mg.

Indications: eradication of tapeworm and *H.nana*.

Cautions:caution in patients with hypersensitivity to niclosamide, in children under 2 years and during pregnancy.

Side effects:nausea or vomiting, stomach pain, bad taste in mouth, dizziness, drowsiness, skin rash and itching may rarely occur.

Dose and Administration: *Oral:* preferably after a light meal or breakfast. Tablets should be crushed or chewed thoroughly and washed down with a small amount of water.

For small children tablets should be grounded as finely as possible and mixed with small amount of water.

In those with chronic constipation a mild laxative may be given before or after administering the drug.

A second course of niclosamide may be given if proglotides and /or ova persist for 7 – 14 days after treatment. Adult: tapeworm: 2g H.nana: 2 g on the first day, followed by 1 g for the following 6 days.

Child: 1 –5 years: 500mg; 6-12 years: 1g

Note: The dose may be given once as a single dose or half the dose first and the other half 1 hour later.

Storage: At room temperature, in a tight container, away from heat and direct light.

Piperazine

Tablet (Adipate), 300mg

Elixir (Citrate), 500mg/5ml, 622.5mg/5ml, 750mg/5ml, 706mg/5ml, 937.5mg/5ml, 1gm/5ml

Indications: for the treatment of round worm (*Ascaris Lumbricoids*) and pinworm (*Enterobius*) infections.

Cautions: caution in patients with epilepsy, impaired renal or hepatic function, and hypersensitivity. Supportive therapy should be given for anemic, dehydrated or malnourished patients prior to administration of the drug. Treat other members of the family paying attention to personal hygiene.

Drug interactions: chlorpromazine.

Side effects:nausea, vomiting, mild diarrhoea, abdominal cramps, headache, and dizziness may occur occasionally.

Dose and Administration:*Oral:* in constipated patients a purgative should be given to ease expulsion of the worm. A single dose is usually enough to treat roundworms. However, the dose may be repeated in 2 days if a patient has large number of roundworms.

*Roundworm infection (Ascariasis):*Adult: 3- 4g (30 – 40ml) or 75mg/kg of body weight as a single dose.

Child: 75mg/kg of body weight as a single dose. Or, 1 –5 years, 1g (10ml) as a single dose. 6 –12 years –2g (20ml) as a single dose. *Pinworm Infection (Enterobiasis, oxyuriasis)*: Adult: 2g (20ml) or 65mg/kg of body weight every 12 hours daily for 7 days.

Child: 65 mg/kg of body weight as a single dose for 7 days. Or, 1 –5 years 750 mg (7.5ml) once daily for 7 days. 6 –12 years –1½ g (15ml) once daily for 7 days. Maximum – 2.5 g once daily.

Storage: at room temperature, in light containers, protected from light.

Pyrantel Pamoate

Tablet, 125mg base

Oral suspension, 250mg base /5ml

Indications: treatment of Ascariasis, enterobiasis (pinworm infection), helminth infection (multiple), hookworm infection

Cautions: pre-existing liver dysfunction, severe malnutrition or anaemia.

Drug interactions: piperazine

Contraindications: hypersensitivity to the drug

Side effects: nausea, vomiting, tenesmus, anorexia, diarrhoea, drowsiness, headache, trouble in sleeping, hypersensitivity (skin rash)

Dose and Administration: Adult: *Ascariasis: Oral:* 11mg (base) per kg of body weight as a single dose may be repeated in 2 or 3 weeks if required.

Enterobiasis: Oral: 11mg (base) per kg of body weight as a single dose. Repeat in 2 or 3 weeks.

Hookworm (infection): Oral: 11mg (base) per kg of body weight once a day for three days.

Trichostrongyliasis: Oral: 11mg (base) per kg of body weight as a single dose. Maximum - up to 1 gm (base)

Child 2 years and over same as adults

Storage: at room temperature in a tight, light resistant container.

Thiabendazole

Tablet, 500mg

Oral suspension, 500mg/ml

Indications: for treatment of strongyloidiasis, cutaneous and visceral larva migrans, dracontiasis, symptoms of trichinosis. It is also used as secondary treatment for threadworm when mixed with above infestations, adjunct in hookworm, whipworm or roundworm (but not suitable for mixed infection involving round worms due to risk of migration). It is not used for prophylactic purpose

Cautions: hepatic and renal function impairment, in elderly. Discontinue if hypersensitivity reaction occur, correct anemia, dehydration or malnutrition preferably before treatment.

Drug interactions: theophylline.

Contraindications: pregnancy, breast-feeding.

Side effects: anorexia, nausea, vomiting, diarrhoea, dizziness, headache, pruritus, drowsiness, hypersensitivity reaction (fever, chills, angioedema, rashes), visual disorder.

Dose and Administration:Adult: *Oral:Cutaneous Larva migrans:* 25mg per kg of body weight two times a day for two days. May be repeated two days after completion of treatment if active lesions are still present.

Visceral Larva migrans: 25mg per kg of body weight 2 times a day for 5-7 days may be repeated in 4 weeks if required.

Strongyloidiasis:Uncomplicated infection: 25mg per kg of body weight 2 times a day for two days. *Hyper infection syndrome:*

8. Anti-Infectives

25mg per kg of body weight 2 times a day for 5-7 days may be repeated if required.

Trichinosis: 25mg per kg of body weight two times a day for 2-4 days based on patient response. Maximum - up to 3 grams daily. Child: (children 13.6kg of body weight and above) - same as adults dose.

Note: Continue medicines for full time of treatment and take after meals.

Storage: at room temperature in a tight container.

9. MEDICINES for ENDOCRINE DISORDERS and CONTRACEPTIVES

9.1. Pituitary Hormone Preparations

Vasopressin, also known as antidiuretic hormone, is used in the treatment of pituitary diabetes insipidus, chiefly as desmopressin. It has documented efficacy in the short-term management of bleeding oesophageal varices and colonic diverticular bleeding.

Desmopressin, a synthetic analogue of vasopressin, differs from vasopressin in being longer-acting and in evoking minimal vasoconstrictor effects. It is used for diagnosis and treatment of diabetes insipidus. Intravenous injection may be used when intranasal or oral administration is considered unsuitable.

Desmopressin Acetate

Tablet, 100 mcg, 200 mcg

Injection, 4 mcg/ml

Nasal spray, 100 mcg/ml, 10 mcg/metre d spray

Indications: diagnosis and treatment of diabetes insipidus; management of mild to moderate haemophilia.

Cautions: renal failure and hypertension; elderly; cystic fibrosis.

Contraindications: cardiac insufficiency and other conditions treated with diuretics.

Side effects: fluid retention and hyponatraemia; abdominal pain, haedache, nausea, vomiting, epistaxis.

Dose and Administration:Adult: *Diabetes insipidus: Oral:* initially 0.1 mg 3 times daily, adjusted to a maximum of 1.2 mg/day in 3 divided doses.*Intranasal:* 10- 20 mcg (0.1- 0.2 ml) 1 - 2 times daily.*IV:* 1 - 4 mcg (0.25 - 1 ml) 1 - 2 times daily.*Enuresis:Oral:* under 65 years, 0.2 mg at bedtime; may be

increased to 0.4 mg if necessary. Child: *Diabetes insipidus*:
Oral: initially 0.1 mg 3 times a day, adjusted to a maximum of 1.2mg/day in 3 divided doses.

Intranasal: 5-10 mcg (0.05-0.1ml) 1-2 times daily. *I.V*: over 1 year, 0.4 - 1mcg 1-2 times daily; under 1year, 0.2 - 0.4mcg 1-2 times daily. *Enuresis*: *Intranasal*: over 5 years, 10-40mcg (0.1-0.4ml) given before sleep. *Oral*: over 5 years, initially 0.2mg at bedtime; may be increased to 0.4 mg if necessary.

Storage: store tablets at room temperature; Injection at 2 - 8⁰c. Nasal solution of desmopressin acetate preserved with benzalkonium chloride should be stored at 20 - 25 °C, nasal solutions preserved with chlorobutanol should be refrigerated at 2-8°C.

Vasopressin

Injection, 20 units/ml in 1 ml ampoule

Indications: treatment of diabetes insipidus, prevention and treatment of postoperative abdominal distention.

Cautions: chronic nephritis, asthma, epilepsy, migraine, heart failure, or other conditions which might be aggravated by water retention.

Drug interactions: cimetidine, chlorpropamide, clofibrate, carbamazepine, fludrocortisone, urea, or tricyclic antidepressants, lithium, heparin, demeclocycline, noradrenaline and alcohol.

Side effects: large parenteral doses cause headache, sweating, tremor, nausea, vomiting, diarrhoea, cramp. In women, cause uterine cramps of a menstrual character. Hyponatraemia with water retention. Hypersensitivity reactions (urticaria and bronchial constriction). Cardiovascular effects (hypertension, arrhythmias).

Dose and Administration:*Diabetes insipidus:* SC or I.M: Adult: 5-10 units 2-4 times/day as needed. Child: 2.5-10 units 2-4 times/day as needed. *Abdominal distention:* Adult: I.M: 5 units stat, 10 units every 3-4 hours.

Storage: store in airtight containers at 2° to 8°C.

9.2. Corticosteroidal Preparations

The corticosteroids are used in physiological (low) doses for replacement therapy in adrenal insufficiency. In pharmacological (high) doses, glucocorticoids decrease inflammation, suppress the immune response, stimulate erythroid cells of the bone marrow, promote protein catabolism, reduce intestinal absorption, increase blood glucose, and elevate blood pressure, increase renal excretion of calcium and promote redistribution of fat and development of cushingoid features.

Systemic administration of corticosteroids is contraindicated in patients with peptic ulcer, osteoporosis, psychoses, or severe psychoneuroses, and they should be used only with great caution in the presence of congestive heart failure or hypertension, in patients with diabetes mellitus, epilepsy, glaucoma, infectious diseases, chicken pox and severe herpeszoster, ocular herpes simplex, chronic renal failure and uremia in elderly persons. Patients with active or doubtfully quiescent tuberculosis should not be given corticosteroids except, very rarely, as adjuncts to treatment with tubercular drugs. Corticosteroids are usually contraindicated in the presence of acute infections, because of the interference with inflammatory and immunological response during long courses of corticosteroid therapy. Patients should be examined regularly and in particular, checked for hypertension, glucosuria, hypocalcaemia, gastric discomfort, and mental changes. Sodium intake may need to be reduced and potassium

supplements may be necessary. Monitoring of the fluid intake and output, and daily weight records may give early warning of fluid retention.

Corticosteroids should not be administered concurrently with barbiturates, carbamazepine, phenytoin, primidone, or rifampicin; potassium depleting diuretics such as thiazide, anticoagulants, antidiabetics antihypertensives, salicylates, antimuscarinics, somatotropin, somatrem & vaccines, live virus, or other immunizations.

Signs of potential side effects upon using of corticosteroid are diabetes mellitus; burning, numbness, pain, or tingling at or near injections site; congestive heart failure (in susceptible individuals); generalized allergic reaction; local allergic reaction or infection at injection site; psychic disturbances; sudden blindness generalized anaphylaxis; cardiac arrhythmias; flushing of face or cheeks; seizures, acne; adrenal suppression; a vascular necrosis; cataracts, posterior subcapsular; Cushing's syndrome effects; cutaneous or subcutaneous tissue atrophy; ecchymosis; fluid and sodium retention; glaucoma with possible damage of optic nerves; growth suppression (in children); hypokalemic syndrome; impaired wound healing; increased intracranial pressure; secondary fungal or viral ocular infection; osteoporosis or bone fractures; pancreatitis; peptic ulceration or intestinal perforation; scaring at injection site; steroid myopathy; tendon rupture; and thin fragile skin.

Note: The risk of adverse effects with pharmacologic doses of corticosteroids generally increases with the duration of therapy and frequency of administration and to a lesser extent, with dosage.

Withdrawal of systemic corticosteroids: Gradual withdrawal should be considered in those whose disease is unlikely to relapse and who have: Recently received repeated courses with

in 1 year of stopping long-term therapy; Other possible causes of adrenal suppression; Received more than 40mg daily prednisolone (or equivalent); Been given repeat doses in the evening; Received more than 3 weeks' treatment.

Abrupt withdrawal may be considered in those whose disease is unlikely to relapse and who have received treatment for 3 weeks or less and are not included in the patient groups described above.

During corticosteroid withdrawal the dose may be reduced rapidly down to the physiological dosage (equivalent to 7.5mg prednisolone daily) and then reduced more slowly. Assessment of the disease may be needed during withdrawal to ensure that relapse does not occur.

Corticosteroids cover during stress. Patients who are unable to take the dose by mouth should receive parenteral corticosteroid cover.

For patients requiring surgery, parenteral hydrocortisone should be administered as follows: 200mg hydrocortisone intramuscularly with premeditation; 100mg hydrocortisone by intravenous infusion in 5000ml 0.9% sodium chloride during surgery; 100mg hydrocortisone intramuscularly every 6 hours for 72 hours after surgery. For patients requiring minor surgical procedures; 100mg by hydrocortisone intramuscularly shortly before and after intervention.

Betamethasone

Tablet, 0.5mg

Indications: inflammatory dermatoses such as seborrheic or atopic dermatitis, neurodermatitis, anogenital pruritus, psoriasis, and inflammatory phase of xerosis.

Cautions, Drug interactions, Contraindications and Side effects: see notes above

Dose and Administration:Adult: *Oral:* 2.4 - 4.8 mg/day in 2-4 doses; range: 0.6-7.2 mg/day.Child: *Oral:* 0.0175-0.25 mg/kg/day divided every 6-8 hours or 0.5-7.5 mg/m²/day divided every 6-8 hours.

Storage:store at 2-30 °C.

Betamethasone Sodium Phosphate + Betamethasone Dipropionate

Injection, 2mg + 5mg/2ml

Indications: Allergic States: Control of various incapacitating allergic conditions intractable to conventional treatment, in serum sickness and allergic reactions to drugs or insect bites.

Contraindications: Systemic fungal infections, hypersensitivity reactions to Betamethasone or other corticosteroids.

Drug interactions: phenobarbital, rifampin, phenytoin, ephedrine, estrogen, amphotericin B, coumarin-type anticoagulants, nonsteroidal anti-inflammatory drugs or alcohol, salicylate concentrations, somatotropin.

Side effects: The same as for other corticosteroids: Abdominal distention, nausea, vomiting, increased appetite, weight gain, pancreatitis, ulcerative esophagitis or peptic ulcer. Impaired wound healing, erythema, hirsutism, increased sweating, suppression of skin test reactions, hyper-pigmentation or hypo-pigmentation, subcutaneous and cutaneous atrophy or sterile abscess in site of injection. Increased intracranial pressure with papilledema, posterior subcapsular cataract, increased intraocular pressure (glaucoma), vertigo or headache. Euphoria, insomnia, mood swings from severe depression to frank psychotic manifestations, personality changes or convulsions. Menstrual irregularities, development of cushingoid state, suppression of fetal intrauterine or childhood growth, secondary adrenocortical and pituitary unresponsiveness

particularly in times of stress (e.g. trauma, surgery or illness) and negative nitrogen balance due to protein catabolism. Decreased carbohydrate tolerance, hyperglycemia, manifestations of latent diabetes mellitus, and increased requirements of insulin or oral hypoglycemic agents in diabetics.

Rare instances of blindness associated with intra-lesional therapy around the head. Joint instability may result from repeated intra-articular injections.

Dose and Administration: *Systemic Administration:* Treatment is initiated with 1-2ml, injected deeply intramuscular in the gluteal region, and repeated as necessary. In severe illness 2ml might be required initially. A wide variety of dermatologic conditions respond to an I.M. injection of 1ml Suspension, to be repeated as necessary. In respiratory tract disorders, effective control of symptoms is obtained in bronchial asthma, hay fever, allergic bronchitis and allergic rhinitis with a dose of 1-2ml I.M. In the treatment of acute or chronic bursitis, 1-2ml I.M. injection. Dose can be repeated as necessary. *Local Administration:* In acute subdeltoid, subacromial, olecranon and prepatellar bursitis an intra-bursal injection of 1-2ml of suspension may relieve pain and restore full range of movement within few hours. Chronic bursitis may be treated with reduced dosage once acute symptoms are controlled. In acute tenosynovitis, tendinitis and peritendinitis, one injection of suspension should alleviate the condition. In chronic forms of these conditions, it may be necessary to repeat the injection as the patient's condition requires. Recommended dose for intra-articular injection varies according to the size of the joint: Large joints (such as knee, hip and shoulder): 1-2ml. Medium joints (such as elbow, wrist and ankle): 0.5-1ml. Small joints (such as foot, hand joints): 0.25-0.5

ml. Recommended doses at intervals of one week in bursitis under calcaneal spur is 0.5ml. In synovial cyst is 0.25-0.5ml. In tenosynovitis, periosteitis of cuboid is 0.5ml and in acute gouty arthritis is 0.5-1ml. After favorable response is obtained the proper maintenance dosage should be determined by decreasing the initial dose in small decrements at appropriate time intervals until the lowest dose which will maintain an adequate clinical response is determined.

Storage: between 2° and 25°C. Protect from freezing.

Dexamethasone

Tablet, 0.5mg, 0.75mg, 1mg, 2mg, 4mg

Injection, 4mg/ml, 25mg/ml, 50mg/ml

Indications: suppression of inflammatory and allergic disorders; shock; diagnosis of Cushing's disease, congenital adrenal hyperplasia; cerebral oedema; nausea and vomiting with chemotherapy; rheumatic disease; see also notes above.

Cautions, Contraindications, Drug interactions and Side effects; see notes above

Side effects: see notes above; perineal irritation may follow intravenous administration of the phosphate ester.

Dose and Administration: *Oral:* usual range 0.5-10mg daily. IM injection or slow IV injection or infusion (as dexamethasone phosphate), initially 0.5-20mg; Child 200-500 micrograms/kg daily. Cerebral oedema (as dexamethasone phosphate), intravenous injection, 10mg initially, then 4mg by intramuscular injection every 6 hours as required for 2-10 days. Shock (as dexamethasone phosphate), intravenous injection or infusion, 2-6mg/kg, repeated in necessary after 2-6 hours. *Note: Dexamethasone 1mg ≈ dexamethasone phosphate 1.2mg ≈ dexamethasone sodium phosphate 1.3 mg*

Storage:at room temperature.

Fludrocortisone Acetate

Tablet, 0.1mg, 0.3 mg

Indications: partial replacement therapy for primary and secondary adrenocortical insufficiency in Addison's disease; treatment of salt-losing adrenogenital syndrome.

Cautions, Contraindications, Drug interactions and Side effects; see notes above.

Dose and Administration: *Oral:*Adult: 0.1-0.2 mg/day with ranges of 0.1 mg 3 times/week to 0.2 mg/day. Addison's disease: initial: 0.1mg/day; if transient hypertension develops, reduce the dose to 0.05 mg/day. Preferred administration with cortisone (10-37.5 mg/day) or hydrocortisone (10-30mg/day). Infant and Child: 0.05-0.1mg/day

Storage:store in well-closed container and at room temperature.

Fluticasone Furoate

Nasal Spray, 27.5mcg

Indications: prophylaxis and treatment of allergic rhinitis and perennial rhinitis; nasal polyps

Cautions: Corticosteroid nasal preparations should be avoided in the presence of untreated nasal infections, and also after nasal surgery (until healing has occurred); they should also be avoided in pulmonary tuberculosis. Patients transferred from systemic corticosteroids may experience exacerbation of some symptoms. Systemic absorption may follow nasal administration particularly if high doses are used or if treatment is prolonged. The height of children receiving prolonged treatment with nasal corticosteroids should be monitored; if growth is slowed, referral to a paediatrician should be considered.

Contraindication: intolerance to corticosteroids, glaucoma, infections (fungal, bacterial or parasitic or systemic viral), nasal septic ulcers, nasal trauma, nasal surgery

Drug interactions: Nelfinavir, Ritonavir

Side effects: Local side-effects include dryness, irritation of nose and throat, nasal ulceration and epistaxis. Raised intra-ocular pressure or glaucoma may occur rarely. Headache, smell and taste disturbances may also occur. Hypersensitivity reactions, including bronchospasm, have been reported.

Dose and Administration: Rhinitis: 100 micrograms (2 sprays) into each nostril once daily, preferably in the morning, increased to maximum twice daily if required; when control achieved reduce to 50 micrograms (1 spray) into each nostril once daily; child 4–11 years, 50 micrograms (1 spray) into each nostril once daily, preferably in the morning, increased to maximum twice daily if required. Nasal polyps: Adult and Adolescent over 16 years, 200 micrograms (approx. 6 drops) into each nostril once or twice daily; consider alternative treatment if no improvement after 4–6 weeks.

Hydrocortisone

Tablet (Acetate), 5mg, 10 mg

Injection (sodium succinate), 50mg/ml in 2ml ampoule, 125mg/ml

Powder for injection, 25mg/amp, 500mg in vial

Indications: adrenocortical insufficiency; hypersensitivity reactions including anaphylactic shock inflammatory bowel disease.

Cautions, Drug interactions, Contraindications and Side effects; see notes above

Dose and Administration: Replacement therapy in adrenocortical insufficiency: *Oral:* Adult: 20 - 30mg daily in

divided doses (usually 20 mg in the morning and 10 mg in early evening), Child, 10 - 30mg.

Acute adrenocortical insufficiency: Slow IV injection or IV infusion: Adult: 100 – 500 mg, 3 - 4 times in 24 hours or as required; Slow IV injection, Child up to 1 year 25mg, 1-5 years 50mg, 6 - 12 years 100mg.

Reconstitution and Administration: According to manufacturer's directions.

Storage: At room temperature, in a tight, light resistant container, protect from freezing. *Note: Reconstituted solutions should be used only if it is clear and should be discarded after 3 days. After reconstitution, protect the solution from light.*

Methylprednisolone Acetate

Injection (aqueous suspension), 40 mg/ml, 80mg/ml in 1 and 2ml ampoules

Indications: treatment of rheumatoid arthritis, osteoarthritis, bursitis and other non-infectious inflammatory conditions. Anti-inflammatory effects may be evident within 12-24 hours and usually last 3-4 weeks.

Cautions, Contraindications, Drug interactions and Side effects; see notes above.

Dose and Administration: Intra-articular, large joints (knees, ankles, shoulders) 20-80mg; medium joints (elbows, wrists) 10-40mg; small joints (metacarpophalangeal, interphalangeal, sternoclavicular, acromioclavicular) 4-10 mg. Soft-tissue injection, up to 60 mg, depending on the amount of inflamed tissue.

Storage: store at room temperature.

Prednisolone

Tablet, 1mg, 3.5mg, 5mg, 10mg

Injection (Sodium Phosphate), 10mg/ml, 25mg/ml in 2ml ampoule

Indications: suppression of inflammatory and allergic disorders; inflammatory bowel disease, asthma, and rheumatic disease, for the treatment of adrenocortical insufficiency and as immune suppression.

Cautions, Contraindications, and Drug interactions and Side effects; see notes above.

Intra articular injection of prednisolone is contraindicated in patients with arthroplasty of joint; blood clotting disorders, intra articular fracture, current or history of periarticular infection, osteoporosis & unstable joint. *Note: owing to its less pronounced mineralocorticoids activity prednisolone is less likely than hydrocortisone to cause sodium retention, electrolyte imbalance, and oedema.*

Dose and Administration:Suppression of inflammatory and allergic disorders: Oral: Adult: initially up to 10 - 20mg daily (severe disease, up to 60mg daily), preferably taken in the morning after breakfast: dose can often be reduced within a few days, but may need to be continued for several weeks or months: maintenance, 2.5 - 15mg daily or higher; cushingoid features are increasingly likely with doses above 7.5mg daily; Child: fractions of adult dose may be used (for example, at 1 year 25% of adult dose, at 7 years 50%, and at 12 years 75%) but clinical factors must be given due weight.

Storage: store in a tight container at room temperature. Protect from freezing and light.

Triamcinolone Acetonide

Tablet, 4mg

Injection, 10mg/ml, 40mg/ml in 1ml vial

Indications: suppression of inflammatory and allergic disorders; rheumatic disease.

Cautions, Drug interactions, Contraindications, Side effects see notes above. Anorexia, weight loss, flushing, depression, and muscle wasting are reported to have been particularly associated with Triamcinolone.

Dose and Administration: Oral: 4 - 48mg daily although daily doses over 32mg is seldom indicated.

Deep intramuscular injection, into gluteal muscle, 40mg of Acetonide for depot effect, repeated at intervals according to the patient's response, maximum single dose 100mg.

Storage: at room temperature. Protect from freezing and light.

9.3. Thyroid Hormones and Antithyroid Agents

Thyroid agents are natural or synthetic agents containing levothyroxine (thyroxine) or liothyronine (tri-iodothyronine). The principal effect is to increase the metabolic rate. They also exert a cardio stimulatory effect which may be the result of a direct action on the heart. The main agent for thyroid replacement and described in this section is thyroxin. It is used in hypothyroidism (myxoedema) and also in diffuse non-toxic goiter, Hashimoto thyroiditis (lymphadenoid goiter) and thyroid carcinoma. Neonatal hypothyroidism requires prompt treatment for normal development.

Thyroxin Sodium (Levothyroxine Sodium) is the treatment of choice for maintenance therapy. It is almost completely absorbed from the gastrointestinal tract but the full effects are not seen for up to 1 to 3 weeks after beginning therapy; there is a slow response to dose change and effects may persist for several weeks after withdrawal. Dosage of thyroxin sodium in infants and children for congenital hypothyroidism and juvenile myxoedema should be titrated according to clinical

response, growth assessment and measurement of plasma thyroxine and thyroid stimulating hormone.

Antithyroid drugs are used for hyperthyroidism either to prepare patients for thyroidectomy or for long-term management.

Antithyroid agents are used to achieve euthyroidism in patients with thyrotoxicosis. Propylthiouracil and carbimazole, interfere with thyroxine synthesis in the thyroid gland and are used mainly to prepare patients for surgery or irradiation, or in the long-term management of hyperthyroidism associated with Grave's disease.

Antithyroid drugs do not block the release of stored thyroid hormones and it is only when the performed hormones are depleted and concentrations of circulating hormones decline that clinical effects become apparent. An additional action of propylthiouracil is inhibition of the peripheral deiodination of thyroxine to tri-iodothyronine.

Propylthiouracil is given in a dose of 200 to 400mg daily in adults and this dose is maintained until the patient becomes euthyroid; the dose may then be gradually reduced to a maintenance dose of 50 to 150mg daily.

Antithyroid drugs only need to be given once daily because of their prolonged effect on the thyroid. Over-treatment with the rapid development of hypothyroidism is not uncommon and should be avoided particularly during pregnancy because it can cause fetal goiter.

Pregnancy and breastfeeding: Propylthiouracil cross the placenta and in high doses may cause fetal goiter and hypothyroidism- the lowest dose that will control the hyperthyroid state should be used (requirements in Graves disease tend to fall during pregnancy). Propylthiouracil appears in breast milk but this does not preclude breastfeeding as long as

neonatal development is closely monitored and the lowest effective dose is used.

Iodine has been used as an adjunct to antithyroid drugs for 10 to 14 days before partial thyroidectomy; however, there is little evidence of a beneficial effect. Iodine should not be used for long-term treatment because its antithyroid action tends to diminish. In patients in whom drug therapy fails to achieve long-term remissions definitive treatment with surgery or (increasingly) radioactive iodine is preferable.

Propranolol is useful for rapid relief of thyrotoxic symptoms and may be used in conjunction with antithyroid drugs or as an adjunct to radioactive iodine. Beta-blockers are also useful in neonatal thyrotoxicosis and in supraventricular arrhythmias due to hyperthyroidism. Propranolol has been used in conjunction with iodine to prepare mildly thyrotoxic patients for surgery but it is preferable to make the patient euthyroid with carbimazole. Laboratory tests of thyroid function are not altered by beta-blockers. Most experience is treating thyrotoxicosis has been gained with propranolol but nadolol is also used.

Iodine + Potassium Iodide (Aqueous Iodine oral solution or Lugol's solution)

Solution, 5% + 10%

Indications: thyrotoxicosis (pre-operative).

Cautions: pregnancy, children; not for long-term treatment.

Contraindications: breastfeeding.

Side effects: hypersensitivity reactions including Coryza - like symptoms, headache, lacrimation, conjunctivitis, pain in salivary glands, laryngitis, bronchitis, rashes; on prolonged treatment depression, insomnia, impotence; goiter in infants of mothers taking iodides.

Dose and Administration: 0.3ml 3 times daily well diluted with milk or water.

Carbimazole

Tablet, 5 mg

Indications: hyperthyroidism.

Cautions: impaired liver function, tracheal obstruction.

Drug interactions: oral anticoagulants and heparin.

Contraindications: hypersensitivity to carbimazole.

Side effects: pruritus, skin rashes, non-specific gastrointestinal disturbances, headache, mild arthralgia, urticaria, alopecia, drug-induced agranulocytosis, cholestatic hepatitis with jaundice, blood dyscrasias and "drug-fever" reactions.

Dose and Administration: *Oral:* Adult: Initially 20 - 60 mg daily until there is euthyroidism. Maintenance: 5 - 15 mg as a single daily dose.

Child: the usual initial daily dose is 15mg per day.

Storage: do not store above 25°C; Store in the original container.

Propranolol

Tablet, 10mg, 40mg

Injection, 1mg/ml in 1ml ampoule

See notes above and section 3.3 under propranolol

Propylthiouracil

Tablet, 25mg, 50mg, 100mg

Indications: hyperthyroidism

Cautions: liver disorders, pregnancy, breast-feeding, reduce dose in renal impairment.

Side effects: nausea, mild gastrointestinal disturbances headache, rashes and pruritus, arthralgia; rarely alopecia, bone

marrow suppression, urticaria, leucopenia; rarely coetaneous viscosities, thrombocytopenia, aplastic anaemia, hepatitis, lupus erythematous - like syndromes.

Dose and Administrations: see notes above

Storage: at room temperature.

Thyroxin Sodium

Tablet, 0.05mg, 0.1mg

Indications: hypothyroidism

Cautions: cardiovascular disorders (myocardial insufficiency or ECG evidence of myocardial infarction); hypopituitarism or predisposition to adrenal insufficiency (must be corrected by corticosteroid prior to initial levothyroxine); elderly, long-standing hypothyroidism, diabetes insipidus, diabetes mellitus (may need to increase dose of insulin or oral antidiabetic drug); pregnancy; breast feeding.

Drug interactions: warfarin.

Contraindications: thyrotoxicosis, cholestyramine or colestipol, sympathomimetics.

Side effects: (usually with excessive dose) anginal pain, arrhythmias, palpitations, tachycardia, skeletal muscle cramps, diarrhea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight and muscular weakness.

Dose and Administration: Hypothyroidism: Oral: Adult: initially 50 - 100micrograms daily (25-50 micrograms for: those over 50 years) before breakfast, increased by 25 - 50 micrograms every 3 - 4 weeks until normal metabolism maintained (usual maintenance dose, 100 - 200 micrograms daily); where there is cardiac disease, initially 25 micrograms daily or 50 micrograms on alternate days, adjusted in steps of 25 micrograms every 4 weeks. Congenital hypothyroidism and

juvenile myxoedema: Oral: Child: up to 1 month, initially 5 - 10 micrograms/kg daily, adjusted in steps of 25 micrograms every 2 - 4 weeks, until mild toxic symptoms appear, then reduce dose slightly.

Storage: at room temperature store in a tight light resistant container.

9.4. Insulin and oral antidiabetic agents

Diabetes mellitus is a disorder of carbohydrate metabolism in which the action of insulin is diminished or absent through altered secretion, decreased insulin activity, or a combination of both factors. There are two principal classes of diabetes (and many sub types not listed here):

Type I diabetes: Type I diabetes, also referred to as insulin dependent diabetes mellitus (IDDM), is due to a deficiency of insulin following autoimmune destruction of pancreatic beta cells. Patients with type I diabetes require administration of insulin.

Type II diabetes: Type II diabetes, also referred to as non-insulin dependent diabetes (NIDDM), is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Although patients may be controlled on diet alone, many require administration of oral antidiabetic drugs or insulin to maintain satisfactory control.

The aim of treatment is to achieve the best possible control of plasma glucose concentration and prevent or minimize complications including microvascular complications (retinopathy, albuminuria, neuropathy).

Diabetes mellitus is a strong risk factor for cardiovascular disease. Other risk factors such as smoking, hypertension, obesity and hyperlipidaemia should also be addressed.

Management of diabetes mellitus

Insulin: Insulin plays a great role in the regulation of carbohydrate, fat and protein metabolism. It is a polypeptide hormone of complex structure. There are differences in the amino acid sequence of animal insulin's, human insulin's and the human insulin analogues. Insulin may be of beef or pork origin or it may be human insulin produced by gene technology or by modification of porcine insulin.

All insulin preparations are to a greater or lesser extent immunogenic in man but immunological resistance to insulin action is uncommon. Human and Porcine insulin are less immunogenic than bovine insulin and where possible most newly diagnosed IDDM patients are now given human insulin. Insulin of whatever origin is formulated to provide a range of preparations offering:

- Short duration which have a relatively rapid onset of action, namely soluble insulin, insulin lispro and insulin aspart.
- Intermediate action, e.g isophane insulin and insulin zinc suspension; and
- Long action which have a relatively slower in onset, e.g. Crystalline insulin Zinc suspension

For those who require administration of insulin, appropriate combinations of insulin therapy will have to be worked out for the individual patient. In pregnancy insulin requirements should be monitored frequently.

Examples of recommended insulin regimens

- Short - acting insulin mixed with intermediate - acting insulin: twice daily (before meals)
- Short - acting insulin mixed with intermediate acting insulin before breakfast: Short-acting insulin before evening meal; and Intermediate-acting insulin: at bed time

- Short-acting insulin: three times daily (before breakfast, midday and evening meal)
- Intermediate - acting insulin at bedtime
- Intermediate-acting insulin with or without short-acting insulin once daily either before breakfast or at bedtime suffices for some patients with type II diabetes who need insulin, sometimes in combination with oral hypoglycemic drugs.

Insulin is inactivated by gastro-intestinal enzymes, and must therefore be given by injection; the subcutaneous route is ideal in most circumstances. It is usually injected in to the upper arms, thighs, buttocks, or abdomen; there may be increased absorption from a limb site if the limb is used in strenuous exercise following the injection. Generally subcutaneous insulin injections cause few problems; fat hypertrophy does however occur but can be minimized by rotating the injection site. Local allergic reactions are now rare. The various types of insulin may also be given intramuscularly when the onset of action is faster than with the subcutaneous route. An even faster onset may be achieved with intravenous administration, but this route is only suitable for fast-acting or soluble insulin.

Hypoglycemia: The most frequent complications of insulin therapy is hypoglycemia and patients taking insulin should be educated about its cause, symptoms, and treatment. Most patients can recognize the early warning signs of hypoglycemia and by taking sugar immediately they can prevent more serious symptoms developing. Comatose patients should be given intravenous glucose or, if this is not practicable, subcutaneous or intramuscular glucagons.

Hypoglycemia can also develop in patients taking oral hypoglycemic, notably the sulphonylureas. Some patients may no longer be able to recognize the warning signs of

hypoglycemia after transferring from animal to human insulin and these patients, if appropriate, should be transferred back to porcine insulin.

Car drivers need to be particularly careful to avoid hypoglycemia. They should check their blood glucose concentrations before driving and, on long journeys, at intervals of approximately two hours; they should ensure that a supply of sugar is always readily available. If hypoglycemia occurs the driver should switch off the ignition until recovery is complete (may be 15 minutes or longer). Driving is not permitted when hypoglycemic awareness has been lost. For sporadic physical activity departing from the patients usual daily routine extra carbohydrate may need to be taken to avert hypoglycemia. Blood glucose should be monitored before, during and after exercise.

Diabetic Ketoacidosis: Diabetic ketoacidosis results from a lack of insulin due to a number of factors and the onset may be over hours or days. It is characterized by hyperglycemia, hyperketonaemia, and acidaemia and is a medical emergency which should be treated promptly with fluid and electrolyte replacement and insulin. However, over vigorous fluid replacement without severe dehydration carries the risk of precipitating cerebral oedema.

Surgery: Insulin dependent diabetics who require surgery should be managed with a continuous intravenous insulin infusion. Insulin is given as normal the night before operation, and switched to either a variable rate infusion via a syringe pump, together with a 10% glucose drip, or to a combined insulin-glucose infusion, on the day of operation. Subsequent conversion back to subcutaneous insulin should be undertaken before breakfast, giving the first subcutaneous dose 30 minutes before stopping continuous infusion. Non - insulin

dependent patients should have any oral treatment omitted on the day of operation, and may be given insulin by a similar regimen if control is poor or deteriorates as can happen with major surgery.

Soluble insulin is a short - acting form of insulin. When injected subcutaneously it has a rapid onset of action (after 30 - 60 minutes), a peak action between 2 and 4 hours, and duration of action up to 8 hours when injected intravenously, soluble insulin has a very short half - life of only about 5 minutes.

When administered subcutaneous, intermediate-acting insulin's have an onset of action of approximately 1 - 2 hours, a maximal effect at 4 - 12 hours and duration of action of 16 - 24 hours. They can be given twice daily together with short - acting insulin or once daily, particularly in elderly patients. They can be mixed with soluble insulin in the syringe, essentially retaining properties of each component.

The duration of action of different insulin preparations varies considerably from one patient to another and this needs to be assessed for every individual. The type of insulin used and its dose and frequency of administration depend on the needs of each patient. For patients with acute onset diabetes mellitus, treatment should be started with soluble insulin given 3 times daily with medium acting insulin at bedtime. For those less seriously ill, treatment is usually started with a mixture of premixed short and medium acting insulin given twice daily. The proportions of soluble insulin can be increased in patients with excessive post-prandial hyperglycaemia. Patients should remain on the same insulin throughout treatment. Regimens should be developed by each country.

Acarbose

Tablet, 50mg, 100mg

Indications: diabetes mellitus inadequately controlled by diet or by diet with oral antidiabetic drugs

Cautions: monitor liver function; may enhance hypoglycaemic effects of insulin and sulfonylureas (hypoglycaemic episodes may be treated with oral glucose but not with sucrose); interactions: Appendix 1 (antidiabetics)

Contraindications: inflammatory bowel disease, predisposition to partial intestinal obstruction; hernia, previous abdominal surgery. Hepatic impairment: avoid. Renal impairment: avoid if eGFR less than 25 mL/minute/1.73 m². Pregnancy and Breast-feeding: avoid

Side-effects: flatulence, soft stools, diarrhoea (may need to reduce dose or withdraw), abdominal distention and pain; *rarely*, nausea, abnormal liver function tests and skin reactions; *very rarely* ileus, oedema, jaundice, and hepatitis

Note: Antacids unlikely to be beneficial for treating side-effects

Dose and administration: adults over 18 years, initially 50 mg daily increased to 50 mg 3 times daily, then increased if necessary after 6–8 weeks to 100 mg 3 times daily; max. 200 mg 3 times daily

Counselling: Tablets should be chewed with first mouthful of food or swallowed whole with a little liquid immediately before food. To counteract possible hypoglycaemia, patients receiving insulin or a sulfonylurea as well as acarbose need to carry glucose (not sucrose—acarbose interferes with sucrose absorption).

Biphasic Insulin (BP)⁺

Injection (highly purified), 100 units/ml in 10ml vial

Indications: diabetes mellitus (intermediate acting)

Cautions, Drug interactions, Side effects: see notes above and under soluble insulin; Protamine may cause allergic reactions

⁺ BP stands for Bovine and porcine

Dose and Administrations:By subcutaneous injection, according to requirements

Storage: store at 2⁰_C to 8⁰_C. Do not allow freezing protect from light.

Note: It should be gently shaken before use.

Biphasic Isophane Insulin (soluble/Isophane Mixture)

Injection, 50/50, 30/70, 100 units/ml in 10ml vial

Indications: diabetes mellitus (intermediate acting)

Cautions, Drug interactions, Side effects; see notes above and under soluble insulin; protamine may cause allergic reactions.

Dose and Administration:By subcutaneous injection, according to requirements

Storage: Store at 2⁰_C to 8⁰_C. Do not allow freezing protect from light.

Note: It should be gently shaken before use.

Insulin soluble /Neutral (HPB)*

Injection 100 units/ml

Indications: diabetes mellitus; diabetic emergencies and at surgery; diabetic ketoacidosis or coma.

Cautions: see notes above; reduce dose in renal impairment; occasionally insulin resistance necessitating large doses; pregnancy and breastfeeding; see also interactions.

Drug interactions: analgesics, antibacterials, antifungals, uricosurics.

Side effects: hypoglycaemia in overdose; localized and rarely generalized, allergic reactions; lipoatrophy at injection site; insulin resistance.

* HPB stands for Human, porcine, and Bovine

Dose and Administration: Diabetes mellitus: SC, IM, IV injection or infusion: Adult and Child according to individual requirements

Storage: store at 2°C to 8°C . Do not allow to freeze protect from light.

Insulin Zinc suspension/Insulin Lente (HPB)*

Injection 100 units/ml

Indications: diabetes mellitus (long acting)

Cautions, Drug interactions, Side effects: see notes above and under soluble insulin.

Dose and Administrations: By subcutaneous injection, according to requirements

Storage: store between 2°C and 8°C protect from freezing.

Isophane/NPH insulin (HPB)*

Injection, 100units/ml

Indications: diabetes mellitus **Cautions, Drug interactions, Side effects;** see notes above and under soluble insulin; Protamine may cause allergic reactions.

Dose and Administrations: By subcutaneous injection, according to requirements. Intravenous injection is contraindicated.

Storage: unopened vials of insulin should be stored at 2°C to 8°C and should not be subjected to freezing. The vial in use may be stored at room temperature; exposure to extremes in temperature or direct sunlight should be avoided.

Oral antidiabetic drugs

If patients with NIDDM have not achieved suitable control after about 3 months old dietary modification and increased physical activity, then oral hypoglycemic may be tried. The two major classes of oral hypoglycemic agents are the **sulphonylureas** and the **biguanides**. Sulphonylureas act mainly by increasing endogenous insulin secretion, whilst biguanides act chiefly by decreasing hepatic gluconeogenesis and increasing peripheral utilization of glucose. Both types of agents only function in the presence of some endogenous insulin production.

Oral treatment of NIDDM is usually begun with a sulphonylureas. Chlorpropamide has more adverse effects than the other sulphonylureas. It has a long half life and hence is considered to have an increased tendency to cause hypoglycaemia, although a recent large study reported that hypoglycaemic episodes were less frequent with chlorpropamide than Glibenclamide. Use of chlorpropamide is therefore inadvisable in the elderly; Glibenclamide is also best avoided for the same reason.

A sulphonylurea with a short half-life, such as tolbutamide, should be used instead in such patients. Unfortunately sulphonylureas can cause weight gain so severely obese patients may be treated with the biguanide metformin rather than a sulphonylurea. Metformin is as effective as the sulphonylurea in terms of blood glucose control but has a rare tendency to cause lactic acidosis in patients with renal failure and should therefore be avoided in patients at risk. Patients with NIDDM who cannot be controlled adequately by oral therapy and diet need to be given insulin either in addition to or in place of the oral therapy.

Contraindications: sulphonylureas should be avoided where possible in severe hepatic and renal impairment and in

porphyria. They should not be used while breast feeding and insulin therapy should be substituted during pregnancy. Insulin therapy should also be instituted temporarily during intercurrent illness (such as myocardial infarction, coma, infection, and trauma). Oral antidiabetic drugs should be omitted on the morning of surgery; insulin is often required because of the ensuing hyperglycaemia in these circumstances. Sulphonylureas are contraindicated in the presence of ketoacidosis.

Side effects: side effects of sulphonylureas are generally mild and infrequent and include gastro-intestinal disturbances such as nausea, vomiting, diarrhoea and constipation. They can occasionally cause a disturbance in liver function, which may rarely lead to cholestatic jaundice, hepatitis and hepatic failure. Hypersensitivity reactions can occur, usually in the first 6 - 8 weeks of therapy; they consist mainly of allergic skin reactions which progress rarely to erythema multiforme and exfoliative dermatitis, fever and jaundice; photosensitivity has rarely been reported with chlorpropamide. Blood disorders are also rare but may include leucopenia, thrombocytopenia, agranulocytosis, pancytopenia, haemolytic anaemia, and aplastic anaemia.

Chlorpropamide has appreciably more side effects, mainly because of its very prolonged duration of action and the consequent hazard of hypoglycaemia and it should generally no longer be used. It may also cause facial flushing after drinking alcohol; this effect does not normally occur with other sulphonylureas. Chlorpropamide may also enhance antidiuretic hormone secretion and very rarely cause hyponatraemia.

Biguanides: The biguanides are agents of first choice in the management of obese type 2 diabetics, but the small risk of lactic acidosis demands that they may be used with caution. Risk factors for lactic acidosis include: impaired renal or hepatic

function, cardiopulmonary insufficiency, presence of infections, excessive alcohol intake, and certain systemic illnesses, e.g. leukaemia.

Metformin is useful in management of obese diabetics because it induces a mild anorexia and so helps to control weight gain. The biguanides include metformin.

Glimepiride

Tablet, 3mg

Indications: treatment of type II diabetes mellitus

Cautions: pregnancy, hypoglycemia may be produced during use.

Drug interactions: CYP2C8/9 inhibitors (e.g. ketoconazole, NSAIDs, pioglitazone), beta blockers, chloramphenicol, cimetidine, fluconazole, salicylates, sulfonamides, tricyclic antidepressants may increase effect of Glimepiride. Glimepiride may increase effects of cyclosporines, CYP2C8/9 inducers may decrease effects of Glimepiride (e.g. carbamazepine, Phenobarbital, phenytoin, rifampin, estrogens, oral contraceptives, thiazides and other diuretics, NSAIDs, isoniazide)

Contraindications: hypersensitivity to glimepiride, other sulfonyl ureas or sulfonamides or to any of the excipients, breast feeding, insulin dependent diabetes, ketoacidosis (with or without coma), severe renal or hepatic function disorders. In case of severe renal or hepatic function disorders, a changeover to insulin is required.

Side effects: dizziness, headache, hypoglycemia, nausea, weakness, anorexia, heartburn, vomiting

Dose and Administration: oral:Adult:Starting dose: 1 mg glimepiride per day. If good control is achieved this dosage should be used for maintenance therapy.If control is

unsatisfactory the dosage should be increased, based on the glycaemic control, in a stepwise manner with an interval of about 1 to 2 weeks between each step, to 2, 3 or 4 mg glimepiride per day. A dosage of more than 4 mg glimepiride per day gives better results only in exceptional cases. *The maximum recommended dose is 6 mg glimepiride per day.*

Storage: at room temperature.

Metformin

Tablet, 500mg, 850mg

Indications: type 2 diabetes mellitus.

Cautions: substitute insulin during severe infection, trauma, surgery; breastfeeding.

Drug interactions: alcohol, cimetidine & other cationic medication excreted by renal tubular transport (such as: amiloride, nifedipine, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, vancomycin); Furosemide; vitamin B12.

Contraindications: renal impairment (withdraw if renal impairment suspected; hepatic impairment; heart failure; severe infections or trauma; dehydration; alcohol dependence; pregnancy.

Side effects: anorexia, nausea and vomiting, diarrhoea patients with renal failure (discontinue); decreased vitamin B12 absorption.

Dose and Administrations: Oral: Adult: 500mg every 8 hours or 850mg every 12 hours with or after food (maximum 2g daily in divided doses).

Storage: Store at room temperature in a light resistant container, unless otherwise specified by manufacturer.

Sulphonamides, Urea Derivatives

Sulphonylureas act mainly by stimulating the release of endogenous insulin. Some pancreatic beta-cell responsiveness should remain intact for these agents to be effective. They may provide good control of blood glucose and have been shown to reduce the microvascular complications of diabetes. They are used in the management of type 2 diabetes not controlled by diet alone, and may be given together with a biguanide if necessary to achieve control. The sulphonylureas in common use include glibenclamide, glimepiride, glipizide, chlorpropamide and tolbutamide.

Chlorpropamide

Tablet, 100mg, 250mg

Indications: type II diabetes mellitus.

Cautions, Contraindications, Side effects; see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administrations: Initially 250mg daily with breakfast (Elderly 100 - 125 mg but avoid - see notes above), adjusted according to response; maximum 500 mg daily.

Storage: Store in a well-closed container at room temperature

Glibenclamide

Tablet, 5mg

Indications: type II diabetes mellitus

Cautions, Side effects, Contraindications: see notes above

Drug interactions: analgesics (azapropazone, phenylbutazone and possibly other NSAIDs enhance effect of sulphonylureas), antibacterial, antifungals, uricosurics.

Dose and Administrations: Initially 5mg daily with or immediately after break fast (Elderly 2.5mg, but avoid - see

notes above), adjusted according to response, maximum 15mg daily.

Glimepiride

Tablet, 1mg, 2mg, 4mg

Indications: management of type 2 diabetes mellitus (NIDDM).

Cautions, Contraindications and Side effects: see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administration: Adult: Oral: initially 1 mg once daily, before breakfast. If necessary the dose may be increased by 1 mg at weekly intervals up to 6 mg daily, according to blood glucose levels; maximum 8 mg daily.

Glipizide

Tablet, 2.5 mg, 5 mg, 10 mg

Indications: management of type 2 diabetes mellitus (NIDDM).

Cautions, Contraindications and Side effects: see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administration: Adult: Oral: initially, 2.5 - 5 mg daily, 15 - 30 minutes before breakfast (2.5 mg in the elderly and in liver impairment), gradually increased, if necessary, to a maximum of 40 mg/day. Amounts exceeding 15 mg/day should be given in divided doses.

Storage: store at controlled room temperature.

Pioglitazone

Tablet, 15mg, 30mg, 45mg

Indications:Type 2 diabetes mellitus (NIDDM), monotherapy: Adjunct to diet and exercise, to improve glycemic control. Type 2 diabetes mellitus (NIDDM), combination therapy with

sulfonyl urea, metformin, or insulin: when diet, exercise, and a single agent alone does not result in adequate glycemic control.

Cautions: should not be used in diabetic ketoacidosis; use in type 1 diabetes is not recommended; anemia; not for use in children < 18 years of age.

Drug interactions: delavirdine, fluconazole, gemfibrozil, ketoconazole, nifedipine, NSAIDs, sulfonamides, amiodarone, fluoxetine, glimepiride, glipizide, phenytoin, sertraline, warfarin.

Contraindications: hypersensitivity reaction, active liver disease, patients who have experienced jaundice during therapy.

Side effects: serum triglycerides decreased, HDL-cholesterol increased, weight gain, upper respiratory tract infection, edema, headache, fatigue, hypoglycemia, anemia, myalgia, sinusitis, pharyngitis.

Dose and Administration: Oral: Adult: Monotherapy: Initial: 15-30 mg once daily; if response is inadequate, the dosage may be increased in increments up to 45mg once daily; maximum recommended dose: 45mg once daily. Combination therapy: Maximum recommended dose: 45mg/day

With sulphonylureas: Initial: 15-30 mg once daily;

With metformin: Initial: 15-30mg once daily

With insulin: Initial: 15-30mg once daily

Rosiglitazone maleate

Tablet, 1mg, 2mg, 4mg, 8mg

Indications: type 2 diabetes mellitus (noninsulin dependent, NIDDM): Monotherapy: improve glycemic control as an adjunct to diet and exercise; combination therapy: in combination with a sulphonylurea, metformin, or insulin when diet, exercise, and a single agent do not result in adequate glycemic control.

Cautions: diabetic ketoacidosis; use in type 1 diabetes; premenopausal, anovulatory women; anemia or depressed leukocyte count; edema.

Drug interactions: delavirdine, fluconazole, gemfibrozil, ketoconazole, nicardipine, NSAIDs, sulfonamides, amiodarone, fluoxetine, glimepride, glipizide, phenytoin, sertraline, warfarin.

Contraindications: active liver disease, patients who previously experienced jaundice during troglitazone therapy.

Side effects: weight gain, increase in total cholesterol, increased LDL-cholesterol, increased HDL-cholesterol, edema, headache, fatigue, hyperglycemia, hypoglycemia, diarrhea, anemia, back pain.

Dose and Administration: Oral: Adult: Monotherapy: Initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily. Combination therapy: With sulfonylureas: initial: 4 mg daily as a single daily dose or in divided doses twice daily; doses of sulfonylurea should be reduced if the patient reports hypoglycemia.

With metformin: initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily. With insulin: initial: 4 mg daily as a single daily dose or in divided doses twice daily. Doses of insulin should be reduced by 10% to 25% if the patient reports hypoglycemia or if the plasma glucose falls to < 100 mg/dl.

Saxagliptin+ Metformine

Tablet, 5mg+500mg, 5mg+1000mg, 2.5mg+1000mg

Indications: type II diabetes mellitus

Cautions: elderly; determine renal function before treatment and periodically thereafter; Hepatic impairment; Renal impairment

Contraindication: Pregnancy, Breast-feeding

Drug Interactions: Alcohol, Anabolic Steroids, Beta-blockers, Corticosteroids, Diazoxide, Diuretics, Loop, Diuretics, Thiazide and related, MAOIs, Oestrogens, Progestogens, Testosterone

Side-effects: vomiting, dyspepsia, gastritis; peripheral oedema; headache, dizziness, fatigue; upper respiratory tract infection, urinary tract infection, gastroenteritis, sinusitis, nasopharyngitis; hypoglycaemia, myalgia; less commonly dyslipidaemia, hypertriglyceridaemia, erectile dysfunction, arthralgia; also reported rash.

Dose: Adult over 18 years, 5 mg once daily

Thiazolidinediones

The thiazolidinediones, such as pioglitazone and rosiglitazone, improve glycaemic control by reducing cellular insulin resistance.

Tolbutamide

Tablet, 500mg

Indications: type II diabetes mellitus

Cautions, Contraindications; see notes above.

Side effects: see notes above, also headache, and tinnitus.

Drug interactions: see under Glibenclamide.

Dose and Administrations: 0.5 to 1.5g (maximum 2g) daily in divided doses; with or immediately after breakfast

Storage: store in a well-closed container at room temperature.

Gliclazide

Tablet (sustained release) 30 mg, 40 mg, 80mg

Indications: type 2 diabetes mellitus

Cautions: may encourage weight gain and should be prescribed only if poor control and symptoms persist despite adequate attempts at dieting

Contraindications: renal and hepatic impairment, pregnancy and breast feeding, should be avoided where possible in acute porphyria. It is contraindicated in the presence of ketoacidosis.

Side-effects: gastro-intestinal disturbances such as nausea, vomiting, diarrhoea, and constipation

Dose and Administration: Initially, 40–80 mg daily, adjusted according to response; up to 160 mg as a single dose, with breakfast; higher doses divided; max. 320 mg daily

9.5. Female Sex hormones and Combination preparations

Therapeutically, oestrogens, progestogens and their derivatives are used alone or in combination:

- In oral contraceptives to suppress ovulation.
- To control abnormalities in ovarian hormone secretion in the treatment of dysfunctional uterine bleeding and primary dysmenorrhoea.
- Peri and postmenopausally to relieve symptoms and to prevent and possibly treat the long-term sequelae of the menopause.
- To induce normal pubertal development in Turner's syndrome and other hypo-oestrogenic states. Patients with delayed puberty should be managed by a specialist as injudicious use of oestrogen can cause abnormal breast development.

They are also used in high doses in the palliative treatment of advanced prostatic carcinoma.

Chorionic Gonadotrophin

Powder for injection, 1500 IU, 5000 IU

Indications: induces ovulation and pregnancy in anovulatory, infertile females; treatment of hypogonadotrophic hypogonadism, prepubertal cryptorchidism; spermatogenesis induction with follitropin alfa or follitropin beta.

Cautions: asthma, epilepsy, migraine, or cardiovascular disorders, including hypertension, or renal disorders.

Contraindications: hypersensitivity to the drug; prostatic carcinoma, precocious puberty.

Side effects: headache, tiredness, changes in mood, depression, restlessness, edema, (especially in males), and pain on injection, gynaecomastia, ovarian hyperstimulation with marked ovarian enlargement or cyst formation, acute abdominal pain, ascites, pleural effusion, hypovolaemia, shock, and thrombo-embolic disorders in severe cases.

Dose and Administration: Adult: *I.M.*: Induction of ovulation: 5000-10,000 units given to mimic the midcycle peak of luteinising hormone. Up to 3 repeat injections of up to 5000 units each may be given within the following 9 days to prevent insufficiency of the corpus luteum. Prepubertal cryptorchidism (males): *IM*: 500-4000 units three times weekly. Delayed puberty associated with hypogonadism in males: *IM*: 500-1500 units twice weekly.

Storage: store at 2° to 15 °C in airtight containers; protect from light.

Conjugated estrogens (equine)

Vaginal cream, 0.625 mg/g base

Tablet, 0.3mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg, 2.5 mg

Indications: for replacement therapy in naturally occurring or surgically induced estrogen deficiency state associated with

menopausal and postmenopausal symptoms; e.g. hot flushes, sleep disturbances and atrophic vaginitis; prostatic cancer, breast cancer, abnormal uterine bleeding.

Cautions: postmenopausal women, endometriosis, asthma, epilepsy, migraine, coronary heart disease, diabetes or renal disorders; gallbladder disease, cholestatic jaundice.

Drug interactions: hydrocortisone, anticoagulants, aminoglutethimide, carbamazepine, phenobarbital, rifampin, nafcillin, nevirapine, phenytoin, ethanol, rifamycins.

Contraindications: hepatic dysfunction; a history of oestrogen dependent neoplasia such as breast or endometrial cancer, endometrial hyperplasia, undiagnosed vaginal bleeding, cerebrovascular accident; thrombosis or thromboembolic disorders; active thrombophlebitis, ophthalmic vascular disease; known or suspected pregnancy.

Side effects: there may be sodium and water retention with oedema, weight gain, tenderness and enlargement of the breasts, changes in libido, menstrual disorders and withdrawal bleeding, alterations in liver function, jaundice, gallstones, depression, headache, migraine, dizziness, a decrease in glucose tolerance, and decrease in tolerance of contact lenses. Nausea and vomiting and other gastro-intestinal disturbances. Skin reactions, cardiovascular effects (risk in blood pressure).

Dose and Administration:Adult:Atrophic vaginitis:

Vaginal cream: PV or Topicaly: 1-2 g daily, on a cyclical basis; maximum 4 g/day.Oral: initial: 0.3 mg/day; the lowest dose that will control symptoms should be used. May be given cyclically or daily, depending on medical assessment of patient.In menopausal and postmenopausal symptoms: Oral: 0.3 to 1.25 mg daily is given in conjunction with a progestogen in women with a uterus.Primary ovarian failure: Oral: 1.25 mg daily. Female hypogonadism: Oral: 2.5 to 7.5 mg daily administered

on a cyclical basis. Palliative treatment of prostatic carcinoma:
Oral: 1.25 to 2.5 mg three times daily. Abnormal uterine bleeding: Oral: 1.25 mg, may repeat every 4 hours for 24 hours, followed by 1.25 mg once daily for 7-10 days.

Storage: store in airtight containers and at room temperature.

Conjugated estrogens (equine) (initial phase) + Conjugated estrogens (equine) and Medroxyprogesterone acetate (second phase)

Biphasic tablet conjugated estrogens 0.625mg and conjugated estrogens 0.625mg / medroxyprogesterone acetate 5mg.

Indications: women with an intact uterus; treatment of moderate to severe vasomotor symptoms associated with menopause; treatment of atrophic vaginitis; osteoporosis (prophylaxis).

Contraindications: pregnancy.

Dose and Administration: *Oral: Adult:* One maroon conjugated estrogen 0.625mg tablet daily on days 1 through 14 and one light blue conjugated estrogen 0.625mg / MPA 5mg tablet daily on days 15 through 28.

Conjugated estrogens and Medroxyprogesterone acetate

Monophasic tablet, 0.3+1.5mg, 0.45+1.5mg, 0.625+2.5mg, 0.625+5mg

Dose and Administration: *Oral: Adult:*

One conjugated estrogen 0.3mg / MPA 1.5mg tablet daily; dose may be increased to one conjugated estrogen 0.625mg / MPA 5mg tablet daily.

Diensterol

Vaginal Cream 0.1%

Indications: treatment of atrophic vaginitis or other vaginal disturbances associated with hypoestrogenic conditions.

Cautions and Contraindications: abnormal vaginal bleeding, breast cancer, active/recent stroke or heart attack, asthma, diabetes, seizures, migraine headaches, liver disease, heart disease (e.g., high blood pressure, heart attacks, congestive heart failure), kidney disease, low thyroid hormone (hypothyroidism), abnormal calcium level in the blood, depression, high blood pressure during pregnancy (toxemia), cholestatic jaundice, uterine fibroids, endometriosis, cholesterol or lipid problems, gallbladder disease, excessive weight gain, certain blood disorder (porphyria), any allergies (especially peanut allergy).

Side effects: vaginal irritation, dizziness, lightheadedness, headache, stomach upset, bloating, nausea, weight changes, increased/decreased interest in sex, and breast tenderness, mental/mood changes (e.g., severe depression, memory loss), calf pain/swelling, sudden severe headache, chest pain, trouble breathing, one-sided weakness, slurred speech, vision changes, breast lumps, swelling of hands or feet, changes in vaginal bleeding, unusual vaginal discharge/itching/odor, yellowing of the eyes or skin, rash, itching, swelling, severe dizziness, trouble breathing.

Dose and Administration: the usual dosage range is one or two applicatorful per day for one or two weeks, then gradually reduced to one half initial dosages for a similar period. A maintenance dosage of one applicatorful, one to three times a week, may be used after restoration of the vaginal mucosa has been achieved.

Storage: store at room temperature and away from light and moisture.

Estradiol Valerate

Tablets, 1 mg, 2 mg

Indications: treatment and prophylaxis of menopausal and postmenopausal disorders, and in menstrual symptoms arising from estrogen deficiency.

Cautions, Contraindications and Side effects: as for the estrogens in general.

Dose and Administration: Adult:Oral: 1 - 2 mg daily, according to severity of symptoms and clinical response.

Storage: store at room temperature.

Estradiol + Estriol +Estrone

Monophasic tablet, 600mcg + 270mcg + 1.4 mg

Dose and Administration:

Menopausal symptoms and Osteoporosis prophylaxis: 1 to 2 tablets daily, with cyclical progestogen for 12 - 14 days of each cycle in women with intact uterus.

Estradiol

Tablet, 2mg

Intravaginal cream, 0.01 %

Pessary, 500 mcg

Indications: actions and uses similar to those described for the oestrogens in general.

Cautions, Contraindications and Side effects; similar to estrogens.

Dose and Administration:

Adult: Oral: initially 2-8 mg daily for 5-7 days; maintenance 2-4 mg daily, cyclically or continuously.

Atrophic vaginitis:PV, 1 applicator (0.5g) daily for 2-3 weeks, maintenance 1 application twice weekly.

Storage: stores in airtight containers.

Ethinyl estradiol

Tablet, 1 mg, 2mg

Indications: hormone replacement for menopausal symptoms, osteoporosis prophylaxis; palliation in breast cancer in men and postmenopausal women; contraception in combination with a progestogen.

Cautions: progestogen may need to be added to regimen to reduce risk of endometrial cancer due to unopposed estrogen; migraine; history of breast nodules of fibrocystic disease; uterine fibroids may increase in size; symptoms of endometriosis may be exacerbated; predisposition to thromboembolism; presence of antiphospholipid antibodies; increased risk of gall bladder disease; porphyria.

Drug interactions: rifampicin, ritonavir, warfarin, doxycycline, nevirapine, phenytoin.

Contraindications: pregnancy; estrogen - dependent cancer; active thrombophlebitis or thromboembolic disorders; undiagnosed vaginal bleeding; breastfeeding; liver disease, Dubin Johnson and Rotot syndromes.

Side effects: nausea and vomiting, abdominal cramps and bloating; weight increase; breast enlargement and tenderness; premenstrual - like syndrome; sodium and fluid retention; changes in liver function; cholestatic jaundice; rashes and chloasma, changes in libido; depression, headache, migraine, dizziness, leg cramps; contact lenses may irritate.

Dose and Administration: Oral: **Adult:** Hormone replacement (female): 10 - 20 mcg daily. Palliation in breast cancer in postmenopausal women: 0.1- 1 mg 3 times daily.

Storage: store at room temperature

Etonogestrol+ Ethinyl estradiol

Vaginal ring, 11.7mg+2.7mg

The ring should be placed in the vagina and left in place for 3 weeks. After 3 weeks, it is removed for a 1-week break; then a new ring is inserted. The directions on the label should be followed carefully. More than one contraceptive ring at a time should never be used. The contraceptive ring should be inserted and removed on the same day of the week and at about the same time of day.

Hydroxyprogesterone Caproate

Injection, 250 mg/ml in 1 ml ampoule

Indications: used for recurrent miscarriage and various menstrual disorders.

Dose and Administration: *Recurrent miscarriage associated with proven progesterone deficiency: IM: 250-500mg weekly given during the first half of pregnancy.*

Norethisterone (Norethindrone)

Tablet, 5 mg

Indications: endometriosis; menorrhagia; severe dysmenorrhoea; contraception (section - 8.4.1); hormone replacement therapy (HRT).

Cautions: epilepsy; migraine; diabetes mellitus; hypertension; cardiac or renal disease and those susceptible to thromboembolism; depression; breast-feeding.

Drug interactions: carbamazepine, ciclosporine, dexamethasone, fludrocortisone, glibenclamide, griseofulvin, hydrocortisone, insulins, metformin, nevirapine, phenobarbital, phenytoin, prednisolone, rifampicin, warfarin.

Contraindications: pregnancy, undiagnosed vaginal bleeding; hepatic impairment or active liver disease; severe arterial disease, breast or genital tract cancer, porphyria; history in

pregnancy of idiopathic jaundice, severe pruritus or pemphigoid gestations.

Side effects: acne, urticaria, fluid retention, weight increase, gastrointestinal disturbances, changes in libido, breast discomfort, premenstrual symptoms, irregular menstrual cycles, depression, insomnia, somnolence, alopecia, hirsutism, anaphylactoid - like reactions; exacerbation of epilepsy and migraine; rarely jaundice.

Dose and Administration: Adult: Oral: Endometriosis: 10 mg daily starting on fifth day of cycle (increased if spotting occurs to 20 - 25 mg daily, reduced once bleeding has stopped).

Menorrhagia: 5 mg three times daily for 10 days to stop bleeding; to prevent bleeding 5 mg twice daily from day 19 to 26 of cycle. *Dysmenorrhoea:* 5 mg 2 - 3 times daily from day 5 to 24 for 3 to 4 cycles.

Storage: protect from light.

9.6. Male sex hormone Preparations and its antagonists

Mesterolone

Tablet, 25 mg

Indications: replacement therapy for adult on set hypogonadism or following parenteral therapy after secondary sexual characteristics have developed

Cautions, Contraindications, Drug interactions and Side effects; see under testosterone.

Dose and Administration: Adult: Oral: initially 25 mg 3 times daily; maintenance 25 mg once or twice daily, depending on individual response.

Storage: protect from light.

Testosterone

Indications: hypogonadism; palliative treatment of advanced breast cancer in women.

Cautions: cardiac, renal or hepatic impairment; elderly, ischaemic heart disease, hypertension, epilepsy, skeletal metastases (risk of hypercalcaemia); regular examination of prostate during treatment; prepubertal boys.

Drug interactions: glibenclamide, insulins, metformin, warfarin.

Contraindications: breast cancer in men, prostate cancer, hypercalcaemia, pregnancy, breastfeeding, nephrosis, and history of primary liver tumours.

Side effects: prostate abnormalities and prostate cancer, headache, depression, gastrointestinal bleeding, nausea, cholestatic jaundice, changes in libido, gynaecomastia, anxiety, asthenia generalized paraesthesia, electrolyte disturbances including sodium retention with oedema and hypercalcaemia; increased bone growth; androgenic effects such as hirsutism, male pattern baldness, seborrhoea, acne, priapism, precocious sexual development and premature closure of epiphyses in prepubertal males, virilism in females, and suppression of spermatogenesis in men.

Storage: protect from light and store at room temperature.

Preparations include:

Testosterone propionate

Injection, 10mg/ml, 100 mg/ml, 250 mg/ml in 1 ml ampoule

Dose and Administration: IM: 50mg two or three times weekly.

**Testosterone propionate + Testosterone phenyl propionate
+Testosterone isocaproate + Testosterone decanoate**

Injection, 30 mg + 60 mg + 60 mg + 100 mg

Dose and Administration: *IM:* usually 1ml every 4 weeks.

9.7. Contraceptives

Hormonal Contraceptives

Hormonal contraceptives are only generally available for women although preparations for men are being evaluated. Oral contraceptives are divided in to 2 main types: combined (containing an oestrogen and a progestogen) and progestogen - only: They produce a contraceptive effect mainly by suppressing the hypothalamic pituitary system resulting in prevention of ovulation. In addition changes in the endometrium make it unreceptive to implantation and changes in the cervical mucus may prevent sperm penetration.

Combined Oral Contraceptives: Oral contraceptives containing an oestrogen and a progestogen are the most effective preparations for general use. Advantages of combined oral contraceptives include:

- Reliable and reversible.
- Reduced dysmenorrhoea and menorrhagia;
- Reduced incidence of premenstrual tension.
- Less symptomatic fibroids and functional ovarian cysts;
- Less benign breast disease
- Reduced risk of ovarian and endometrial cancer
- Reduced risk pelvic inflammatory disease, which may be a risk with intra uterine devices.

An association between the amount of estrogen and progestogen in oral contraceptives and an increased risk of adverse cardiovascular effects has been observed.

The oestrogen content ranges from 20 to 50 micrograms and generally a preparation with the lowest oestrogen and progestogen content which gives good cycle control and minimal side - effects in the individual woman is chosen.

The risk of hypertension increases with increasing duration of oral contraceptive use and they should be discontinued if the woman becomes hypertensive during use. Combined oral contraceptives are associated with an increased risk of thromboembolic and thrombotic disorders and an increase in risk of cerebrovascular disorders including stroke and subarachnoid hemorrhage.

Risk factors for venous Thromboembolism or Arterial disease: Risk factors for venous thromboembolism include family history of venous thromboembolism in first degree relative age less than 45 years, obesity, long-term immobilization and varicose veins.

Risk factors for arterial disease: Risk factors for arterial disease include family history of arterial disease in first - degree relative age under 45 years, diabetes mellitus, hypertension, smoking, age over 35 years, obesity and migraine.

If 2 or more factors for either venous thromboembolism or arterial disease are present, combined oral contraceptives should be avoided. Combined oral contraceptives are contraindicated if there is severe or focal migraine

Estrogen containing oral contraceptives should be discontinued four weeks prior to major elective surgery and all surgery to the legs. When discontinuation is not possible consideration, should be given to the prophylactic use of subcutaneous heparin.

Reasons to Stop Combined Oral Contraceptives Immediately: Combinedestrogen-containing oral contraceptives

should be stopped immediately if any of the following symptoms occur.

- Sudden severe chest pain (even if not radiating to left arm):
- Sudden breathlessness (or cough with blood stained sputum)
- Severe pain in calf of one leg
- Severe stomach pain
- Serious neurological effects including unusual, severe, prolonged headache especially if first time or getting progressively worse or sudden partial or complete loss of vision or sudden disturbance of hearing or other perceptual disorders or dysphagia or bad fainting attack or collapse or first unexplained epileptic seizure or weakness, motor disturbances, very marked numbness suddenly affecting one side or one part of body:
- Hepatitis, jaundice, liver enlargement;
- Severe depression
- Blood pressure above systolic 160mmHg and diastolic 100mmHg;
- Detection of a risk factor.

Diarrhea and vomiting: Diarrhea and vomiting up to 3 hours after taking an oral contraceptive or very severe diarrhea can interfere with its absorption. Additional precautions should therefore be used during and for 7 days after recovery. If the vomiting and diarrhoea occurs during the last 7 tablets, the next pill - free intervals should be omitted (in the case of every day tablets the inactive ones should be omitted).

Interactions: The effectiveness of both combined and progestogen only oral contraceptives may be considerably reduced by interaction with drugs that induce hepatic enzyme activity (e.g carbamazepine, griseofulvin, modafinil, nelfinavir, nevirapine, oxcarbazepine, phenytoin, phenobarbital, primidone, ritonavir, topiramate, and above all, rifabutin and rifampicin);

advice on the possibility of interaction with newer antiretroviral drugs should be sought from HIV specialists: some broad-spectrum antibiotics (eg. Ampicillin, doxycycline) may reduce the efficacy of combined oral contraceptives by impairing the bacterial flora responsible for recycling of ethinylestradiol from the large bowel.

Effectiveness of oral progestogen only preparations is not affected by broad-spectrum antibiotics but is reduced by enzyme inducing drugs.

Progestogen-only contraceptives: Progestogen only contraceptives, such as oral levonorgestrel may offer a suitable alternative when estrogens are contraindicated but the oral progestogen only preparations do not prevent ovulation in all cycles and have a higher failure rate rather than combined estrogen containing preparations. Progestogen - only contraceptives carry less risk of thromboembolic and cardiovascular disease than combined oral contraceptives and are preferable for women over 35 years, for heavy smokers, and for those with hypertension, valvular heart disease, diabetes mellitus, and migraine, they can be used as an alternative to estrogen containing combined preparations prior to major surgery. Menstrual irregularities (oligomenorrhoea, menorrhagia, and amenorrhoea) are common. Injectable preparations of Medroxy progesterone acetate or norethisterone enanthate may be given intramuscularly. They have prolonged action and should only be given with full counseling and manufacturer's information leaflet.

One tablet daily, on a continuous basis, starting on day 1 of cycle and taken at the same time each day (if delayed by longer than 3 hours contraceptive protection may be lost). Additional contraceptive precautions are not necessary when initiating treatment.

Changing from a combined oral contraceptive: start on the day following completion of the combined oral contraceptive course without a break (or in the case of every day tablets omitting the inactive ones).

After childbirth: start any time after 3 weeks postpartum (increased risk of breakthrough bleeding if started earlier) - lactation is not affected.

Emergency contraception: Emergency contraception can be obtained using levonorgestrel, one tablet of 750 micrograms should be taken as soon as possible (within 72 hours) after unprotected intercourse followed 12 hours later by another one tablet. Under those circumstances it prevents about 86% of pregnancies that would have occurred if no treatment had been given. Adverse effects include nausea, vomiting, headache, dizziness, breast discomfort, and menstrual irregularities. If vomiting occurs within 2-3 hours of taking the tablets, replacement tablets can be given orally with an antiemetic. It should be explained to the woman that her next period may be early or late; that she needs to use a barrier contraceptive method until her next period, and that she should return promptly if she has any lower abdominal pain or if the subsequent menstrual bleed is abnormally light, heavy, brief or absent. There is no evidence of harmful effects to the fetus if pregnancy should occur.

9.7.1. Combined Oral Contraceptives

Drospirenone+Ethinyl Estradiol

Tablet (film coated), 3mg+0.03mg, 3mg+0.02mg

Indications: oral contraceptive

Contraindications: hypersensitivity to ethinyl estradiol; drospirenone or any components of the formulation; severe hypertension history of or current thrombophlebitis or venous

thromboembolic disorder cerebral vascular disease; coronary artery disease.

Side effects: nausea; withdrawal bleeding may occur. **Dose and Administration:** *oral:* 1 tablet daily for 28 consecutive days. Dose should be taken at the same time each day either after the evening meal or at bed time.

Storage: store at 25⁰ c

Levonorgestrel (D-Norgestrel) + Ethinylestradiol and Iron tablets* *Tablet, (0.15mg + 0.03mg, 0.25mg + 0.05mg, 0.5mg + 0.05mg; 0.3mg + 0.03mg), 0.05mg+0.03mg (6tablets), 0.075mg+0.05 (5tablets), 0.125mg+0.03mg (10 tablets)*

Norethindrone (Norethisterone) + Ethinylestradiol*
Tablet, 0.5mg + 0.035m

Norethindrone (Norethisterone) + Mestranol and iron tablets* *Tablet, 1mg + 0.05mg)*

Indications: contraception, menstrual symptoms, endometriosis.

Cautions: risk factor for venous thromboembolism and arterial disease (see notes above); migraine; hyperprolactinaemia (seek specialist advice); some types of hyperlipidaemia; gallbladder disease; depression; long-term immobilization, sickle-cell disease; inflammatory bowel disease including crohn disease; see also interactions

Drug interactions: see notes above

* Each iron Tablet contains: Ferrous fumarate 75 mg

Contraindications: pregnancy; twenty-one days postpartum; breastfeeding until weaning or for first 6 months postpartum; personal history of venous or arterial thrombosis, heart disease associated with pulmonary hypertension or risk of embolism; migraine; history of sub-acute bacterial endocarditis; ischaemic cerebrovascular disease; liver disease, including disorders of hepatic secretion such as Dubin - Johnson or Rotor syndromes, infections hepatitis (until liver function normal); porphyria; systemic lupus erythematosus; liver adenoma; history of cholestasis; gall stones: estrogen - dependent neoplasms; neoplasms of breast or genital tract; undiagnosed vaginal bleeding; history during pregnancy of pruritus, chorea, herpes, deteriorating otosclerosis; cholestatic jaundice; pemphigoid gestationis; diabetes mellitus (if either retinopathy, neuropathy or if more than 20 years duration); after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values)

Side effects: nausea, vomiting, headache, breast tenderness, increase in body weight, thrombosis, changes in libido, depression, chorea, skin reaction, chloasma, hypertension, impairment of liver function, 'spotting' in early cycles, absence of withdrawal bleeding, irritation of contact lenses; rarely, photosensitivity and hepatic tumours; breast cancer (small increase in risk of breast cancer during use which reduces during the 10 years after stopping; risk factor seems related to age at which contraceptive is stopped rather than total duration of use; small increase in risk of breast cancer should be weighed against the protective effect of the ovary and endometrium)

Dose and Administrations: Contraception (21 - day combined (monophasic) preparations), by mouth, Adult (female), 1 tablet ('pill') daily for 21 days; subsequent courses repeated after 7 - day pill - free interval (during which withdrawal bleeding

occurs). Administration each tablet (pill') should be taken at approximately the same time each day; if delayed by longer than 24 hours contraceptive protection may be lost. It is important to bear in mind that the critical time for loss of protection is when a pill is omitted at the beginning or end of a cycle (which lengthens the pill - free interval).

Note: The following advice is recommended. If you forget a pill, take it as soon as you remember, and the next one at the normal time. If you are 12 or more hours late, the pill may not work; as soon as you remember, continue normal pill - taking, but for 7 days an additional method of contraception such as the sheath will be required. If the 7 days run beyond the end of your packet, start the next packet when you have finished the present one - do not have a gap between packets.

Storage: at room temperature, in a well - closed container.

9.7.2 Progestogen - only contraceptives

Indications: contraception

Cautions: heart disease, sex-steroid dependent functional ovarian cysts, active liver disease, recurrent cholestatic jaundice, history of jaundice in pregnancy; see also interactions

Drug interactions: see notes above under interaction and progestogen only contraceptives notes.

Contraindications: pregnancy, undiagnosed vaginal bleeding; severe arterial disease; liver adenoma, porphyria; after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values); see notes above

Side effects: menstrual irregularities (see also notes above); nausea, vomiting, headache dizziness, breast discomfort, depression, skin disorders, disturbance of appetite, weight changes, changes in libido.

Breast cancer: There is a small increase in the risk of having breast cancer diagnosed in women using or who have recently

used, a progestogen - only contraceptive pill; this relative risk may wholly or partly be due to an earlier diagnosis. The most important risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years.

Dose and Administrations: See under preparation

Oral Preparations

Norethindrone (Norethisterone)

Tablet, 0.35mg

Dose and Administration: 1 tablet daily at same time each days starting on day 1 of cycle then continuously; if administration delayed for 3 hours or more it should be regarded as a 'missed pill'.

Parental preparations

Medroxyprogesterone Acetate,

Injection (aqueous suspension), 150mg/ml in 1 ml vial

Dose and Administration: by deep intramuscular injection, 150mg within first 5 days of cycle or within first 5 days after parturition (delay until 6 weeks after parturition if breast-feeding); for long-term contraception, repeated every 12 weeks (if interval greater than 12 weeks and 5 days, exclude pregnancy before next injection and advise patient to use additional contraceptive measures (e.g barrier) for 14 days after the injection).

Norethindrone (Norethisterone) Enanthate

Injection (oily), 200mg/ml in 1 ml ampoule

Dose and Administration: by deep intramuscular injection given very slowly into gluteal muscle, short-term contraception, 200mg with in first 5 days of cycle or immediately after parturition (duration 8 weeks); may be repeated once after 8 weeks (withhold breast-feeding for neonates with severe or persistent jaundice requiring medical treatment).

Implants

Etonogestrel

Implant (subdermal) 68 mg/capsule, pack of 1 capsule.

Dose and Administration: *by subdermal implantation*, no previous hormonal contraceptive, 1 implant inserted during first 5 days of cycle; parturition or abortion in second trimester, 1 implant inserted between days 21 - 28 after delivery or abortion (if inserted after 28 days additional precautions necessary for next 7 days); abortion in first trimester, 1 implant inserted immediately; changing from an oral contraceptive, consult product literature; remove within 3 years of insertion.

Levonorgestrel (D-Norgestrel)

Tablet, 0.03mg, 0.075mg

Implant capsule (subdermal); 108mg/capsule pack of 2 capsules; 75mg/capsule pack of 2 capsules.

Intra uterine device, 52mg

Dose and Administration: *Implant capsule -by subdermal implantation*, set of 6 implant capsules inserted within first 5 days of cycle (preferably on 1st day after 1st day additional precautions necessary for following 7 days) or 21st day after parturition (after this any additional, precautions necessary for following 7 days), remove within 5years of insertion.

Intra uterine device: To be inserted into uterine cavity; should be inserted within 7 days of onset of menstruation or immediately after 1st trimester abortion; release 20mcg

lovonorgestrel/day over 5 years. May be removed and replaced with a new unit at anytime during menstrual cycle; do not leave any one system in place for 5years.

Note: Inserted in the uterine cavity, to a depth of 6-9cm, with the provider insertion device; should not be forced into the uterus.

9.7.3. Contraceptive Devices, Barriers, and Spermicides

Condoms (male and female)

Indications: as a primary method of contraception to prevent pregnancy at times when oral contraceptives or intrauterine devices may not be effective or are contraindicated or as an adjuvant to the periodic abstinence (rhythm) method of contraception. Also for prevention (prophylactic) of Sexually transmitted diseases (STDs)

Cautions: in medical or psychosocial conditions where a critical need exists for highly effective contraception. Persons must be sufficiently counseled regarding the need for consistent and correct use of condoms if they are to be effective in preventing pregnancy.

Contraindication: sensitivity to latex condom

Side effect: burning, stinging, warmth, itching, other irritation of the Skin, penis, rectum, or vagina, vaginal dryness or malodor, allergic vaginitis, contact dermatitis.

Note: Condoms should be completely unrolled into the penis before any genital contact occurs and remain intact throughout intercourse

Copper T 380 A

Indications: Copper T 380 A is an intra-uterine device used for prevention of pregnancy, most suitable in parous women but should be a last-resort contraceptive for young nulliparous women because of the increased risk of pelvic inflammatory disease and infertility.

Cautions: caution should be taken in those with anaemia, heavy menses, history of pelvic inflammatory disease, diabetes,

valvular heart disease (antibiotic cover needed) - avoid if prosthetic valve or past attack of infective endocarditis; epilepsy, increased risk of expulsion if inserted before uterine involution; there should be gynaecological examination before insertion, 6 weeks after (or sooner if there is a problem), then after 6 months, then yearly. The IUD should be removed if pregnancy occurs.

Contraindications: Pregnancy, severe anaemia, known HIV infection, very heavy menses, history of ectopic pregnancy or tubal surgery, distorted or small uterine cavity, genital malignancy, pelvic inflammatory disease, immunosuppressive therapy, copper allergy, Wilson's disease, medical diathermy.

Side effects: Uterine or cervical perforation, displacement, pelvic infection may be exacerbated, heavy menses, dysmenorrhoea, allergy, some pain on insertion (pain helped by giving NSAIDs half an hour before insertion) bleeding, occasionally, epileptic seizures, vasovagal attack. *Note: Copper T 380A should be fitted into uterine cavity after the end of menstruation and before the calculated time of implantation. An intrauterine device should not be removed in mid cycle unless an additional contraceptive was used for the previous 7 days.*

Diaphragm with spermicides

Indications: Diaphragm is a mechanical barrier method of contraception designed to hold spermicides near the cervical os, which is particularly important in the event that the diaphragm is dislodged or does not form a complete seal around the cervix.

Cautions: Caution is required in cases where there was recent abortion or parturition, in chronic allergic conditions, in genital contact dermatitis.

Drug interactions: Avoid use of diaphragm (with spermicides) with vaginal or topical medications, and vaginal douch products.

Contraindications: Allergy to spermicides (Nonoxinol, octoxinol), menstruation, toxic-shock syndrome.

Side effects: Vulvovaginal candidiasis (thick, white or curd like vaginal discharge), toxic shock syndrome (dizziness, fever, lightheadedness, chills, sunburn-like rash followed by peeling of the skin, muscle aches, hypotension, unusual redness of the mucous membrane inside of the mouth, nose, throat, vagina or conjunctiva; confusion)

Dose and Administration:*Nonoxinol 9 vaginal cream with diaphragm:* Intravaginal, Initially 1 applicatorful (approximately 1 teaspoonful of 0.5% cream placed into cup (diaphragm) and additional spermicides spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into the vagina just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.*Nonoxinol 9 vaginal foam with diaphragm:* Intravaginal, initially 1 applicatorful placed into vagina and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than one hour prior to intercourse. An additional applicatorful should be inserted into vagina just prior to, and not longer than one hour before, each repeat of intercourse.

Nonoxinol 9 vaginal gel with diaphragm: Intravaginal, initially 2 teaspoonful of a 2% gel placed into cup and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vagina, just prior to each repeat act of intercourse or if intercourse takes place later than six hours after initial diaphragm placement.*Octoxinol 9 vaginal cream with diaphragm:* Intravaginal, initially 2 teaspoonful placed into cup

and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vaginal just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.

Octoxinol 9 vaginal jelly with diaphragm: Intravaginal, initially 1 applicatorful placed into cup and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vagina just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.

Storage: at room temperature.

Nonoxinol, octoxinol,

Creams, Foams, Gels

Indications: Vaginal spermicides are used as chemical barrier contraceptive for prevention of pregnancy.

Also used for prevention of sexually transmitted diseases when used in combination with latex condoms.

Cautions: Caution is required in chronic allergy (local), genital contact dermatitis, in medical or psychosocial conditions where a critical need exists for highly effective contraception. Caution should also be taken in recent parturition or abortion.

Drug interactions: vaginal or topical medication, especially those containing aluminium, citrate, cotton dressing, hydrogen peroxide, iodide, lanolin, nitrates, permanganates, salicylates, silver salts, sulfonamides. Avoid also use of spermicides with vaginal douche products or other vaginal or local cleansing products.

Contraindications: allergy to octoxinol, nonoxinol, and benecellonium chloride, menstruation, history of toxic-shock syndrome, Genital ulcer, vaginal epithelial irritation.

Side effects: burning, stinging, warmth, itching, or other irritation of the skin, penis, rectum, or vagina, vaginal discharge (transient), vaginal dryness or odor, Allergic vaginitis (persistent vaginal redness, irritation, rash, dryness, or whitish discharge), contact dermatitis (persistent skin rash, redness, irritation or itching), urinary tract infection (female) - due to change in vaginal flora.

Dose and Administration:*Nonoxinol 9 vaginal cream* - *Intravaginal*, 1 applicatorful of 5% cream inserted just prior to intercourse. An additional applicatorful should be inserted into vagina just prior to each repeat act of intercourse.*Nonoxinol 9 vaginal Foam* - *Intravaginal*, 1 applicatorful of inserted just prior to and not longer than one hour prior to each act of intercourse.*Nonoxinol 9 vaginal Gel* - *Intravaginal*, 1 applicatorful of a 4% gel inserted just prior to and not longer than one hour prior to intercourse.

Storage: at room temperature, in a well-closed container (cream and gel), protect from freezing.

Nonoxynol

Pessaries, 5%

Indication: Prevention of pregnancy

Dose and Administration: Insert 1 pessary vaginally at least 10 minutes prior to intercourse; effective for 1 hour.

9.8. Medicines affecting Gonadotrophins

Danazole

Capsules, 100 mg, 200 mg

Indications: in the management of endometriosis, benign breast disorders such as fibrocystic disease, gynaecomastia and pre-pubertal breast hypertrophy; hereditary angioedema.

Cautions: seizure, migraine, or conditions influenced by edema.

Drug interactions: carbamazepine, cyclosporine, and warfarin.

Contraindications: undiagnosed genital bleeding; pregnancy; breast-feeding; porphyria; markedly impaired hepatic, renal, or cardiac function.

Side effects: greasy skin, acne, voice changes and possibly signs of virilisation (when therapy should be stopped immediately).

Dose and Administration:Adult: *Oral:Endometriosis:* 200 - 800 mg daily in divided doses, adjusted according to response, usually for 3 - 6 months (maximum 9 months).*Cyclical breast pain and nodularity:* 100 mg twice daily for a maximum of 3 months.

Storage: store at room temperature.

9.9. Medicines used for impotence

The phosphodiesterase type 5 (PDE5) inhibitors, sildenafil, tadalafil are equally effective in mild to moderate erectile dysfunction. The choice of drug depends on the patient's requirements and the side-effect profile of the drug. Tadalafil is the longest lasting with efficacy up to 36 hours. Tadalafil can be taken with food and alcohol, whilst sildenafil has delayed and reduced absorption when taken with a high fat meal. Failure with one drug does not imply that the others will be ineffective as well. These drugs are strongly contraindicated in patients taking vasodilator nitrates.

Sildenafil is a phosphodiesterase type 5 inhibitor. The neurotransmitter produced in the penis as the result of erotic stimulation is nitric oxide, which promotes the production of

cGMP causing vasodilation. By blocking the action of PDE5 (which breaks down cGMP), sildenafil allows the concentration of cGMP to build up during erotic stimulation. Sildenafil reacts to a lesser degree with other isoenzymes of PDE, which accounts for some of the side effects.

Sildenafil Citrate

Tablet, 25 mg, 50 mg, 100 mg

Indications: male erectile dysfunction.

Cautions: predisposition to priapism (e.g. sickle cell disease, leukaemia); hepatic or severe renal impairment, elderly.

Drug interactions: nitrates; agents that inhibit cytochrome P450 (eg. itraconazole, ketoconazole, erythromycin and cimetidine); other agents for erectile dysfunction.

Contraindications: concurrent use with nitrates or nitric oxide donors (combination can be fatal); severe ischaemic heart disease; retinitis pigmentosa (possible disorders of retinal PDE).

Side effects: cardiovascular effects related to vasodilation (headache, flushing, dizziness and hypotension); dyspepsia; mild and transient abnormal vision and sensitivity to light priapism has been reported.

Dose and Administration: Adult: Oral: Initially 50 mg taken 1 hour before anticipated sexual activity; titrate upwards to 100 mg if effect is inadequate or downwards to 25 mg if severe side-effects occur. The maximum dosing frequent is once per day and maximum dose is 100mg. Hepatic or renal impairment, the **elderly**, and concomitant use with agents known to inhibit cytochrome P450: Initially 25 mg.

Storage: store at room temperature.

Tadalafil

Tablet, 5mg, 10mg, 20mg

Indications, Cautions, Drug interactions, Contraindications and Side effects; See under sildenafil and notes above.

Dose and Administration: Adult: *Oral:* 20mg from 16 minutes to 36 hours before sexual activity. Maximum 20 mg once in 24 hours. Mild to moderate hepatic impairment (avoid if severe): Maximum 10mg once daily.

Vardenafil

Tablet, 5 g, 10mg, 20mg

Indications: erectile dysfunction

Cautions: hepatic impairment, renal impairment; bleeding disorders or active peptic ulceration; susceptibility to prolongation of QT interval (including concomitant use of drugs which prolong QT interval), should be used with caution in cardiovascular disease, left ventricular outflow obstruction, anatomical deformation of the penis (e.g. angulation, cavernosal fibrosis, Peyronie's disease), and in those with a predisposition to priapism (e.g. in sickle-cell disease, multiple myeloma, or leukaemia). *Concomitant treatment with a phosphodiesterase type-5 inhibitor and an alpha-blocker can increase the risk of postural hypotension: initiate treatment with a phosphodiesterase type-5 inhibitor (at a low dose) only once the patient is stable on the alpha-blocker*

Drug interactions: alpha blockers, calcium channel blockers, ketoconazole, itraconazole, nifedipine, indinavir erythromycin, nitrates, ritonavir saquinavir, and grape juice.

Contra-indications: contra-indicated in patients receiving nitrates, in patients in whom vasodilation or sexual activity are inadvisable, or in patients with a previous history of non-arteritic anterior ischaemic optic neuropathy. In the absence of information, manufacturers contra-indicate this drug in hypotension (avoid if systolic blood pressure below 90 mmHg),

recent stroke, unstable angina, and myocardial infarction. Also hereditary degenerative retinal disorders

Side-effects: dyspepsia, nausea, vomiting, headache (including migraine), flushing, dizziness, myalgia, back pain, visual disturbances (non-arteritic anterior ischaemic optic neuropathy has been reported—stop drug if sudden visual impairment occurs), and nasal congestion. Less common side-effects include painful red eyes, palpitation, tachycardia, hypotension, hypertension, and epistaxis. Other rarely side-effects include syncope, hypersensitivity reactions (including rash, facial oedema, and Stevens-Johnson syndrome), and priapism. Serious cardiovascular events (including arrhythmia, unstable angina, and myocardial infarction), seizures, sudden hearing loss (discontinue drug and seek medical advice), and retinal vascular occlusion. Less commonly drowsiness, dyspnoea, increased lacrimation, photosensitivity; rarely anxiety, seizures, transient amnesia, hypertonia, and raised intra-ocular pressure

Dose and administration: adults over 18 years, initially 10 mg (elderly and patients on alpha-blocker therapy 5 mg) approx. 25– 60 minutes before sexual activity, subsequent doses adjusted according to response up to maximum 20 mg as a single dose; maximum 1 dose in 24 hours. *Note: Onset of effect may be delayed if taken with high-fat meal.*

10. OBSTETRIC and GYNAECOLOGICAL MEDICINES

Medicines used in obstetrics: medicines may be used to modify uterine contractions. These include oxytocic medicines to stimulate uterine contractions both in induction of labour and to control postpartum haemorrhage and beta₂-adrenoceptor agonists used to relax the uterus and prevent premature labour.

Postpartum haemorrhage: Ergometrine and oxytocin differ in their actions on the uterus. In moderate doses oxytocin produces slow generalized contractions with full relaxation in between; ergometrine produces faster contractions superimposed on a tonic contraction. High doses of both substances produce sustained tonic contractions. Oxytocin is now recommended for routine use in postpartum and post-abortion haemorrhage since it is more stable than ergometrine. However, ergometrine may be used if oxytocin is not available or in emergency situations.

Premature labour: Salbutamol is a beta₂-adrenoceptor agonist which relaxes the uterus and can be used to prevent premature labour in uncomplicated cases between 23 and 24 weeks of gestation. Its main purpose is to permit a delay in delivery of at least 48 hours. The greatest benefit is obtained by using this delay to administer corticosteroid therapy or to implement other measures known to improve perinatal health. Prolonged therapy should be avoided since the risk to the mother increase after 48 hours and the response of the myometrium is reduced.

Treatment of vaginal and vulval conditions: Anti-infective drugs: Candidal vulvitis can be treated locally with cream but is almost invariably associated with vaginal infection which should also be treated. Vaginal candidiasis is treated primarily with antifungal pessaries or cream inserted high into

the vagina (including during menstruation) local irritation may occur on application of vaginal antifungal products.

Imidazole drugs (clotrimazole, miconazole) are effective in short courses of 3 to 14 days according to the preparation used; single dose preparations after an advantage when compliance is a problem. Vaginal applications may be supplemented with antifungal cream for vulvitis and to treat other superficial sites of infection.

Nystatin is a well established treatment (but stain clothing yellow). One or two pessaries are inserted for 14 to 28 nights; they may be supplemented with cream for vulvitis and to treat other superficial sites of infection.

Trichomonal infections: Commonly involve the lower urinary tract as well as the genital system and need systemic treatment with metronidazole or tinidazole. Bacterial infections with Gram - negative organisms are particularly common in association with gynaecological operations and trauma. Metronidazole is effective against certain Gram - negative organisms, especially *Bacteroides spp.* and may be used prophylactically in gynaecological surgery. Metronidazole is also indicated for bacterial vaginosis.

Aminocaproic Acid

Injection, 100 mg/ml in 1 ml ampoule.

Indications: treatment of excessive bleeding from fibrinolysis.

Cautions: cardiac, renal or hepatic disease.

Drug interactions: oral contraceptives, estrogens.

Contraindications: hypersensitivity to aminocaproic acid; disseminated intravascular coagulation (without heparin); evidence of an intravascular clotting process.

Side effects: arrhythmia, bradycardia, hypotension, peripheral ischemia, syncope, confusion, thrombosis, fatigue,

hallucinations, headache, rash, pruritus, abdominal pain, anorexia, cramps, GI irritation, nausea, dry ejaculation, agranulocytosis, bleeding time increased, watery eyes, vision decreased, tinnitus, failure, myoglobinuria, dyspnea, nasal congestion, pulmonary embolism.

Dose and Administration:Adult: *IV:* 4 - 5 g during the first hour, followed by 1 g/hour for 8 hours or until bleeding controlled (maximum daily dose: 30 g).

Storage: store at room temperature.

Bromocriptine Mesylate

Tablet, 2.5 mg

Indications: galactorrhoea, amenorrhoea and infertility associated with hyperprolactinaemia, and certain cases of acromegaly (adjunctive therapy). It is used to suppress lactation after stillbirth or abortion, or when breast - feeding is contraindicated.

Cautions: psychotic disorders, parkinsonism with dementia, compromised cerebral circulation, ischaemic heart disease, liver disease, peptic ulcers.

Drug interactions: metoclopramide, domperidone, antipsychotic agents, tricyclic antidepressants, methyl dopa, reserpine, antihypertensive agents, alcohol.

Contraindications: hypersensitivity to ergot alkaloids, toxemia of pregnancy, uncontrolled hypertension or severe cardiovascular disease.

Side effects: nausea, postural hypotension, drowsiness and dizziness, especially early in therapy. Hypertension, myocardial infarction, seizures and stroke, dyskinesia, hallucinations, confusion and behavioral disturbances, urticaria, skin rashes, peptic ulceration, nasal stuffiness, visual disturbance,

impotence and urinary retention, retroperitoneal fibrosis, pleural thickening and effusions, and digital vasospasm.

Dose and Administration:*Oral: Adult:Suppression of lactation:* 2.5 mg twice daily for 2 weeks, starting not before 4 hours after parturition, and provided that viral signs have established. If lactation recurs 2 - 3 days after treatment is stopped, it may be reinstated and continued for another week.*Hypogonadism or amenorrhoeal, galactorrhoea syndromes:* initially 1.25 mg once daily at bedtime; gradually increases to an average of 2.5mg 2- 3 times daily.

Storage: store at a temperature less than 25°C.

Bupivacaine Hydrochloride

Injection, 0.5% in 10ml vial

Indication: long-acting local anaesthetic agent. Particularly useful for producing prolonged analgesia during labour and caesarean section, where the interval between doses is usually 2-3 hours.

Cautions, Contraindications, Drug interactions, Side effects and Dose and Administration; see section 5.4 (local anaesthetic).

Clomiphene Citrate

Tablet, 50 mg

Indications: management of anovulatory or oligo - ovulatory infertility in women with an intact hypothalamic - pituitary - ovarian axis.

Cautions: ectopic pregnancy, breast-feeding.

Contraindications: hepatic dysfunction, ovarian cysts, undiagnosed abnormal uterine bleeding, pregnancy.

Side effects: reversible ovarian enlargement and cyst formation (withdraw therapy); hot flushes, abdominal discomfort and

pain, nausea and vomiting, breast discomfort, abnormal uterine bleeding, headache, skin rashes, weight gain; CNS effects such as dizziness, nervousness, depression, fatigue, insomnia, visual disturbances (blurring of vision, diplopia and photophobia), reversible hair loss, hepatotoxicity.

Dose and Administration: *Oral:*

Adult: initially 50 mg daily for 5 days, starting on day 3 to 5 of the menstrual cycle or after an induced bleed. If ovulation is confirmed but conception fails, the same dose may be repeated during the next cycle. If ovulation fails, the dose may be increased to 100 mg daily (as a single dose) for 5 days.

Storage: store at room temperature.

Clotrimazole

Cream (vaginal), 1%

Tablet (vaginal), 100mg, 500mg

Indications: in the local treatment of vulvovaginal candidiasis caused by *Candida albicans* and other species of candida in pregnant (second and third trimester only) and non-pregnant women.

Note: It is not effective in the treatment of vulvovaginitis caused by other common pathogens such as Trichomonas vaginitis.

Cautions: pregnancy and labour and in those patients who are allergic to clotrimazole and its family. Use hygienic measures to cure infection and prevent reinfection by wearing cotton panties instead of synthetic underclothes and wearing only freshly washed under clothes. Sex partners should be advised to use condom.

Contraindications: hypersensitivity to clotrimazole

Side effects: vaginal burning, itching, discharge, or other irritation not present before therapy, abdominal or stomach

cramps or pain, burning or irritation of penis of sexual partner; headache.

Dose and Administration: *cream:* Intravaginal, 50mg (1 applicatorful of 1% vaginal cream), once a day, preferably at bed time, for six to fourteen consecutive days. *Tablets:* *Non-pregnant patients:* Intravaginal, 500mg as a single dose, preferably at bedtime or 100mg once a day preferably at bedtime, for six or seven consecutive days. *Pregnant patients:* Intravaginal (100mg once a day), preferably at bedtime, for seven consecutive days.

Storage: vaginal cream - store between 2 and 30⁰c in a collapsible tube or in a tight container. Vaginal tablet - at room temperature in a well-closed container

Dienogest

Tablet, 2mg

Indications: Management of pelvic pain associated with endometriosis

Cautions: bleeding, breast cancer, carbohydrate intolerance, chloasma, Cholestatic jaundice, Hepatic tumors, ovarian cysts, pruritus, retinal vascular lesions, venous thromboembolism (VTE).

Drug interactions: CYP3A4 inducers, CYP3A4 inhibitors, barbiturates, benzodiazepines, phenytoin, rifamycin derivatives.

Contraindications: hypersensitivity to dienogest or any component of the formulation; undiagnosed abnormal vaginal bleeding; active venous thromboembolic disorder; history of or current arterial and cardiovascular disease (eg, MI, CVA); diabetes mellitus with vascular involvement; history of or current severe hepatic disease where liver function tests remain abnormal; history of or current hepatic neoplasia (benign or malignant); known or suspected sex-hormone-dependent

malignancy; ocular lesions due to ophthalmic vascular disease, such as partial or complete vision loss or defect in visual fields; current or history of migraine with focal aura; breast-feeding; known or suspected pregnancy.

Side effects: headache, depression, sleep disturbance, irritability, migraine, nervousness, acne, alopecia, breast discomfort, ovarian cyst, libido decreased, nausea, weight gain, abdominal pain, vaginal bleeding, weakness.

Dose and administration: Adult: *Endometriosis:* Oral: 2 mg once daily. Administer without regard to meals. If a dose is not absorbed due to vomiting and/or diarrhea within 3-4 hours of administration, repeat dose.

Storage: Store in original packaging at 15°C to 30°C

Dinoprostone (prostaglandin E₂)

Tablet (vaginal), 3 mg

Suppository (vaginal), 20mg

Indications: *Suppositories:* Terminate pregnancy from 12th through 28th week of gestation; evacuate uterus in cases of missed abortion or intrauterine fetal death.

Vaginal insert: Initiation and/or cervical ripening in patients at or near term in whom there is a medical or obstetrical indication for the induction of labor.

Cautions: cervicitis, infected endocervical lesions, acute vaginitis, compromised (scarred) uterus or history of asthma, hypertension or hypotension, epilepsy, diabetes mellitus, anemia, jaundice, cardiovascular, renal, or hepatic disease.

Drug interactions: oxytocin may augment the activity of oxytocic agents and their concomitant use is not recommended. A dosing interval of at least 30 minutes is recommended for the sequential use of oxytocin following the removal of the dinoprostone vaginal insert. A 6 hours interval is needed

between the insertion of dinoprostone and initiation of oxytocin infusion.

Contraindications: hypersensitivity to prostaglandins, fetal distress, unexplained vaginal bleeding during this pregnancy, acute pelvic inflammatory disease, uterine fibroids, and cervical stenosis.

Side effects: headache, vomiting, diarrhea, nausea, bradycardia, fever, back pain, bronchospasm, cardiac arrhythmia, chills, cough, dizziness, dyspnea, flushing, hot flushes, hypotension, pain, shivering, syncope, tightness of the chest, vasomotor and vasovagal reactions, wheezing.

Dose and Administration: *Abortifacient:* Insert 1 suppository high in vagina, repeat at 3- 5 hour intervals until abortion occurs up to 240 mg (maximum dose); continued administration for longer than 2 days is not advisable. *Cervical ripening:* *Suppositories:* *Intracervical:* 2 - 3 mg. *Vaginal Tablet:* induction of labour, inserted high in to posterior fornix, 3 mg, followed after 6-8 hours by 3 mg if labour is not established; maximum 6 mg.

Storage: store suppositories at a temperature not exceeding 20 °C.

Ergometrine maleate

Injection, 0.25 mg/ml, 0.5mg/ml

Tablet, 0.25mg, 0.5mg

Indications: prevention and treatment of postpartum and postabortion hemorrhage in emergency situations. Oxytocin and ergometrine combined are more effective in early pregnancy than either drug alone.

Cautions: cardiovascular diseases, hypertension, renal and hepatic function impairment, multiple pregnancy, sepsis, or hypersensitivity.

Drug interactions: adrenaline. Tobacco smoking should also be avoided.

Contraindications: induction of labour, first and second stages of labour, coronary artery disease, eclampsia or preeclampsia or pregnancy.

Side effects: dizziness, mild and transient headache, ringing in the ears and hypertension may occur rarely. Abdominal pain, nausea, vomiting and uterine cramping may also occur, especially after intravenous injection.

Dose and Administration:Adult: *Prevention and treatment of postpartum haemorrhage, when oxytocin is not available:IM injection:* 200 mcg when the anterior shoulder is delivered or immediately after birth

Excessive uterine bleeding: Slow IV injection: 250-500 mcg when the anterior shoulder is delivered or immediately after birth.*Secondary postpartum haemorrhage:Oral:* 0.2-0.4 mg 2-4 times daily, usually for 48 hours.

Storage: Injection: 2-8⁰C, or as specified by manufacturer. Protect from light and freezing. Tablets: Store at room temperature, in tight container and protect it from light.

Note: Discoloured solution or solutions containing visible particles should not be used.

Estradiol Valerate

Injection, 10mg/ml in 1ml ampoule

Indications: Treatment of moderate to severe vasomotor symptoms associated with menopause, treatment of vulvar and vaginal atrophy, abnormal uterine bleeding due to hormonal imbalance.

Cautions: cardiovascular disease, hypertension, familial defects of lipoprotein metabolism, breast feeding mother.

Contraindications: Hypersensitivity to estradiol or any component of the formulation, undiagnosed abnormal vaginal bleeding, history of or current thrombophlebitis or venous thromboembolic disease (eg, stroke), carcinoma of the breast, estrogen-dependent tumor, hepatic dysfunction and pregnancy.

Side effects: as for the estrogens in general.

Dose and Administration: *Moderate to severe vasomotor symptoms associated with menopause and female hypogonadism (due to hypogonadism):* 10-20mg every 4 weeks

Storage: store at room temperature.

Isoconazole

Vaginal tablet, 300mg, 600mg

Cream, 1%, 2%

Indications: treatment of vaginal mycoses, particularly due to *Candida spp.*

Cautions: pregnancy.

Side effects: local reactions including burning or itching may occur following the application of isoconazole.

Dose and Administration: *Pessaries:* 600mg or 300mg daily for 3 days.

Storage: protect from light.

Magnesium Sulfate

Injection, 2%, 5%, 10 %, 20 %, 50 % in 20 ml

Indications: prevention of recurrent seizures in eclampsia.

Cautions: hepatic impairment, renal failure.

Drug interactions: alcuronium, nifedipine, suxamethonium, vecuronium.

Contraindications: hypersensitivity to magnesium sulfate.

Side effects: generally associated with hypermagnesaemia, nausea, vomiting, thirst, flushing of skin, hypotension, arrhythmias, coma, respiratory depression, drowsiness, confusion, loss of tendon reflexes, muscle weakness.

Dose and Administration: Adult: *IV injection:* initially 4 g over 5 - 10 minutes followed by IV infusion at a rate of 1 g every hour for at least 24 hours after the last seizure; recurrence of seizures may require additional IV bolus of 2g.

Storage: store at room temperature.

Methylergometrine Maleate

Injection, 0.2mg/ml

Tablet, 0.12mg

Indications: prevention and treatment of postpartum or postabortal uterine bleeding due to uterine atony or subinvolution. Its use is not recommended prior to delivery of the placenta since placental entrapment may occur. It is also used to lessen expulsion of uterine contents in cases of incomplete abortion. It is not indicated for induction or augmentation of labor, to induce abortion, or in cases of threatened spontaneous abortion because of its propensity to produce non-physiologic, tetanic contractions and its long duration of action.

Cautions: hepatic and renal function impairment, hypocalcaemia, mitral valve stenosis, venoatrial shunts and in those patients that are allergic to methylergometrine or ergot alkaloids.

Drug interactions: general anaesthetic especially halothane, bromocriptine, other ergot alkaloids, nicotine, tobacco smoking, nitroglycerine, vasoconstrictors and vasopressors.

Contraindications: pregnancy, labour and delivery, unstable anginal pectoris, recent myocardial infarction, history of

cerebrovascular accident, history of transient ischemic attack, cardiovascular disease, coronary artery disease, eclampsia or preeclampsia, (history of) severe hypertension, occlusive peripheral vascular disease, severe raynaud's phenomenon.

Side effects: nausea, vomiting, abdominal pain, diarrhoea, uterine cramping dizziness, sweating, tinnitus (ringing in the ears)

Dose and Administration:Adult:*uterine stimulant: Oral:* 0.2 to 0.4mg two or four times a day until the danger of uterine atony and hemorrhage has passed.

IV or IM: 0.2mg repeated in two or four hours if necessary, up to five doses.

Storage: at room temperature in a tight container (tablets), protect from light and from freezing.

Metronidazole

Intravenous infusion, 5mg/ml in 100ml

Syrup, 4% w/v, 250mg/5ml

Tablet, 250mg

Tablet (vaginal), 500mg

Indications: used for the treatment of bacterial vaginosis (formerly called, *Haemophilus vaginitis*, *Gardnerella vaginitis*, non-specific vaginitis, *Carynebacterium vaginitis*, or anaerobic vaginosis) which is a non-inflammatory vaginal syndrome characterized by replacement of the normal vaginal flora (predominantly hydrogen producing lactobacillus) with a mixed flora including *Gardnerella vaginalis*. It is also used in the treatment of female pelvic infections, including endometritis, endomyometritis, tube-ovarian abscess, and liver abscess caused by bacteriodes species, including the *B. fragilis* group, clostridium species, petpococcus species, and

peptostreptococcus species. See also section 7.1.2 & 7.4.2 for other uses.

Cautions: abnormal neurologic symptoms, history of blood dyscrasias. Reduce dosage in patients with hepatic impairment. Use the drug during pregnancy with caution when it is clearly needed. Breast feeding should be interrupted in nursing mothers.

Drug interactions: alcohol, anticoagulants (cumarin - or indandione - derivatives), cimetidine, disulfiram, phenobarbital, phenytoin.

Contraindications: history of hypersensitivity to the drug or other nitroimidazole derivatives.

Side effects: nausea, vomiting, diarrhoea, loss of appetite, dry mouth, sharp unpleasant metallic taste, constipation, abdominal discomfort, numbness, tingling, pain, or weakness in hands or feet, seizures, leucopenia, thrombocytopenia, vaginal candidiasis (any vaginal irritation, discharge, or dryness not present before therapy).

Dose and Administration: Adult: *Vaginosis (bacteria):* Oral: 2 g as a single dose or 500 mg twice daily for 7 days. *Intravaginal:* 500mg placed high into the vagina every night for ten or twenty consecutive days. *IV-infusion,* 15mg (base) per kg of body weight initially, then 7.5mg per kg of body weight up to a maximum of 1gm, every six hours for seven days or longer. *Pelvic inflammatory disease:* Oral: 500mg of metronidazole twice daily with ofloxacin given orally in a dosage of 400mg twice daily. Therapy should be continued for 14 days. *Note: Metronidazole may cause dizziness. Patients should be advised to avoid alcoholic beverages and to comply with full time of treatment.*

Storage: at room temperature in a well-closed, light-resistant container.

Metronidazole + Miconazole

Vaginal pessary, 750mg +200mg

Indications:vaginal candidiasis due to *Candida albicans*, bacterial vaginitis due to anaerobic bacteria and *Gardnerella vaginalis*, trichomonal vaginitis due to *Trichomonas vaginalis* and in mixed vaginal infections.

Cautions:alcohol, vaginal contraceptives (diaphragms or condoms), renal failure, liver failures, hepatic encephalopathy, pregnancy and lactation.

Contraindications: hypersensitive to the drug, first trimester of pregnancy, porphyria, epilepsy and serious liver function disorders; Children.

Side effects:Hypersensitivity reactions (skin rash). Miconazole nitrate can cause vaginal irritation (burning, itching) as all other imidazole derivative antifungal drugs applied intravaginally (2-6%). If there is severe irritation, treatment should be discontinued. Side effects due to systemic use of metronidazole are hypersensitivity reactions (rare), leukopenia, ataxia, mental changes, peripheral neuropathy at overdose and after long period of usage, convulsion, diarrhea (seldom), constipation, dizziness, headache, lack of appetite, vomiting, nausea, abdominal pain or cramp, taste changes (seldom), dry mouth, metallic or bad taste, tiredness. These side effects occur very rarely, because of low blood levels of metronidazole after intravaginal application.

Drug Interactions:Alcohol, oral anticoagulants, phenytoin, phenobarbital, disulfiram, cimetidine, lithium, astemizole, terfenadine, theophylline and procainamide.

Dose and Administration: one pessary should be inserted high into the vagina at night for 7 days.In recurrent cases, or when the vaginitis has been resistant to other treatments, application

of one pessary at night for 14 days is recommended.

Storage: store at room temperature

Miconazole Nitrate

Tablet (vaginal), 200mg, 400mg

Cream (vaginal), 2%

Indications: treatment of Vulvovaginal candidiasis caused by *Candida albicans* and other species of candida in pregnant (second and third trimesters only) and non-pregnant women.

Cautions, Contraindications, Side effects: Same as clotrimazole

Dose and Administration:Adult:*Vaginal cream: Intravaginal*, one applicatorful once a day at bed time for seven or fourteen days. It may be repeated if needed.*Vaginal tablets: Intravaginal*, 100mg once a day at bed time for seven days. It may be repeated for seven days if needed or 200mg or 400mg once a day at bedtime for three days. It may be repeated if needed.

Storage: at room temperature in a tight container

Mifepristone

Tablet, 200 mg

Indications: medical termination of intrauterine pregnancy, through day 49 of pregnancy. Patients may need treatment with misoprostol and possibly surgery to complete therapy.

Cautions: severe anemia.

Drug interactions: substrate of CYP3A4, progestin.

Contraindications: hypersensitivity to mifepristone, misoprostol, other prostaglandins, chronic adrenal failure, porphyrias, hemorrhagic disorder or concurrent anticoagulant therapy, pregnancy termination greater than 49 days, IUD in place, ectopic pregnancy or undiagnosed adnexal mass,

concurrent long term corticosteroid therapy, inadequate or lack of access to emergency medical services, inability to understand effects and/or comply with treatment.

Side effects: vaginal bleeding and uterine cramping, bleeding or spotting occurs in most women for a period of 9-16 days, headache, dizziness, abdominal pain, nausea, vomiting, and diarrhea.

Dose and Administration: *Oral: Adult:* Termination of pregnancy: treatment consists of three visits by the patient; the patient must read medication guide and sign patient agreement prior to treatment:

Day 1: 600 mg (three 200 mg tablets) taken as a single dose under physician supervision.

Day 3: patient must return to the healthcare provider 2 days following administration of mifepristone; if termination of pregnancy cannot be confirmed using ultrasound or clinical examination, 400 mcg (two 200 mcg tablets) of misoprostol can be given. Patient may need treatment for cramps or gastrointestinal symptoms at this time. Day 14: patient must return to the healthcare provider in approximately 14 days after administration of mifepristone to confirm complete termination of pregnancy by ultrasound or clinical examination. Surgical termination is recommended to manage treatment failures.

Storage: store at room temperature.

Misoprostol

Tablet, 100mcg, 200mcg, 400mcg, 800mcg

Tablet (vaginal), 25mcg

Indication: It is used to induce abortion; intravaginal use ripens the cervix before surgical abortion

Cautions, Drug interactions, Contraindications, Side effects and Storage see section 1.2 under misoprostol.

Dose and administration

For gestation up to 9 weeks, mifepristone 200 mg by mouth followed 1–3 days later by misoprostol 800 micrograms vaginally; in women at more than 7 weeks gestation (49–63 days), if the abortion has not occurred 4 hours after misoprostol, a further dose of misoprostol 400 micrograms may be given vaginally or by mouth. **For gestation between 9 and 13 weeks**, mifepristone 200 mg by mouth followed 36–48 hours later by misoprostol 800 micrograms vaginally followed if necessary by a maximum of 4 further doses at 3-hourly intervals of misoprostol 400 micrograms vaginally or by mouth. **For gestation between 13 and 24 weeks**, mifepristone 200 mg by mouth followed 36–48 hours later by misoprostol 800 micrograms vaginally then a maximum of 4 further doses at 3-hourly intervals of misoprostol 400 micrograms by mouth.

Neomycin + Polymixin B + Nystatin

Tablet (vaginal), 35000IU +35000IU +100000IU

Indications: Topical treatment of vaginal infections

Cautions: pregnancy, renal failure

Drug interactions: spermicidal products and condoms

Contraindications: breast-feeding, allergy to one of its ingredients or another substance of the same family, use of latex diaphragms or condoms

Side effects: Possibility of contact allergic eczema or away from the site of application in case of prolonged use.

Dose and Administration: *vaginal:* **Adult:** Place one tablet deep in the vagina for 12 days. Do not stop treatment during menstrual periods.

Storage: Store below 25°C.

Nystatin

Cream (vaginal), 100,000 units

Pessary (ovules), 100,000 units

Indications: local treatment of vulvovaginal candidiasis caused by *Candida (monilia) albicans* and other candida species.

Note: It is not effective against *Trichomonas Vaginalis* or *Gardnerella vaginalis (Haemophilus Vaginalis)*.

Cautions: discontinue treatment with nystatin therapy if irritation or sensitization occurs. They are also advised against interrupting or discontinuing vaginal nystatin therapy during a prescribed regimen even during menstruation or if symptomatic relief occurs after only a few days of therapy unless otherwise instructed by their physician.

Contraindications: sensitivity to nystatin

Side effects: vaginal irritation not present before therapy

Dose and Administration:Adult:*Nystatin vaginal cream: Intravaginal*, insert 1-2 applicatorfuls at night for at least 14 nights.*Nystatin vaginal pessary: Intravaginally*, insert 1-2 pessaries at night for at least 14 nights.

Storage: at room temperature in a tight, light-resistant container.

Oxytocin

Injection, 1unit/ml, 5units/ml, 10units/ml

Indications: for nonselective induction of labour for medical reasons and for stimulation or reinforcement of labour in patients with dysfunctional inertia. Parenteral oxytocin is also indicated for management of incomplete or therapeutic abortion, as well as to produce uterine contractions during the third stage of labour. Oxytocin is also indicated to control postpartum bleeding or hemorrhage.

Cautions: particular caution needed when given for induction or enhancement of labour in presence of borderline

cephalopelvic disproportion (avoid if significant), mild or moderate pregnancy-induced hypertension or cardiac disease, women over 35 years or with history of lower-uterine segment caesarean section, fetal death in utero or meconium-stained amniotic fluid, avoid tumultuous labour (may cause amniotic fluid embolism). Avoid large infusion volumes and restrict fluid intake by mouth (risk of water intoxication and hyponatraemia), effects enhanced by concomitant administration of prostaglandins (very careful monitoring of urine activity), caudal block anaesthesia (may enhance hypertensive effects of sympathomimetic vasopressors). See also interaction.

Drug interactions: hydrocarbon, inhalation anesthetics such as enflurane, halothane, isoflurane, and with vasopressors, other oxytocics.

Contraindications: significant cephalopelvic disproportion, cord presentation, total placenta previa, vasa previa, where vaginal delivery is contraindicated, fetal distress, hypertonic uterine patterns, obstetrical emergencies requiring surgical intervention, uterine inertia or severe toxemia on prolonged use.

Side effects: fast or irregular heartbeat, nausea or vomiting

Dose and Administration:**Adult:***Induction or stimulation of labour: IV infusion:* initially at an initial rate 0.5 to 4 milliunits (0.0005 to 0.004 unit) per minute, and then increased gradually at intervals every 20-60 minutes in increments of 1 to 2 milliunits (0.001-0.002 unit) per minute until a contraction pattern similar to that of normal labour is obtained. The rate of up to 6 milliunits per minute is reported to produce plasma oxytocin concentrations comparable to those in natural labour but doses of up to 20 milliunits (0.02 units) or more per minute may be required. The rate may be reduced gradually once labour is induced.*Incomplete or therapeutic abortion: IV*

infusion: 10 units at a rate of 20 to 40 milliunits (0.02 to 0.04 units) per minute. *Control of postpartum uterine bleeding: IV infusion*: 10 units at a rate of 20 to 40 milliunits per minute following delivery of the infant(s) and preferably placenta(s). A rate of 20-100 milliunits per minute may be used following abortion.

Storage: store oxytocin at 2 to 8°C, protect from freezing. 10units/ml (1ml) may also be stored at 15 to 25°C for up to 30 days.

Oxytocin + Ergometrine Maleate

Injection, 5 units + 500mcg in each ml

See notes under ergometrine maleate

Dose: *IM injection*: 1ml; *IV injection*, no longer recommended

Ritodrine Hydrochloride

Injection, 10mg/ml in 5ml ampoule

Indications: prevention of premature labour and abortion.

Cautions: mild-to-moderate preeclampsia, hypertension, or diabetes.

Drug interactions: atropine, beta-adrenergic blockers, corticosteroids, magnesium sulfate, diazoxide, meperidine, general anesthetics, sympathomimetics.

Contraindications: before 20th week of pregnancy and when continuation of pregnancy is hazardous to mother or fetus, hypersensitivity, pre-existing maternal conditions that would be seriously affected by pharmacologic properties of beta-mimetic agent.

Side effects: palpitations, chest pain or tightness;, heart murmur, angina pectoris, myocardial ischemia, alterations in BP, pulmonary edema, sinus bradycardia upon drug withdrawal, arrhythmias, drowsiness, weakness, mild

tachycardia, tremor, headache (including migraines), nervousness, restlessness, emotional upset, anxiety, malaise, hyperventilation, erythema, rash, nausea, constipation, diarrhea, vomiting, epigastric distress, ileus, bloating, leucopenia, agranulocytosis, hemolytic icterus, impaired liver function, lactic acidosis, glycosuria, dyspnea, sweating, chills, hypokalemia, hyperglycemia.

Dose and Administration: *IM:* 10 mg every 3 to 8 hours and continued for 12 to 48 hours after the contractions have stopped.

Storage: store at room temperature and protect from excessive heat.

Salbutamol

Injection, 0.5mg/ml in 1ml ampoule

Indications: arrest uncomplicated premature labour between 24-33 weeks gestation; see also section 2.2.

Cautions: suspected cardiac disease, hypertension, hyperthyroidism, hypokalaemia, diabetes mellitus, mild to moderate pre-eclampsia. The patient's state of hydration and heart rate should be monitored carefully.

Drug interactions: corticosteroids, diuretics, theophylline.

Side effects: nausea, vomiting, flushing, sweating, tremor, hypokalemia, tachycardia, muscle cramps, palpitation and hypotension, increased tendency to uterine bleeding, pulmonary oedema, chest pain or tightness, arrhythmias, headache.

Contraindications: cardiac disease, eclampsia and severe pre-eclampsia, intra-uterine infection, antepartum haemorrhage (requires immediate delivery), placenta praevia, cord compression, not used in first or second trimesters.

Dose and Administration: *Premature labour:*
Adult:*intravenous infusion:* 10 micrograms/minute gradually

increased to maximum of 45 micrograms/minute until contractions have ceased, then gradually reduced; or *by intravenous or intramuscular injection*, 100 – 250 micrograms repeated according to patient's response; subsequently *by mouth* 4 mg every 6 – 8 hours:

Storage: Store at room temperature. Protect from light.

11. ANTINEOPLASTICS and ADJUVANTS

The treatment of cancer with medicines, radiotherapy and surgery is complex and should only be undertaken by an oncologist. For this reason the following information is provided merely as a guide. Chemotherapy may be given as a curative or palliative intent of treatment. Where the condition can no longer be managed with cytotoxic therapy, alternative palliative treatment should be considered. For some tumours, single drug chemotherapy may be adequate, but for many malignancies a combination of medicines provides the best response. Examples of combination therapy include:

- 'CHOP' is the acronym for a chemotherapy regimen used in the treatment of non-Hodgkin lymphoma. CHOP consists of (Cyclophosphamide, Hydroxydaunorubicin (also called doxorubicin or Adriamycin), Oncovin (Vincristine), Prednisone or Prednisolone).
- 'ABVD' is a chemotherapy regimen used in the first-line treatment of Hodgkin lymphoma, supplanting the older MOPP protocol. It consists of concurrent treatment with the chemotherapy drugs: Adriamycin (doxorubicin/hydroxydaunorubicin), Bleomycin, Vinblastine, Dacarbazine (similar to procarbazine).
- 'MOPP' (Mustargen (Chlormethine), Oncovin (Vincristine), Procarbazine, Prednisolone) for Hodgkin's disease.

Cytotoxic medicines are often combined with other classes of medicines in the treatment of malignant conditions. Such medicines include hormone agonists and antagonists, corticosteroids and immunostimulant medicines. Combinations are, however, more toxic than single medicines. The following information covers medicines that have specific anti-tumor activity. However, they are toxic medicines which should be used with great care and monitoring.

Precautions and Contraindications: treatment with cytotoxic medicines should be initiated only after baseline tests of liver and kidney function have been performed and baseline blood counts established. It may be necessary to modify (adjust doses) or delay treatment cycle by one week in certain circumstances. The patient should also be monitored regularly during chemotherapy and cytotoxic medicines should be withheld if there is significant deterioration in bone marrow, liver or kidney function.

Cytotoxic medicines should be administered with care to avoid undue toxicity to the patient or exposure during handling by the health care provider.

Many cytotoxic medicines are teratogenic and should not be administered during pregnancy especially in the first trimester. Contraceptive measures are required during therapy and possibly for a period after therapy has ended.

General adverse effects: Antineoplastic agents exert their effect on rapidly dividing cells (malignant cells, bone marrow, mucous membranes, hair follicles) and therefore have common toxicities, despite different modes of action. Toxicities depend on dose, schedule and route of administration as well as predisposing factors in the patient. Potential benefit of particular regimen needs to be weighed against toxicity for each individual patient.

The acute effects of antineoplastic medication frequently include nausea and vomiting, which may be severe.

Bone Marrow suppression: Malignant tumours may develop as a long term complication of cytotoxic therapy. These include acute myeloid leukaemia, solid tumours, Hodgkin's disease, ovarian cancer and gastric cancer.

Reproductive toxicity: Most cytotoxic medicines are teratogenic. In most men receiving chemotherapy the sperm

count will return to normal within 2 years of subsequent recovery of spermatogenesis.

Hyperuricaemia may complicate treatment of conditions such as non-Hodgkin lymphomas and leukaemia. Renal damage may result from the formation of uric acid crystals. Patients should be adequately hydrated and hyperuricaemia may be managed with allopurinol initiated 24 hours before cytotoxic treatment and continued for 7 to 10 days afterwards.

Alopecia is common.

11.1. Alkylating Agents

Alkylating medicines are among the most widely used medicines in cancer chemotherapy. They act by damaging DNA and therefore interfering with cell replication. However, there are two complications.

1. They affect gametogenesis and may cause permanent male sterility; in women, the reproductive span may be shortened by the onset of a premature menopause.

2. A marked increase in the incidence of acute non-lymphocytic leukaemia, in particular when combined with extensive radiation therapy.

Alkylating agents include; busulfan, chlorambucil, cyclophosphamide, mechlorethamine hydrochloride, melphalan and thiotepa.

Busulfan

Tablets, 0.5 mg, 2 mg

Indications: chronic myeloid leukaemia, conditioning regimens for bone marrow transplantation.

Cautions: seizures, patients recently given other myelosuppressive drugs or radiation treatment.

Drug interactions: azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, nocardipine, propofol, protease inhibitors, quinidine, verapamil, aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin, rifamycins.

Contraindications: pregnancy, hypersensitivity to busulfan.

Side effects: sterility, ovarian suppression, amenorrhea, testicular atrophy, malignant tumors, leukopenia, thrombocytopenia, anemia, nausea, vomiting, diarrhea, alopecia, amenorrhea, hyperpigmentation, bone marrow suppression.

Dose and Administration: (refer to individual protocols)

Oral: For remission induction of CML:

Adult: 4 - 8 mg/day (may be as high as 12 mg/day).

Child: 0.06 - 0.12 mg/kg/day or 1.8 - 4.6 mg/m²/day;

Bone Marrow Transplant –ablative conditioning regimen:

Adult and Child: 1mg/kg/dose every 6 hours for 16 doses.

Storage: store in a well-closed container at room temperature.

Chlorambucil

Tablet, 2 mg, 5 mg

Indications: chronic lymphocytic leukaemia; Hodgkin and low grade non-Hodgkin's lymphomas; breast, ovarian and testicular carcinoma, thrombocythemia.

Cautions: seizure and bonemarrow suppression.

Drug interactions: live vaccines, ethanol.

Contraindications: pregnancy.

Side effects: myelosuppression (leukopenia, thrombocytopenia, anemia) skin rash, hyperuricemia, menstrual changes, nausea, vomiting, diarrhea, oral ulceration, agitation, ataxia, confusion, fever.

Dose and Administration: (refer to individual protocols):

Oral: Adult: 0.1- 0.2 mg/kg/day **or** 3 - 6 mg/m²/day for 3-6

weeks, then adjust dose on basis of blood counts **or** 0.4 mg/kg and increased by 0.1mg/kg biweekly or monthly **or** 14 mg/m²/day for 5 days, repeated every 21-28 days.**Child:** general short courses: 0.1- 0.2 mg/kg/day or 4.5 mg/m²/day for 3 - 6 weeks for remission induction (usual: 4-10mg/day); maintenance therapy: 0.03 - 0.1mg/kg/day.*Chronic lymphocytic leukaemia (CLL):* Biweekly regimen: Initial: 0.4 mg/kg/dose every 2 weeks; increase doses by 0.1mg/kg every 2 weeks until a response occurs and/or myelosuppression occurs. Monthly regimen: Initial: 0.4 mg/kg, increase dose by 0.2 mg/kg every 4 weeks until a response occurs and /or myelosuppression occurs. *Malignant lymphomas: Non-Hodgkin's lymphoma:* 0.1mg/kg/day. *Hodgkin's lymphoma:* 0.2mg/kg/day. **Storage:** store in refrigerator at 2-8°C; protect from light.

Cyclophosphamide

Powder for injection, 200 mg, 500 mg, 1000mg in vial

Tablet, 50 mg

Indications: malignant lymphomas including non-Hodgkin's lymphoma, lymphocytic lymphoma; multiple myeloma; leukaemias, mycosis, fungoides; neuroblastoma; adenocarcinoma of the ovary, retinoblastoma; breast cancer; severe rheumatoid arthritis.

Cautions: hepatic, renal, or bone marrow damage.

Drug interactions: allopurinol, succinyl choline, halothane, chloramphenicol, carbamazepine, nevirapine, phenytoin, suxamethonium, phenobarbitol, thiazide, digoxine, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, protease inhibitors, quinidine, verapamil, aminoglutethimide, phenobarbitol.

Contraindications: pregnancy and breast feeding

Side effects: sterility, amenorrhea, leukopenia, thrombocytopenia, anemia, nausea, vomiting, anorexia, mucositis, acute hemorrhagic cystitis, renal tubular necrosis, headache, skin rash, nasal congestion, diarrhea, alopecia, amenorrhea.

Dose and Administration: Adult and Child: *Oral:* 50-100 mg/m²/day as continuous therapy or 400-1000 mg/m² in divided doses over 4-5 days as intermittent therapy. *IV:* single dose: 400-1800 mg/m² (30-50 mg/kg) per treatment course (1-5 days) which can be repeated at 2-4 week intervals. Continuous daily doses: 60-120 mg/m² (1-2.5mg/kg) per day.

Storage: store at a temperature not exceeding 25°C.

Mechlorethamine Hydrochloride (Nitrogen Mustard)

Powder for injection, 10 mg in vial

Indications: Hodgkin's disease, non-Hodgkin's lymphoma, malignant effusions.

Cautions: Local reactions to extravasation of into the subcutaneous tissue result in a severe, brawny, tender induration that may persist for a long time.

Drug interactions: vaccines, ethanol.

Contraindications: pre-existing profound myelosuppression or infection, pregnancy, breast feeding.

Side effects: delayed menses, oligomenorrhea, amenorrhea, impaired spermatogenesis, nausea, vomiting, myelosuppressive, fever, vertigo, alopecia, hyperuricemia, diarrhea, anorexia, metallic taste, ototoxicity, precipitation of herpes zoster.

Dose and Administration: (refer to individual protocols): **Adult:** *IV:* 0.4 mg/kg or 12-16 mg/m² for one dose or divided into 0.1 mg/kg/day for 4 days, repeated at 4-6 week intervals. **Adult and Child:** *I.V:* 6 mg/m² on days 1 and 8 of a 28 day cycle (MOPP regimen)

Storage: store intact vials at room temperature.

Melphalan

Tablet, 2 mg, 5 mg

Indications: multiple myeloma, ovarian carcinomas and malignant melanoma.

Cautions: impaired renal function, elderly.

Drug interactions: cimetidine, cyclosporine, ethanol.

Contraindications: pregnancy, severe bone marrow suppression.

Side effects: leukopenia, thrombocytopenia, anemia, rash, nausea, vomiting, diarrhea, vasculites, alopecia, pruritus, sterility, amenorrhea, bladder irritation, hemorrhagic cystitis, agranulocytosis, hemolytic anemia, hepatitis, jaundice, pulmonary fibrosis.

Dose and Administration: (refer to individual protocols)**Adult:** *Multiple myeloma:* Oral 6 mg/day initially adjusted as indicated **or** 0.15 mg/kg/day for 7 days **or** 0.25 mg/kg/day for 4 days; repeat at 4-6 week intervals. *Ovarian carcinoma:* Oral: 0.2 mg/kg/day for 5 days, repeat every 4-5 weeks.

Storage: store in refrigerator at 2-8°C; protect from light.

Temozolomide

Capsule: 5mg, 20mg, 100mg, 140mg, 180mg, 250mg

Indications: first line for glioblastoma multiforme in adults in combination with radiotherapy and subsequently as monotherapy; adult patients with refractory (first relapse) anaplastic astrocytoma who have experienced disease progression on nitrosourea and procarbazine. ;. It is also licensed for second-line treatment of malignant glioma in adults and children over 3 years.

Cautions: Hepatic and renal impairment

Drug-interaction: Valproate, clozapine, food

Contraindications: Hypersensitivity to temozolomide and Dacarbazine or any component of the formulation; pregnancy and breast-feeding.

Side effect: Oral mucositis, tumour lysis syndrome, Hypericaemia, nausea and vomiting, alopecia, bone marrow suppression, fatigue, headache, convulsions, anorexia, constipation, rash, abdominal pain, stomatitis.

Dose and administration: (refer to individual protocols):*Anaplastic astrocytoma (refractory)*: Initial dose: 150mg/m²/day for 5 days; repeat every 28 days. Subsequent doses of 100-200mg/m²/day; based upon hematologic tolerance. This monthly-cycle regimen may be preceded by a 6 to 7 week regimen of 75mg/m²/day.

glioblastoma multiforme (high-grade glioma):

Concomitant phase: 75mg/m²/day for 42 days with radiotherapy. ANC \geq 1500/mm³, platelet count \geq 100,000/mm³, and common toxicity criteria (CTC) nonhematological toxicity \leq grade 1 (excludes alopecia, nausea/vomiting):75mg/m²/day may be continued throughout the 42-day concomitant period up to 49 days.

Maintenance phase (consist of 6 treatment cycles): Begin 4 weeks after concomitant phase completion. Note: Each subsequent cycle is 28 days (consisting of 5 days of drug treatment followed by 23 days without treatment). Cycle1:150mg/m²/day for 5 days

Elderly: Patients \geq 70 years of age had a higher incidence of grade 4 neutropenia and thrombocytopenia in the first cycle of therapy than patients < 70 years of age.

Storage: Store capsules at room temperature (15-25°C)

Thiotepa

Powder for injection, 15 mg/vial

Indications: superficial tumors of the bladder; palliative treatment of breast and ovarian carcinomas and malignant lymphomas.

Cautions: hepatic, renal, or bone marrow damage.

Drug interactions: other alkylating agents, succinylcholine and other neuromuscular agents.

Contraindications: pregnancy, breast feeding, severe myelosuppression.

Side effects: myelosuppression (anaemia, pancytopenia) dizziness, fever, rash, pruritus, headache, hyperpigmentation, hyperuricemia, anorexia, nausea, vomiting, hemorrhagic cystitis, pain at injection site, hematuria.

Dose and Administration: (*refer to individual protocols*): **Adult:** Bladder tumors: Intra vesically 30-60 mg instilled (in 60 ml of sterile water) once weekly for four weeks or $12\text{mg}/\text{m}^2$ IV bolus every three weeks: *IM, I.V, SC:* 30-60 mg/m^2 once weekly. **Breast and ovarian carcinoma I.V:** 0.3-0.4 mg/kg by rapid IV administration every 1-4 weeks **or** 0.2 mg/kg or 6-8 mg/ m^2 /day for 4-5 days every 2-4 weeks. **Child:** *Sarcomas: I.V:* 25-65 mg/ m^2 as a single dose every 21 days.

Storage: store intact vials under refrigeration (2-8°C) and protect from light.

11.2. Cytotoxic antibiotics

Medicines used in this group are widely used. Many cytotoxic antibiotics act as radiomimetics and simultaneous use of radiotherapy should be avoided as it may result in markedly enhanced toxicity.

Daunorubicin Hydrochloride, Doxorubicin hydrochloride (Adriamycin), Epirubicin are anthracycline antibiotics. Other cytotoxic antibiotics include actinomycin-D and bleomycin.

The anthracyclines can cause acute cardiotoxicity (arrhythmias) and long-term dose-related cardiomyopathy, which is often reversible. Assessment of adequate left ventricular function and careful monitoring for cardiac symptoms and signs is required during the following treatment. The anthracyclines are contraindicated in patients with pre-existing cardiac disease or severe hepatic or renal impairment. The elderly are at special risk of developing cardiac complications with this group of drugs.

Actinomycin-D (Dactinomycin)

Formulations: Powder for injection, 0.5 mg in vial

Indications: trophoblastic tumours, wilm tumour, Ewing sarcoma, rhabdomyosarcoma.

Cautions: hepatobiliary dysfunction.

Drug interactions: Live vaccines, radiation therapy.

Contraindications: infants <6 months of age, herpeszoster.

Side effects: fatigue, malaise, fever, lethargy, alopecia, skin eruptions, acne, increased pigmentation, hypocalcemia, severe nausea, vomiting, anorexia, myelosuppression, anemia, mucositis, stomatitis, diarrhea, abdominal pain, hepatitis.

Dose and Administration: (*refer to individual protocols*): **Adult:** I.V. 2.5 mg/m² in divided doses over 1 week, repeated every 2 weeks or 0.75-2 mg/m² every 1-4 weeks or 400-600 mcg/m²/day for 5 days, repeated every 3-6 weeks. **Child** (> 6 months): IV 15 mcg/kg/day or 400-600 mcg/m²/day for 5 days every 3-6 weeks.

Storage: protect from light and humidity and store at room temperature (15-25°C).

Bleomycin

Formulations: Powder for injection (lyo-philised), 15 unit in vial.

Indications: adjunct to surgery and radiotherapy in palliative treatment of Hodgkin's and non-Hodgkin's lymphomas; reticulum cell sarcoma and lymphoma; carcinomas of the head, neck, larynx, cervix, penis, skin, vulva, testicles including embryonal cell carcinoma, choriocarcinoma and teratoma, malignant effusions, germ cell tumors of the ovary, kaposi's sarcoma.

Cautions: pulmonary diseases.

Drug interactions: lomustine, cisplatin, digoxin, phenytoin, oxygen, live vaccines.

Contraindications: pregnancy and breast feeding.

Side effects: Raynaud's phenomenon, pain at the tumor site, phlebitis, peeling of the skin, hyperkeratosis, hyperpigmentation, alopecia, stomatitis, mucositis, anorexia, weight loss, tachypnea, pulmonary fibrosis, hypoxia, rash, anaphylactoid reactions.

Dosage and Administration: (refer to individual protocols): **Adult and Child:** Single agent therapy: I.M, I.V, and SC: Squamous cell carcinoma, lymphoma, testicular carcinoma: 0.25-0.5 units/kg (10-20 units/m²) 1-2 times/week. Combination agent therapy: I.M, I.V: 3-4 Units/m². I.V: (ABVD): 10 units/m² on days 1 and 15

Pleural sclerosing: 60-240 units as a single infusion

*1unit = 1mg

Storage: store at 2 - 8°C Refrigeration.

Daunorubicin Hydrochloride

Powder for injection, 20 mg in vial

Indications: acute leukaemias

Cautions: impaired hepatic, renal, or biliary function.

Drug interactions: Live vaccines

Contraindications: congestive heart failure or arrhythmias; bone marrow suppression, pregnancy.

Side effects: alopecia, mild nausea or vomiting, discolouration of urine, darkening or redness of skin, hyperuricemia, diarrhea, GI ulceration, myelosuppressive.

Dosage and Administration: (refer to individual protocols)
Adult and Child: *I.V.*: 30-60 mg/m²/day for 3-5 days, repeat dose in 3-4 weeks.

Storage: store at room temperature.

Doxorubicin hydrochloride (Adriamycin)

Powder for injection, 10 mg, 50 mg in vial.

Indications: acute leukaemias; carcinomas of the breast, bladder, ovary and thyroid; neuroblastoma; wilm tumour, Non-Hodgkin's and Hodgkin's lymphomas; soft tissue sarcomas, osteosarcoma.

Cautions: hepatic impairment.

Drug interactions: cyclosporin, phenytoin, stavudine, live vaccines, allopurinol, cyclophosphamide, mercaptopurine, verapamil, promethazine, azole antifungals, chlorpromazine, erythromycin, ciprofloxacin.

Contraindications: pregnancy and breast feeding; bone marrow suppression.

Side effects: cardiovascular diseases, alopecia, nausea, vomiting, mucositis, ulceration, anorexia, diarrhea, esophagitis, discolouration of urine (red), myelosuppression, leukopenia, arrhythmias, heart block, facial flushing, hyperpigmentation of nail beds, hyperuricemia.

Dosage and Administration: (refer to individual protocols)
Adult: *As a single therapy I.V. I.:* 50-75 mg/m² repeat every 21 days or 20-30 mg/m²/days for 2-3 days, repeat in 4 weeks or 20 mg/m² once weekly.

In Combination therapy: *I.V. I.* 40-60 mg/m² every 21-28 days. Multiple Myeloma: Combination therapy: *I.V.I* 9mg/m² /day on days 1-4 (in VAD regimen)

Child: As a single therapy: I.V.I. 35-75 mg/m² as a single dose, repeat every 21 days or 20-30 mg/m² once weekly or 60-90 mg/m² given as a continuous infusion over 96 hours every 3-4 weeks. In Combination therapy: *I.V. I.* 40-60 mg/m² every 21-28 days.

Storage: store at room temperature (15-25°C).

Doxorubicin (Liposomal)

Injection, 10mg, 50mg in vial

Indications: Treatment of AIDS-related Kaposi's sarcoma, breast cancer, ovarian cancer, solid tumors

Cautions: In patient with high cumulative doses of anthracyclines, anthracenediones, and cyclophosphamide; patients with previous thoracic radiation or who have pre-existing cardiac disease.

Drug interactions: Cyclosporine, allopurinol, cyclophosphamide, mercaptopurine, streptozocin, verapamil, paclitaxel, progesterone, bupropion, promethazine, propofol, selegiline, sertraline, and other CYP2B6 substrates, azol antifungals, chlorpromazine, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, quinine, ritonavir, aminoglutethimide, carbamazepine, nafcillin, nevirapine, Phenobarbital, phenytoin, rifamycins and other CYP3A4 inducers, digoxin, zidovudine, live vaccines.

Contraindications: Hypersensitivity to doxorubicin, other anthracyclines, or any component of the formulation; breast-feeding, pregnancy.

Side effects: Peripheral edema, fever, headache, pain, alopecia, palmar-plantar, erythrodysesthesia/hand-foot syndrome, rash,

II. Antineoplastic And Adjuvants

stomatitis, vomiting, nausea, constipation, anorexia, neutropenia, leucopenia, cytopenia, anemia, weakness, agitation, confusion, acne, dry skin

Dosage and Administration: *AIDS-related Kaposi's sarcoma:*

IV: 20 mg/m²/dose once every 3 weeks

Breast cancer: IV: 20-80mg/m²/dose every 8 weeks

Ovarian cancer: IV: 50 mg/m²/dose every 4 weeks

Solid tumors: IV: 50-60 mg/m²/dose every 3-4 weeks

Epirubicin

Powder for injection, 50 mg in vial, Injection, 2mg/ml

Indications: adjuvant therapy for primary breast cancer, Hodgkin's diseases, Non-Hodkin's lymphoma, carcinoma of esophagus, ovarian carcinoma.

Cautions: hepatic impairment, renal dysfunction, cardiac disease.

Drug interactions: cimetidine, ethanol.

Contraindications: severe myocardial insufficiency, severe arrhythmias, pregnancy, lactation.

Side effects: lethargy, alopecia, amenorrhea, nausea, vomiting, mucositis, diarrhea, leucopenia, hot flashes, anemia, thrombocytopenia, conjunctivitis, infection, fever, rash, skin changes, anorexia.

Dosage and Administration: Adult: I.V: 100-120 mg/m² once weekly every 3-4 weeks or 50-60 mg/m² days 1 and 8 every 3-4 weeks

Storage: store in refrigerator (2-8°C).

11.3. Antimetabolites

Antimetabolites are incorporated into new nuclear material or combine irreversibly with vital cellular enzymes, preventing normal cellular division. Antimetabolites include: capecitabine, cytarabine, fluorouracil, mercaptopurine and methotrexate.

Capecitabine

Tablet, 150mg, 500mg

Injection, 26mg/ml

Indications: treatment of metastatic colorectal cancer, metastatic breast cancer, gall bladder cancer, colangio carcinoma

Cautions: bone marrow suppression, poor nutritional status, on warfarin therapy, ≥ 80 years of age, or renal or hepatic dysfunction.

Drug interactions: warfarin.

Side effects: edema, fatigue, fever, dermatitis, diarrhea, mild to moderate nausea, vomiting, stomatitis, decreased appetite, anorexia, abdominal pain, constipation, anemia, lymphopenia, thrombocytopenia, dyspnea.

Dose and Administration: (refer to individual protocols): **Adult:** *Oral:* 2500 mg/m²/day in 2 divided doses (~12 hours apart) at the end of a meal for 14 days followed by a 1 or 2 week rest period.

Storage: store at room temperature (15-25°C).

Cytosine Arabinoside (Cytarabine)

Formulations: Powder for injection, 20 mg in vial

Indications: acute lymphoblastic leukaemia; chronic myeloid leukaemia; meningeal leukaemia; erythroleukemia; non-Hodgkin's lymphoma, CNS lymphoma.

Cautions: hepatic impairment.

Drug interactions: alkylating agents, methotrexate, gentamicin, flucytosin, digoxin.

Contraindications: hypersensitivity to cytarabine.

Side effects: Myelo suppression (leukopenia, thrombocytopenia, anemia), cerebral toxicity, conjunctivitis, corneal keratitis, pulmonary edema, pericarditis, seizures, oral/anal ulceration, rash, nausea, vomiting, anorexia, stomatitis, bleeding, hepatic dysfunction, mild jaundice, dizziness, headache, confusion, itching, hyperuricemia, diarrhea, urinary retention, hepatotoxicity, megaloblastic thrombophlebitis, myalgia, peripheral neuropathy.

Dosage and Administration: (refer to individual protocols):**Adult and Child:***Remission induction: IV:* 100-200 mg/m²/day for 5-10 days; a second course, beginning 2-4 weeks after the initial therapy.*Remission maintenance: IV:* 70-200 mg/m²/day for 2-5 days at monthly intervals.*IM, SC:* 1-2.5 mg/kg single dose for maintenance at 1-4 week intervals.*I.T.:* (meningeal leukaemia, CNS lymphoma): 5-75 mg/ m² every two weeks.

Storage: store at room temperature (15-25°C).

Fluorouracil

Injection, 250 mg/5ml, 500mg/10ml ampoule

Indications: carcinomas of the colorectum, breast, stomach, pancreas, cervix, prostate, ovary and endometrium; liver tumours; head and neck tumours actinic keratoses.

Cautions: impaired kidney and liver function.

Drug interactions: cimetidine, warfarin, metronidazole, phenytoin, live vaccines.

Contraindications: depressed bone marrow function, thrombocytopenia, potentially serious infections, dihydropyrimidine dehydrogenase (DPD) enzyme deficiency, pregnancy.

Side effects: rash, alopecia, nausea, vomiting, anorexia, diarrhea, stomatitis, esophagitis, leukopenia, dry skin, GI ulceration, peripheral neuropathy

Dosage and Administration: (refer to individual protocols):

Adult:*IV bolus:* 500-600 mg/m² every 3-4 weeks or 425 mg/m² on days 1-5 every 4 weeks. *Continuous IV infusion:* 1000 mg/m²/day for 4-5 days every 3-4 weeks or 2300-2600 mg/m² on day 1 every week or 300-400 mg/m²/day or 225 mg/m²/day for 5-8 weeks (with radiation therapy).

Storage: store at room temperature (15-25°C).

Mercaptopurine

Tablet- 50 mg

Indications: acute leukaemias.

Cautions: hepatic impairment, elderly.

Drug interactions: allopurinol, phenytoin, sulfamethoxazole+trimethoprim, live vaccines, doxorubicin, warfarin, sulfasalazine.

Contraindications: severe bone marrow suppression, pregnancy, breast feeding.

Dose and Administration: (refer to individual protocols):

Adult: *Oral:* Induction: 2.5 - 5 mg/kg/day (100-200mg). Maintenance: 1.5 - 2.5 mg/kg/day or 80 - 100 mg/m²/day given once daily

Child:*Oral:* Induction: 2.5 - 5 mg/kg/day or 70 - 100 mg/m²/day given once daily. Maintenance: 1.5 - 2.5 mg/kg/day or 50 - 75 mg/m²/day given once daily

Storage: store at room temperature (15-25°C).

Methotrexate

Powder for injection, 5 mg, 50mg in vial

Injection, 2mg/ml, 4mg/ml, 8mg/ml

Tablets, 2.5 mg, 10mg

Indications: carcinoma of the breast, head and neck, and lung, trophoblastic tumours; acute lymphoblastic leukaemia, meningeal leukaemia, non-Hodgkin's lymphomas; advanced cases of mycosis fungoides; non-metastatic osteosarcoma; psoriasis, severe rheumatoid arthritis.

Cautions: renal and hepatic impairment.

Drug interactions: acetyl salicylic acid, amoxicillin, ampicillin, benzyl penicillin, cyclosporin, dexamethasone, fludrocortisone, hydrocortisone, ibuprofen, phenoxymethylpenicillin, phenytoin, prednisolone, pyrimethamine, sulfadiazine, sulfadoxine + pyrimethamine, sulfamethoxazole + trimethoprim.

Contraindications: breast feeding, pregnancy, sexually active males avoid empringating females during and for a minimum of three months after therapy.

Side effects: headache, vomiting, fever, seizure, reddening of skin, hyperuricemia, defective oogenesis or spermatogenesis, ulcerative stomatitis, glossitis, nausea, vomiting, diarrhea, anorexia, mucositis, renal failure, nephropathy, pharyngitis, vasculitis, dizziness, malaise, encephalopathy, fever, chills, rash, diabetes, cystitis, hemorrhage, myelosuppressive, cirrhosis, blurred vision, renal dysfunction, pneumonitis.

Dosage and Administration: (refer to individual protocols):

Adult:Trophoblastic tumours: Oral, I.M: 15-30 mg/day for 5 days; repeat in 7 days for 3-5 courses.I.V: 11 mg/m² days 1 through 5 every 3 weeks.

Head and neck cancer: Oral, IM, IV: 25-50 mg/m² once weekly.**Mycosis fungoides:** Oral, IM: initial (early stage): 5-

50 mg once weekly or 5-37.5 mg twice weekly.**Bladder cancer:** IV: 30 mg/m² day 1 and 8 every 3 weeks or 30mg/m² day 1, 15, and 22 every 4 weeks.**Breast cancer:** IV: 30-60mg/m² days 1 and 8 every 3-4 weeks.**Gastric cancer:** IV:

1500mg/m² every 4 weeks.**Non-Hodgkin's lymphomas:** IV: 30mg/m² days 3 and 10 every 3 weeks or 120mg/m² day 8 and 15 every 3-4 weeks.**Sarcoma:** IV: 8-12g/m² weekly for 2-4 weeks.**Severe Rheumatoid arthritis:** Oral: 7.5mg once weekly or 2.5 mg every 12 hours for 3 doses perweek, not to exceed 20mg/week.

Psoriasis: Oral: 2.5-5mg/dose every 12 hours for 3 doses given weekly or Oral, IM: 10-25mg/dose given once weekly.

Storage: store in well-closed containers at 15 - 30°C.

Note: Calcium Folate (folinic acid) is used as an antidote for toxicity and side effects of methotrexate (see below and section 12.4 about folinic acid for details)

Calcium Folate (Leucovorin Calcium)

Powder for injection, Folinic Acid (Calcium salt), 15mg

Injection, 15mg, 50mg/vial

Tablet, 15mg

Indications: high-dose methotrexate therapy (folate rescue, inadvertent overdose of methotrexate); used to counteract the folate-antagonist action of methotrexate and thus speed recovery from methotrexate-induced mucositis or myelosuppression ('folinic acid rescue'); with fluoruracil in the palliative treatment of advanced colorectal cancer for better response.

Cautions: pernicious anemia or other megaloblastic anemias due to vitamin B₁₂ deficiency; pregnancy; breastfeeding.

Drug interactions: phenobarbital, phenytoin, and cotrimoxazole.

Contraindications: hypersensitivity to leucovorin.

Side effects: allergic reactions; pyrexia after parenteral administration.

Dose and Administration: (refer to individual protocols):

Adult and Child: *IM or IV injection or infusion: Antidote to methotrexate* (usually started 24 hour after methotrexate), up to 120 mg in divided doses over 12 to 24 hours, then 12 to 15 mg by IM every 6 hours for 48 - 72 hours or 15mg by mouth every 6 hours for 48-72 hours. Methotrexate overdose (started as soon as possible, preferably within 1 hour of methotrexate), by IV injection or infusion, Adult and Child, dose equal to or higher than that of methotrexate, at rate not exceeding 160mg/minute. *With fluorouracil* in colorectal cancer, consult specialist literature.

Storage: store at room temperature (15-25°C) and protect from light.

Vinca Alkaloids and Etoposide

The vinca alkaloids vinblastine and vincristine are used to treat acute leukaemia, lymphomas, and breast and lung cancer. Reversible dose-limiting neurotoxicity is found: peripheral neuropathy with paraesthesiae, cranial nerve palsies, muscle weakness, loss of deep tendon reflexes, paralytic ileus, and grandmal seizures. Pre-existing neurological disease may predispose to severe neuropathy. Etoposide is useful in small cell carcinoma of the bronchus, testicular cancer and lymphomas. It has been used in Kaposi's sarcoma.

Etoposide (Phosphate)

Capsules, 50 mg, 100 mg

Concentrate for infusion, 20 mg/ml.

Powder for injection, 100 mg/vial

Indications: testicular tumours; lung cancer.

Cautions: hepatic or renal impairment; elderly.

Drug interactions: Live vaccines.

Contraindications: intrathecal administration, pregnancy, breast feeding.

Side effects: alopecia, diarrhea, nausea, vomiting, anorexia, anemia, leukopenia, mucositis, hypotension, unusual fatigue, stomatitis, hepatic dysfunction.

Dosage and Administration: (refer to individual protocols):

Adult: *Lung cancer: IV:* 35 mg/m²/day for 4 days or 50 mg/m²/day for 5 days every 3-4 weeks total dose ≤ 400 mg/day. *Oral:* Twice the IV dose rounded to the nearest 50 mg given once daily if total dose ≤ 400 mg or in divided doses if > 400 mg. *Testicular cancer: IV:* 100 mg/m² every other day for 3 doses repeated every 3-4 weeks

Storage: store intact vials of injection at room temperature (15-25°C) and oral capsules in refrigeration (2-8°C).

Vinblastine (Sulphate)

Powder for injection, 10 mg, in vial

Indications: treatment of Hodgkin's and non-Hodgkin's lymphoma; advanced testicular carcinoma, breast carcinoma; palliative treatment of Kaposi's sarcoma, trophoblastic tumours.

Cautions: hepatic impairment

Drug interactions: Live vaccines, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, propofol, protease inhibitors, quinidine, and verapamil, aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin and rifamycins.

Contraindications: pregnancy and breastfeeding.

Side effects: alopecia, diarrhea, stomatitis, anorexia, metallic taste, severe bone marrow suppression, granulocytopenia, thrombocytopenia, hypertension, Raynaud's phenomenon, depression, malaise, headache,

seizure, rash, dermatitis, hyperuricemia, abdominal pain, nausea, vomiting, urinary retention, bronchospasm.

Dose and Administration: (refer to individual protocols):

Adult and Child: *IV*: 4-20 mg/m² (0.1-0.5mg/kg) every 7-10 days **or** 5 day continuous infusion of 1.5 to 2 mg/m²/day or 0.1-0.5 mg/kg/week.

Storage: store at in refrigerators (2 - 8°C).

Vincristine Sulfate

Powder for injection, 1mg, 5mg in vial

Indications: acute lymphoblastic leukaemia; neuroblastoma, wilm tumour, Hodgkin and non-Hodgkin lymphomas; rhabdomyosarcoma, Ewing sarcoma; mycosis fungoides.

Cautions: hepatic impairment.

Drug interactions: phenytoin, live vaccines.

Contraindications: pregnancy and breastfeeding.

Side effects: alopecia, orthostatic hypotension or hypertension, seizure, headache, CNS depression, fever, rash, hyperuricemia, constipation, anorexia, nausea, vomiting, weightloss, diarrhea, bladder atony, photophobia

Dose and Administration: Adult: 0.4-1.4 mg/m², may repeat every week **or** 0.4-0.5 mg/day continuous infusion for 4 days every 4 weeks **or** 0.25-0.5 mg/m²/day for 5 days every week.

Storage: store at 2 - 8°C.

Hormones and Antihormones

Anastrozole

Tablet, 1mg (film coated)

Indications: treatment of locally-advanced or metastatic breast cancer (ER-positive or hormone receptor unknown) in postmenopausal women; treatment of advanced breast cancer in postmenopausal women with disease progression following

tamoxifen therapy; adjuvant treatment of early ER-positive breast cancer in postmenopausal women.

Caution: hyperlipidemias.

Drug interactions: estrogen, tamoxifen.

Contraindications: pregnancy (risk factor D), hypersensitivity reaction.

Side effects: vasodilation, headache, depression, hot flashes, arthritis, arthralgia, back pain, cough increased, pharyngitis, peripheral edema, hypertension, insomnia, dizziness, anxiety, rash, vomiting, constipation, diarrhea, anorexia, anemia, dyspnea.

Dose and Administration: *Breast cancer: Adult: Oral* (refer to individual protocols): 1 mg once daily.

Storage: store at room temperature.

Bicalutamide

Tablet, 50mg, 150mg

Indications: locally advanced prostate cancer at high risk of disease progression, either alone or as adjuvant treatment to prostatectomy or radiotherapy; locally advanced, non-metastatic prostate cancer when surgical castration or other medical intervention inappropriate; advanced prostate cancer in combination with gonadorelin analogue or surgical castration

Cautions: hepatic impairment, also consider periodic liver function tests

Drug interactions: Coumarins

Side effects : nausea, diarrhoea, cholestasis, jaundice; asthenia, weight gain; gynaecomastia, breast tenderness, hot flushes, impotence, decreased libido; anaemia; alopecia, dry skin, hirsutism, pruritus; less commonly vomiting, abdominal pain, dyspepsia, interstitial lung disease, pulmonary fibrosis, depression, haematuria, thrombocytopenia, hypersensitivity

reactions including angioneurotic oedema and urticaria; rarely cardiovascular disorders (including angina, heart failure, and arrhythmias), and hepatic failure

Dose and administration: Locally advanced prostate cancer at high risk of disease progression: 150 mg once daily. Locally advanced, non-metastatic prostate cancer when surgical castration or other medical intervention inappropriate: 150 mg once daily. Advanced prostate cancer: in combination with goserelin analogue or surgical castration, 50 mg once daily (started at the same time as surgical castration or at least 3 days before goserelin therapy)

Tamoxifen Citrate

Tablet, 10 mg, 20mg

Indications: adjuvant treatment of estrogen - receptor-positive breast cancer; metastatic breast cancer; reduce the incidence of breast cancer in women at high risk.

Cautions: leukopenia, thrombocytopenia, or hyperlipidemias.

Drug interactions: warfarin, allopurinol, cyclosporine, delavirdine, fluconazole, gemfibrozil, ketoconazole, NSAIDs, sulfonamides, chlorpromazine, miconazole, fluoxetine, quinidine, quinine, ritonavir, erythromycin, ciprofloxacin, diclofenac, doxycycline, isoniazid, verapamil, carbamazepine, phenobarbital, phenytoin, rifampin, nevirapine.

Contraindications: pregnancy; breast-feeding.

Side effects: hot flushes; endometrial changes (symptoms such as vaginal bleeding and other menstrual irregularities, vaginal discharge, pelvic pain); increased pain and hypercalcaemia with bony metastases; tumour flare; nausea and vomiting; liver enzyme changes; thromboembolic events; decreased platelet count; oedema; alopecia; rash; headache; visual disturbances; rarely hypersensitivity reactions.

Dosage and Administration:Adult:*Breast cancer: Metastatic:* 20 mg/day; *Prevention (high-risk females):* 20mg/day for 5 years.

Storage: store in well closed containers at controlled room temperature.

Testosterone Propionate

Tablet (buccal), 10 mg

Indications: used for replacement therapy

Cautions: cardiac impairment, elderly, ischaemic heart disease, hypertension, epilepsy, migraine, diabetes mellitus, skeletal metastases (risk of hypercalcaemia), undertake regular examination of the prostate and breast during treatment; monitor full blood count, lipid profile and liver function. Women: Regularly assess for androgenic side-effects; women should be advised to report any signs of virilisation e.g. deepening of the voice or hirsutism.

Drug Interactions: Antidiabetics, coumarins, phenindione.

Contra indications: breast cancer in men, prostate cancer, history of primary liver tumours, hypercalcaemia, nephrotic syndrome, Hepatic impairment and avoid if possible—fluid retention and dose-related toxicity, renal impairment, Pregnancy; Breast-feeding; **child and adolescents** under 18 years.

Side effects: prostate abnormalities and prostate cancer, headache, depression, gastro-intestinal bleeding, nausea, vomiting, cholestatic jaundice, changes in libido, gynaecomastia, polycythaemia, anxiety, irritability, nervousness, asthenia, paraesthesia, hypertension, electrolyte disturbances including sodium retention with oedema and hypercalcaemia, weight gain; increased bone growth, muscle cramps, arthralgia; androgenic effects such as hirsutism, male-

pattern baldness, seborrhoea, acne, pruritus, excessive frequency and duration of penile erection, precocious sexual development and premature closure of epiphyses in pre-pubertal males, suppression of spermatogenesis in men and virilism in women; *rarely* liver tumours; sleep apnoea also reported; *with patches, buccal tablets, and gel*, local irritation and allergic reactions (including burn-like lesions with *patches*), and taste disturbances

Dose and Administration: hypogonadism, 30 mg every 12 hours. *Note: Place rounded side of tablet on gum above front teeth and hold lip firmly over the gum for 30 seconds. If tablet detaches within 4 hours of next dose, replace with new tablet which is considered the second dose for the day.*

Raloxifene Hydrochloride

Tablet, 30mg

Indication: Prevention and treatment of osteoporosis in postmenopausal women, prophylaxis of invasive breast cancer in post menopausal women at high risk

Cautions: History of venous thromboembolism/ pulmonary embolism; patients with cardiovascular disease; history of cervical/uterine carcinoma; renal/hepatic insufficiency; concurrent use of estrogens; women with a history of elevated triglycerides in response to treatment with oral estrogens.

Contraindications: Hypersensitivity to the medicine or any component of the formulation; active thromboembolic disorder; pregnancy, breast feeding.

Drug Interactions: Highly protein-bound medicines, warfarin, clofibrate, indomethacin, naproxen, ibuprofen, diazepam, phenytoin, tamoxifen, ampicillin, cholestyramine.

Side effects: Hot flashes, arthralgia, sinusitis, infection, chest pain, fever, migraine, depression, insomnia, rash, peripheral edema, nausea, dyspepsia, vomiting, GI disorder

Dosage and Administration: Adults: Female; *Oral*: 60mg per day which may be administered any time of the day without regard to meals

Monoclonal Antibodies

Bevacizumab

Injection, 25 mg/ml, 25mg/ vial

Indications: metastatic colorectal cancer as a component of multidrug therapy, breast cancer and lung cancer

Cautions: cardiovascular disease.

Drug interactions: it may potentiate the cardiotoxic effects of anthracyclines.

Contraindications: hypersensitivity reactions.

Side effects: hypertension, hypotension, thromboembolism, headache, dizziness, alopecia, weight loss, hypokalemia, abdominal pain, vomiting, diarrhea, anorexia, constipation, stomatitis, dyspepsia, flatulence, leukopenia, epistaxis, gastrointestinal hemorrhage, neutropenia, myalgia, dyspnea.

Dosage and Administration:*IV:Adult:Colorectal cancer: 5-10 mg/kg every 2 weeks*

Storage: store vials at 2 - 8 °C. Protect from light; do not freeze or shake.

Rituximab

Injection, 100 mg/10ml

Indications: relapsed or refractory CD20 positive, B-cell non-Hodgkin's lymphoma, chronic lymphoid leukemia

Cautions: cardiac or pulmonary disease and hypersensitivity reactions.

Side effects: abdominal pain, anemia, dyspnea, hypotension, and neutropenia are more common in patients with bulky disease. Central nervous system (fever, chills, headache, pain),

rash, pruritus, angioedema, nausea, abdominal pain, lymphopenia, cough, rhinitis.

Dosage and Administration:Adult: *I.V infusion* Manufacturer's labeling: 375 mg/m² once weekly for 4 - 8 weeks. or 100 mg/m² IV day 1, then 375 mg/m² 3 times/week for 11 doses has also been reported (cycles may be repeated in patients with refractory or relapsed disease).Retreatment following disease progression: 375 mg/m² once weekly for 4 doses.

Storage: store vials under refrigeration (2 - 8 °C).

11.4. Cytotoxic immunosuppressants

Azathioprine

Tablet, 50 mg

Indications: organ transplantation, in combination with steroids and/or other immunosuppressants; auto immune diseases such as systemic lupus erythematosus, refractory rheumatoid arthritis, idiopathic thrombocytopenia purpura, autoimmune haemolytic anemia and chronic active hepatitis.

Cautions: liver and renal impairment, monitor hematologic function closely.

Drug interactions: allopurinol, sulfasalazine, warfarin.

Contraindications: pregnancy.

Side effects: myelosuppression with occasional thrombocytopenia and anaemia; severe red cell megaloblastosis, hepatotoxicity, hypersensitivity reactions, including anaphylaxis, may occur.

Dose and Administration:Adult and **Child:***Renal transplantation: Oral:* 2-5 mg/kg/day to start, then 1-3 mg / kg / day maintenance.**Adult: Rheumatoid arthritis: Oral:** 1 mg/kg/day for 6-8 weeks; increase by 0.5 mg/kg every 4 weeks until response or up to 2.5 mg/kg/day.

Storage: store at room temperature.

11.5. Other Antineoplastics

Cisplatin

Powder for injection, 10 mg, 50 mg/ vial

Injection, 10mg, 50mg/vial

Indications: treatment of head and neck, breast, testicular and ovarian cancer; Hodgkin's and non-Hodgkin's lymphoma; neuroblastoma, sarcomas, bladder, gastric, lung, esophageal, cervical, and prostate cancer; myeloma, melanoma, mesothelioma, small cell lung cancer, and osteosarcoma.

Cautions: renal impairment, myelosuppression, hearing impairment.

Drug interactions: acetazolamide, amiloride, furosemide, gentamicin, hydrochlorothiazide, phenytoin, spironolactone, streptomycin, vancomycin, vaccine (live).

Contraindications: pregnancy.

Side effects: peripheral neuropathy, mild alopecia, nausea and vomiting, myelosuppressive, elevation of liver enzymes, nephrotoxicity, ototoxicity, arrhythmias, blurred vision, bradycardia, cerebral blindness, hemolytic anemia, electrolyte imbalance.

Dosage and Administration: (refer to individual protocols) *I.V.* in not less than 4 hours and it needs prehydration. **Adult:** *Advanced bladder cancer:* 50-70 mg/m² every 3-4 weeks. *Head and neck cancer:* 100-120 mg/m² every 3-4 weeks. *Metastatic ovarian cancer:* 75-100 mg/m² every 3 weeks. *Testicular cancer:* 10-20 mg/m²/day for 5 days repeated every 3-4 weeks.

Storage: store at room temperature and protect from light.

Dacarbazine

Powder for injection, 100mg, 200mg, 500mg, 600mg, 1000mg/vial

Indications: treatment of malignant melanoma, hodgkin's disease, soft-tissue sarcomas, medullary carcinoma of the thyroid, and neuroblastoma.

Dose and Administration: (refer to individual protocols)
I.V.: Hodgkin's disease, ABVD: 375mg/m² days 1 and 15 every 4 weeks or 100 mg/m²/day for 5 days. *Metastatic melanoma (alone or in combination with other agents):* 150-250mg/m² days 1-5 every 3-4 weeks. *Metastatic melanoma:* 850mg/m² every 3 weeks

Storage: store intact vials under refrigeration (2-8°C) and protect from light.

Hydroxycarbamide (hydroxyurea)

Capsule, 500 mg

Indications: treatment of metastatic disease, chronic myeloid leukaemia, haemoglobinopathies including sickle cell disease and tumours of the head and neck, an adjunct to nucleoside reverse transcriptase inhibitor in the treatment of HIV disease.

Cautions: renal impairment, bone marrow suppression, erythrocytic abnormalities, and elderly.

Drug interactions: zidovudine, zalcitabine, didanosine, fluorouracil, cytarabine, and stavudine.

Contraindications: severe anemia, pregnancy.

Side effects: edema, drowsiness, hallucinations, headache, dizziness, disorientation, seizure, fever, chills, erythema of hands and face, rash, pruritus, hyperpigmentation, dry skin, skin cancer, hyperuricemia, nausea, vomiting, stomatitis, anorexia, diarrhea, constipation, pancreatitis, dysuria, myelosuppression, hepatotoxicity, peripheral neuropathy, dyspnea, pulmonary fibrosis.

Dose and Administration: (*refer to individual protocols*):
Oral:Adult:Solid tumors: Intermittent therapy: 80 mg/kg as a single dose every third day.

Continuous therapy: 20-30 mg/kg/day given as a single dose/day. *Concomitant therapy with irradiation:* 80 mg/kg as a single dose every third day starting at least 7 days before initiation of irradiation.*Resistant chronic myelocytic leukemia:* Continuous therapy: 20-30 mg/kg as a single daily dose. *HIV (in combination with ARV agents):* 1000-1500 mg daily in a single dose or divided doses.*Sickle cell anemia: initial:* 15 mg/kg/day, increased by 5 mg/kg every 12 weeks if blood counts are in an acceptable range until the maximum tolerated dose of 35 mg/kg/day is achieved.

Storage: store at room temperature.

Procarbazine

Capsule, (as hydrochloride) 50 mg

Indications: treatment of Hodgkin's disease.

Cautions: renal and hepatic impairment.

Drug interactions: foods containing high amounts of tyramine, epinephrine, amphetamine, antidepressants, narcotics, phenothiazines, and other CNS depressants.

Contraindications: pre-existing bone marrow aplasia; ethanol ingestion; pregnancy.

Side effects: mental depression, manic reactions, hallucinations, dizziness, headache, nervousness, insomnia, nightmares, ataxia, confusion, CNS stimulation, amenorrhea, nausea, vomiting, anorexia, abdominal pain, stomatitis, dysphagia, diarrhea, constipation, thrombocytopenia, hemolytic anemia, myelosuppressive, paresthesia, neuropathies, nystagmus, pleural effusion, cough, hepatotoxicity, peripheral neuropathy, alopecia, hyperpigmentation.

Dose and Administration: (refer to individual protocols):
Oral: Adult: Initial: 2-4 mg/kg/day in single or divided doses for 7 days then increase dose to 4-6 mg/kg/day until response is obtained. *Child: BMT aplastic anemia conditioning regimen:* 12.5 mg/kg/dose every other day for 4 doses. *Hodgkin's disease: MOPP/IC-MOPP regimens:* 100 mg/m²/day for 14 days and repeated every 4 weeks. *Neuroblastoma and medulloblastoma:* dose as high as 100-200 mg/m²/day once daily have been used.
Storage: store in tight, light - resistant containers and at room temperature.

Miscellaneous

Filgrastin

Injection, 300 mcg/ml, 300 mcg/0.5ml syringe, 480 mcg/1.6ml, 480 mcg /0.8 ml syringe, 30mu/0.5ml

Indications: stimulation of granulocyte production in patients with malignancies, including myeloid malignancies; receiving myelosuppressive therapy associated with a significant risk of neutropenia; severe chronic neutropenia (SCN); receiving bone marrow transplantation (BMT); undergoing peripheral blood progenitor cell (PBPC) collection.

Cautions: complete blood count and platelet count should be obtained prior to chemotherapy.

Drug interactions: medicines which may potentiate the release of neutrophils (e.g. lithium)

Contraindications: concurrent myelosuppressive chemotherapy or radiation therapy, pregnancy, breast feeding

Side effects: neutropenic fever, alopecia, nausea, vomiting, diarrhea, mucositis, chest pain, fluid retention, headache, anorexia.

Dosage and Administration: Refer to individual protocols: *IV or SC: Myelosuppressive therapy:* 5 mcg/kg/day – doses may be

increased by 5 mcg/kg according to the duration and severity of the neutropenia. *BMT*: 5 to 10 mcg/kg/day doses may be increased by 5 mcg/kg according to the duration and severity of neutropenia. *PBPC*: 10 mcg/kg/day or 5 to 8 mcg/kg twice daily in donors. *Severe chronic neutropenia: Congenital*: 6mcg/kg twice daily

Idiopathic/Cyclic: 5 mcg/kg/day

Storage: store in refrigerator at 2 – 8 °C.

Granisetron Hydrochloride

Tablet, 1mg, 2 mg

Injection, 1mg, 3mg in ampoule

Indications: prophylaxis of chemotherapy - related emesis; prophylaxis of nausea and vomiting associated with radiation therapy, including total body irradiation and fractionated abdominal radiation; prophylaxis of postoperative nausea and vomiting (PONV).

Cautions: chemotherapy -related emesis; liver diseases or in pregnancy.

Drug interactions: substrate of CYP3A4.

Contraindications: hypersensitivity reactions.

Side effects: headache, constipation, hypertension, dizziness, insomnia, anxiety somnolence, fever, abdominal pain, diarrhea, dyspepsia, elevated liver enzymes.

Dose and Administration: *Oral: Adult: Prophylaxis of chemotherapy-related emesis:* 2 mg once daily up to 1 hour before chemotherapy or 1 mg twice daily; the first 1 mg dose should be given up to 1 hour before chemotherapy. *Prophylaxis of radiation therapy-associated emesis:* 2 mg once daily given 1 hour before radiation therapy.

Storage: store at room temperature and protect from light.

Ondansetron

Tablet, 4mg, 8mg

Syrup, 4mg/5ml

Injection, 2mg/ml, 4mg/ml, 8mg/ml

Suppository, 16mg

Indications: management of nausea and vomiting induced by chemotherapeutic agents and radiotherapy; prevention and treatment of post-operative nausea and vomiting.

Cautions: previous hypersensitivity to other selective 5HT₃-receptor antagonists; hepatic impairment; subacute intestinal obstruction; porphyria; pregnancy; lactation.

Contraindications: known hypersensitivity to the product.

Side effects: headache, flushing, hiccups, constipation, transient, asymptomatic increase in aminotransferases. Hypersensitivity reactions (anaphylaxis, bronchospasm, hypotension, shock, angioedema, urticaria).transient visual disturbances and dizziness with rapid IV administration; pain, redness at injection site.

Dosage and Administration: **Adult:** *Highly emetogenic chemotherapy (e.g. cisplatin):* Slow IV or IM, 8mg immediately before treatment, followed by 2 further IV or IM doses of 8mg 2-4 hours apart (or by a continuous IV infusion of 1mg/hour for up to 24 hours). Alternatively, a single dose of 32mg diluted in 50-100ml 0.9% sodium chloride solution and infused over not less than 15 minutes immediately before chemotherapy. To protect against delayed or prolonged emesis after the first 24hours, continue with oral, 8mg 12hourly for up to 5 days.*Less emetogenic chemotherapy: Oral:* 8mg 1-2 hours before treatment (or *slow IV or IM*, 8mg immediately before treatment), followed by oral, 8mg 12 hourly for up to 5 days.*Post-operative nausea and vomiting: immediately before*

induction of anaesthesia or postoperatively, 4mg IM or IV over 2-5 minutes. Alternatively, 16mg orally 1 hour before induction. Repeat dosing has not been studied. *Moderate to severe hepatic impairment*: total daily dose of 8mg should not be exceeded. *Child: Emetogenic chemotherapy*: >4 years, IV, 5mg/m² given over 15 minutes, immediately before treatment, followed by oral, 4mg 12 hourly for up to 5 days. *Post-operative nausea and vomiting*: ≥ 2 years, slow IV, 0.1mg/kg up to a maximum of 4 mg, prior to, at, or after, induction of anaesthesia.

Ibandronate

Tablet, 50mg, 150mg

Indications: Hypercalcemia of malignancy, reduce bone pain and skeletal complications from metastatic bone disease.

Cautions, Drug interactions, Contraindications, Side effects and Dose and Administration: See under bone modulating medicine under Ibandronate

Zoledronic acid

4mg/5ml injection

Indication: for treatment of hypercalcemia associated with malignant neoplasms and adjunct to antineoplastic therapy for the treatment of bone metastases of solid tumors and osteolytic lesions of multiple myeloma.

Cautions: renal impairment, serum concentration of calcium, phosphate, magnesium, potassium, and other electrolytes, and also hematocrit and hemoglobin should be monitored carefully. Aspirin-sensitive asthmatic patients, breastfeeding, children and elderly.

Contraindication: known hypersensitivity to zoledronic acid, other bisphosphonates, or any ingredient in the formulation.

II. Antineoplastic And Adjuvants

Side effects: fever, nausea, constipation, anemia, dyspnea, diarrhea, progression of cancer, abdominal pain, insomnia, vomiting, urinary tract infection, anxiety, hypophosphatemia, confusion, agitation, hypokalemia, skeletal pain, cough, hypotension. Hypomagnesemia.

Drug interaction: loop diuretics, aminoglycosides, nephrotoxic agents, thalidomide.

12. BLOOD PRODUCTS and MEDICINES AFFECTING the BLOOD

12.1. Anticoagulants

Anticoagulants are used to prevent thrombus formation or extension of an existing thrombus in the slower-moving venous side of the circulation, where the thrombus consists of a fibrin web enmeshed with platelets and red cells. They are therefore used widely in the prevention and treatment of deep-vein thrombosis in the legs, prophylaxis of embolization in rheumatic heart disease and atrial fibrillation and to prevent thrombi forming on prosthetic heart valves.

Dalteparin

Injection, (Antifactor Xa), 5,000U; 10,000U; 25,000U; 75,000U

Prefilled syringe, 5000U, 7500U, 10,000U

Indications: Prevention of deep vein thrombosis (DVT) which may lead to pulmonary embolism, in patients requiring abdominal surgery who are at risk for thromboembolism complications (eg, patients >40 years of age, obesity, patients with malignancy, history of DVT or pulmonary embolism, and surgical procedures requiring general anesthesia and lasting >30 minutes); prevention of DVT in patients undergoing hip-replacement surgery; patients immobile during an acute illness; prevention of ischemic complications in patients with unstable angina or non-Q-wave myocardial infarction on concurrent aspirin therapy; in patients with cancer, extended treatment (6 months) of acute symptomatic venous thromboembolism (DVT and/or PE) to reduce the recurrence of venous thromboembolism

Cautions and Side effects; see under heparin.

Dosage and Administration: Note: Each 2500 units of anti-Xa activity is equal to 16 mg of dalteparin.

Adult: SC: DVT prophylaxis: Note: In morbidly obese patients (BMI ≥ 40 kg/m²), increasing the prophylactic dose by 30% may be appropriate (Nutescu, 2009):

Abdominal surgery: Low-to-moderate DVT risk: SC: 2500 units 1-2 hours prior to surgery, then once daily for 5-10 days postoperatively. High DVT risk: SC: 5000 units the evening prior to surgery and then once daily for 5-10 days postoperatively. Alternatively in patients with malignancy: 2500 units 1-2 hours prior to surgery, 2500 units 12 hours later, then 5000 units once daily for 5-10 days postoperatively. General surgery with risk factors for VTE: 2500 units 1-2 hours preoperatively followed by 2500-5000 int. units every morning (may administer 2500 units no sooner than 4 hours after surgery and 8 hours after previous dose provided hemostasis has been achieved) or if other risk factors are present (eg, malignancy, heart failure), then may administer 5000 units the evening prior to surgery followed by 5000 units every evening postoperatively; continue treatment until patient is mobilized (approximately $\geq 5-7$ days).

Total hip replacement surgery: SC: *Note: Three treatment options are currently available. Dose is given for 5-10 days, although up to 14 days of treatment have been tolerated in clinical trials. The American College of Chest Physicians (ACCP) recommends a minimum duration of at least 10-14 days; extended duration of up to 35 days is suggested.*

Postoperative regimen: Initial: 2500 units 4-8 hours after surgery (or later if hemostasis not achieved). The ACCP recommends initiation ≥ 12 hours after surgery if postoperative regimen chosen. Maintenance: 5000 int. units once daily; allow at least 6 hours to elapse after initial postsurgical dose (adjust

administration time accordingly).**Preoperative regimen (starting day of surgery):**Initial: 2500 int. units within 2 hours before surgery. The ACCP recommends initiation ≥ 12 hours before surgery if preoperative regimen chosen. At 4-8 hours after surgery (or later if hemostasis not achieved), administer 2500 int. units.Maintenance: 5000 units once daily; allow at least 6 hours to elapse after initial postsurgical dose (adjust administration time accordingly)

Preoperative regimen (starting evening prior to surgery):Initial: 5000 int. units 10-14 hours before surgery. The ACCP recommends initiation ≥ 12 hours before surgery if preoperative regimen chosen. At 4-8 hours after surgery (or later if hemostasis not achieved), administer 5000 int. units.Maintenance: 5000 int. units once daily, allowing 24 hours between doses.Immobility during acute illness: 5000 units once daily.

Unstable angina or non-Q-wave myocardial infarction: SC: 120 units/kg body weight (maximum dose: 10,000 units) every 12 hours for up to 5-8 days with concurrent aspirin therapy. Discontinue dalteparin once patient is clinically stable.Obesity: Use actual body weight to calculate dose; dose capping at 10,000 units recommended.

Venous thromboembolism, extended treatment in cancer patients: SC:Initial (month 1): 200 units/kg (maximum dose: 18,000 units) once daily for 30 days.Maintenance (months 2-6): ~150 units/kg (maximum dose: 18,000 units) once daily. If platelet count between 50,000-100,000/mm³, reduce dose by 2,500 units until platelet count recovers to $\geq 100,000$ /mm³. If platelet count $< 50,000$ /mm³, discontinue dalteparin until platelet count recover to $> 50,000$ /mm³.

Note: If increased bleeding risk, may give 100 units/kg SC twice daily. Concomitant treatment with a vitamin-K antagonist is usually initiated immediately.

Storage: Store at temperatures of 20°C to 25°C. Multidose vials may be stored for up to 2 weeks at room temperature after entering.

Enoxaparin

Injection, 20mg/0.2ml, 40mg/0.4ml, 60mg/0.6ml, 80mg/0.8ml, 100mg/ml

Indications: Acute coronary syndromes: Unstable angina (UA), non-ST-elevation (NSTEMI), and ST-elevation myocardial infarction (STEMI).DVT prophylaxis: Following hip or knee replacement surgery, abdominal surgery, or in medical patients with severely-restricted mobility during acute illness who are at risk for thromboembolic complications. DVT treatment (acute): Inpatient treatment (patients with and without pulmonary embolism) and outpatient treatment (patients without pulmonary embolism).

Note: High-risk patients include those with one or more of the following risk factors: >40 years of age, obesity, general anesthesia lasting >30 minutes, malignancy, history of deep vein thrombosis or pulmonary embolism

Cautions and Side effects:see under heparin.

Dose and Administration: One mg of enoxaparin is equal to 100 units of anti-Xa activity (World Health Organization First International Low Molecular Weight Heparin Reference Standard).**Adult:DVT prophylaxis:** Note: In morbidly obese patients (BMI \geq 40 kg/m²), increasing the prophylactic dose by 30% may be appropriate for some indications or bariatric surgery, dose increases may be >30% based on clinical trial data. SubQ:**Hip replacement surgery:** Twice-daily dosing: 30 mg every 12 hours, with initial dose within 12-24 hours after

surgery, and every 12 hours for at least 10 days or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively or ≥ 12 hours postoperatively; extended duration of up to 35 days suggested. Once-daily dosing: 40 mg once daily, with initial dose within 9-15 hours before surgery, and daily for at least 10 days (or up to 35 days postoperatively) or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively or ≥ 12 hours postoperatively; extended duration of up to 35 days suggested (Guyatt, 2012). **Knee replacement surgery:** 30 mg every 12 hours, with initial dose within 12-24 hours after surgery, and every 12 hours for at least 10 days or until risk of DVT has diminished or the patient is adequately anticoagulated on warfarin. The American College of Chest Physicians recommends initiation ≥ 12 hours preoperatively or ≥ 12 hours postoperatively; extended duration of up to 35 days suggested. **Abdominal surgery:** 40 mg once daily, with initial dose given 2 hours prior to surgery; continue until risk of DVT has diminished (usually 7-10 days).

Heparin

Injection (solution for injection) 1000U/ml, 5000 U/ml, 10,000U/ml, 12,500 U/ml, 25,000U/ml

Injection, 1000IU in 500ml Normal Saline.

Indications: Prophylaxis and treatment of thromboembolic disorders; as an anticoagulant for extracorporeal and dialysis procedures.

Cautions: hepatic impairment and renal failure; spinal or epidural anaesthesia risk of spinal haematoma; pregnancy;

diabetes mellitus, acidosis, concomitant potassium-sparing drugs increased risk of hyperkalaemia.

Drug interactions: acetylsalicylic acid, captopril and ibuprofen, nitroglycerin, omega-3 fatty acids

Contraindications: Hypersensitivity to heparin or any component of the formulation (unless a life-threatening situation necessitates use and use of an alternative anticoagulant is not possible); severe thrombocytopenia; uncontrolled active bleeding except when due to disseminated intravascular coagulation (DIC); not for use when appropriate blood coagulation tests cannot be obtained at appropriate intervals (applies to full-dose heparin only)

Note: Some products contain benzyl alcohol as a preservative; their use in neonates, infants, or pregnant or nursing mothers is contraindicated by some manufacturers.

Side effects: immune-mediated thrombocytopenia usually developing 6 to 10 days after commencement of therapy; haemorrhage, skin necrosis, hypersensitivity reactions including urticaria, angioedema and anaphylaxis, osteoporosis after prolonged use and rarely alopecia.

Dosage and Administration: Many concentrations of heparin are available ranging from 1 unit/mL to 20,000 units/ml. Carefully examine each prefilled syringe or vial prior to use ensuring that the correct concentration is chosen. Heparin lock flush solution is intended only to maintain patency of I.V. devices and is not to be used for anticoagulant therapy.**Acute coronary syndromes:** I.V. infusion (weight-based dosing per institutional nomogram recommended):STEMI: Adjunct to fibrinolysis (full-dose alteplase, reteplase, or tenecteplase) (Antman, 2008): Initial bolus of 60 units/kg (maximum: 4000 units), then 12 units/kg/hour (maximum: 1000 units/hour) as continuous infusion. Check aPTT every 4-6 hours; adjust to

target of 1.5-2 times the upper limit of control (50-70 seconds). Duration of heparin therapy depends on concurrent therapy and the specific patient risks for systemic or venous thromboembolism. Unstable angina (UA)/non-ST-elevation myocardial infarction (NSTEMI) (Anderson, 2007): Initial bolus of 60 units/kg (maximum: 4000 units), followed by an initial infusion of 12 units/kg/hour (maximum: 1000 units/hour). Check aPTT every 4-6 hours; adjust to target of 1.5-2 times the upper limit of control (50-70 seconds). Continue for 48 hours in low risk patients managed with a conservative strategy (ie, no diagnostic angiography or PCI) (Jneid, 2012). **Percutaneous coronary intervention:** No prior anticoagulant therapy: If no GPIIb/IIIa inhibitor use planned: Initial bolus of 70-100 units/kg or If planning GPIIb/IIIa inhibitor use: Initial bolus of 50-70 units/kg. Prior anticoagulant therapy: If no GPIIb/IIIa inhibitor use planned: Additional heparin as needed (eg, 2000-5000 units) or If planning GPIIb/IIIa inhibitor use: Additional heparin as needed (eg, 2000-5000 units) (target ACT 200-250 seconds regardless of device). **Thromboprophylaxis** (low-dose heparin): SubQ: 5000 units every 8-12 hours. Note: The American College of Chest Physicians recommends a minimum of 10-14 days for patients undergoing total hip arthroplasty, total knee arthroplasty, or hip fracture surgery. **Treatment of venous thromboembolism:** Note: Start warfarin on the first or second treatment day and continue heparin until INR is ≥ 2 for at least 24 hours (usually 5-7 days). **Intermittent I.V. Anticoagulation:** Intermittent I.V.: Initial: 10,000 units, then 50-70 units/kg (5000-10,000 units) every 4-6 hours. Maintenance of line patency (line flushing): When using daily flushes of heparin to maintain patency of single and double lumen central catheters, 10 units/mL is commonly used for

younger infants (eg, <10 kg) while 100 units/mL is used for older infants, children, and adults. Capped PVC catheters and peripheral heparin locks require flushing more frequently (eg, every 6-8 hours). Volume of heparin flush is usually similar to volume of catheter (or slightly greater). Additional flushes should be given when stagnant blood is observed in catheter, after catheter is used for drug or blood administration, and after blood withdrawal from catheter.

Storage: store at room temperature.

Warfarin Sodium

Tablets, 2 mg, 5 mg, 10mg

Indications: prophylaxis of embolization in rheumatic heart disease and atrial fibrillation; prophylaxis after insertion of prosthetic heart valve; prophylaxis and treatment of venous thrombosis and pulmonary embolism; transient ischaemic attacks.

Cautions: hepatic or renal failure, recent surgery, breastfeeding.

Drug interactions: acetylsalicylic acid, alcohol, allopurinol, amoxicillin, ampicillin, azathioprine, carbamazepine, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, ciprofloxacin, contraceptives, dexamethasone, doxycycline, erythromycin, fluconazole, fludrocortisone, glibenclamide, griseofulvin, hydrocortisone, ibuprofen, levonorgestrol, levothyroxine, medroxy progesterone, metronidazole, naldixic acid, norethisterone, ofloxacin, phenobarbital, phenytoin, phytomenadione, prednisolone, proguanil, quinidine, rifampicin, ritonavir, sulfadiazine, tamoxifen, testosterone.

Contraindications: Hypersensitivity to warfarin or any component of the formulation; hemorrhagic tendencies (eg, patients bleeding from the GI, respiratory, or GU tract; cerebral

aneurysm; cerebrovascular hemorrhage; dissecting aortic aneurysm; spinal puncture and other diagnostic or therapeutic procedures with potential for significant bleeding; history of bleeding diathesis); recent or potential surgery of the eye or CNS; major regional lumbar block anesthesia or traumatic surgery resulting in large, open surfaces; blood dyscrasias; severe uncontrolled or malignant hypertension; pericarditis or pericardial effusion; bacterial endocarditis; unsupervised patients with conditions associated with a high potential for noncompliance; eclampsia/pre-eclampsia, threatened abortion, pregnancy (except in women with mechanical heart valves at high risk for thromboembolism)

Side effects: haemorrhage, hypersensitivity, rash, alopecia, diarrhea, unexplained drop in haematocrit, 'purple toes', skin necrosis, jaundice, hepatic dysfunction, nausea, vomiting and pancreatitis.

Dose and Administration:*Oral:Adult:* initially 5 - 10 mg daily for 2 - 5 days or until, the desired prothrombin activity is reached. Maintenance is determined by individual response and is usually 2 - 10 mg daily (taken at the sametime each day).

Infants and Child: 0.05-0.34mg/kg/day; infants < 12 months of age may require doses at or near the high end of this range; consistent anticoagulation may be difficult to maintain in children < 5 years of age.

Storage: protect from light and store at room temperature.

12.2. Antiplatelets

Antiplatelet agents are medications that block the formation of blood clots by preventing the clumping of platelets. This antiplatelet effect is used to prevent blood clot formation inside arteries, particularly in individuals who have atherosclerosis (narrowing of the blood vessels) of their arteries, or are otherwise prone to develop blood clots in their arteries.

Acetylsalicylic Acid

Tablet, 75mg, 81mg, 100mg (enteric coated)

Indications: It is used for prophylaxis of platelet aggregation and prevention of thrombosis. That is, it interferes with the clotting process by inhibiting the action of an enzyme that is involved in the production of a chemical that causes platelets to clump together.

Cautions, Drug interactions, Contraindications, Side effects and storage: see section 4.1 under acetylsalicylic acid.

Dose and Administration: For most cardiovascular uses, typical maintenance dosing of aspirin is 81 mg once daily.

Acute coronary syndrome (ST-segment elevation myocardial infarction [STEMI], unstable angina (UA)/non-ST-segment elevation myocardial infarction [NSTEMI]): Oral: Initial: 162-325 mg given on presentation (patient should chew nonenteric-coated aspirin especially if not taking before presentation); for patients unable to take oral, may use rectal suppository (300 mg). Maintenance (secondary prevention): 75-162 mg once daily indefinitely.

Note: When aspirin is used with ticagrelor, the recommended maintenance dose of aspirin is 81 mg/day.

UA/NSTEMI: Concomitant antiplatelet therapy:*If invasive strategy chosen:* Aspirin is recommended in combination with either clopidogrel, ticagrelor, (or prasugrel if at the time of PCI) or an I.V. GP IIb/IIIa inhibitor (if given before PCI, eptifibatid and tirofiban are preferred agents).*If noninvasive strategy chosen:* Aspirin is recommended in combination with clopidogrel or ticagrelor.**Analgesic and antipyretic:** Oral: 325-650 mg every 4-6 hours up to 4 g/day; Rectal: 300-600 mg every 4-6 hours up to 4 g/day. **Anti-inflammatory:** Oral: Initial: 2.4-3.6 g/day in divided doses; usual maintenance: 3.6-

5.4 g/day; monitor serum concentrations. **Aortic valve repair**(*unlabeled use*): Oral: 50-100 mg once daily.

Clopidogrel

Tablet, 75mg

Indications: Reduces rate of atherothrombotic events (myocardial infarction, stroke, vascular deaths) in patients with recent MI or stroke, or established peripheral arterial disease; reduces rate of atherothrombotic events in patients with unstable angina (UA) or non-ST-segment elevation MI (NSTEMI) managed medically or with percutaneous coronary intervention (PCI) (with or without stent) or CABG; reduces rate of death and atherothrombotic events in patients with ST-segment elevation MI (STEMI) managed medically.

Dose and Administration: *Oral: 75mg daily.* A loading dose of 300mg is conventionally prescribed for patients with acute coronary syndromes or those having a stent placed. Some authorities advise a loading dose of 600mg. **Recent MI, recent stroke, or established peripheral arterial disease (PAD):** Oral: 75 mg once daily. *Note: The ACCF/AHA guidelines for PAD recommend clopidogrel as an alternative to aspirin.* **Coronary artery disease (CAD), established:** Oral: 75 mg once daily. *Note: Established CAD defined as patients 1-year post ACS, with prior revascularization, coronary stenosis >50% by angiogram, and/or evidence for cardiac ischemia on diagnostic testing.*

Secondary prevention of cardioembolic stroke (patient not candidate for oral anticoagulation): Oral: 75 mg once daily (in combination with aspirin).

Acute coronary syndrome (ACS): Oral: Unstable angina, non-ST-segment elevation myocardial infarction (UA/NSTEMI): Initial: 300 mg loading dose, followed by 75

mg once daily for up to 12 months (in combination with aspirin indefinitely) (Jneid, 2012). The American College of Chest Physicians recommends combination aspirin dose of 75-100 mg. ST-segment elevation myocardial infarction (STEMI): 75 mg once daily (in combination with aspirin 162-325 mg initially followed by 81-162 mg/day or 75-100 mg/day).

Percutaneous coronary intervention (PCI) for acute coronary syndrome (eg, UA/NSTEMI or STEMI): Loading dose: 600 mg given as early as possible before or at the time of PCI, followed by 75 mg once daily (in combination with aspirin 81 mg/day).

12.3. Hemostatic Agents

Absorbable Gelatin Sponge

Indication: as a haemostatic agent by providing a physical meshwork within which clotting can occur.

Side effects: increase incidence of infection, compression of surrounding tissue due to fluid absorption, granuloma formation, and fibrosis. Generally, gelatin sponges cause little tissue reaction and can be applied to bone, dura, and pleural tissue.

Dose and Administrations: gelatin sponge can be applied dry or soaked in saline or thrombin solutions when applied to skin wounds the gelatin liquifies within 2 to 5 days; when implanted into tissues it is absorbed with in 4 to 6 weeks.

Aminocaproic Acid

Injection, 250 mg/ml in 20ml ampoule

For full profile; see section 9 under aminocaproic acid.

Fibrinogen

Powder, 1g in vial

Indications: for the control of bleeding and prophylactic treatment of patients' deficient in fibrinogen or for treatment of

haemorrhage in congenital hypofibrinogenaemia or afibrinogenaemia.

Note: Fibrinogen is prepared from human plasma

Cautions: risk of thrombosis, Pregnancy, Breast-feeding

Side-effects: Rarely fever, allergic reactions; very rarely thromboembolic events (including myocardial infarction and pulmonary embolism)

Phytomenadione (vitamin K1)

Injection, 1mg/0.5ml, 10mg/ml in 1 ml ampoule.

Indications: for the treatment of hemorrhage due to Vitamin k deficiency.

Cautions: severe liver diseases.

Drug interactions: antacids (aluminium hydroxide), wide spectrum antibiotics, quinidine, quinine, high doses of salicylates, antibacterials like sulfonamides, coumarin or indandione - derivative anticoagulants (such as dicumarol), and other hemolytics.

Side effects: flushing of face, redness, pain, or swelling at place of injection, unusual taste.

Dose and Administration:*Subcutaneously or intramuscularly.*

It should not be given repeatedly to patient with severe liver diseases, once the response to the initial dose is unsatisfactory. **Adult:***I.M. or S.C.*, 2.5 to 10mg (up to 25mg), may be repeated after 6-8 hours if necessary. **Child:Infants -** *IM or SC*, 1-2 mg; **Child***IM or SC*, 5-10mg.

Storage: at room temperature. Protect from light and freezing.

12.4. Antianemic Agents

Iron-deficiency anaemia: Anaemia is usually understood to mean a lowering of haemoglobin concentration, red cell count, or packed cell volume to below 'normal' values but the criteria

for normality are somewhat arbitrary and difficult to establish. Before initiating treatment for anaemia it is essential to determine which type is present. Iron salt may be harmful and result in iron over load if given alone to patients with anemias other than those due to iron deficiency.

Treatment is only justified in the presence of a demonstrable iron - deficiency state. Before starting treatment, it is important to exclude any serious underlying cause of the anaemia (e.g gastric erosion, colonic carcinoma). Prophylaxis is justifiable in pregnancy only for women who have additional risk factors for iron deficiency (e.g poor diet), menorrhagia, after subtotal or total gastrectomy, and in the management of low birth - weight infants such as premature babies, twins, and in infants delivered by caesarean section.

Ferrous salt: many iron compounds have been used for this purpose, but do not offer any real advantage over the simple ferrous fumarate, gluconate, or sulphate salts.

The usual adult dose is sufficient of these salts to supply about 100 to 200mg of elemental iron daily. The approximate elemental iron content of various ferrous salts is ferrous fumarate 200mg (65mg iron), ferrous gluconate 300mg (35mg iron), ferrous succinate 100mg (35mg iron), ferrous sulfate 300mg (60mg iron), and dried ferrous sulfate 200mg (65mg iron)

Iron intake in the evening has been reported to improve its absorption. Iron intake with meals may reduce bioavailability but improve tolerability and adherence.

If adverse effects arise with one salt, dosage can be reduced or a change made to an alternative iron salt.

The hemoglobin concentration should rise by about 100 - 200mg/100ml per day. After the haemoglobin has risen to normal, treatment should be continued for a further three

months in an attempt to replenish the iron stores. Gastrointestinal irritation may occur. Nausea and epigastric pain are dose related. Oral iron may exacerbate diarrhoea in patients with inflammatory bowel disease but care is also needed in patients with intestinal strictures and diverticulae. Iron as iron dextran or iron sorbitol should be given parenterally only if the patient has severe gastrointestinal adverse effects with oral preparations, continuing severe blood loss or malabsorption. Parenteral iron may cause more harm than benefit. Provided that the oral iron preparation is taken reliably and is absorbed then the haemoglobin response is not significantly faster with the parenteral route than the oral route.

Megaloblastic anaemias; these are due to lack of either vitamin B₁₂ (hydroxycobalamin) or folate or both. The clinical features of folate deficient megaloblastic anaemia are similar to those of vitamin B₁₂ deficiency except the accompanying severe neuropathy does not occur; it is essential to determine which deficiency is present and underlying cause is established in every case.

Preparations containing ferrous salt and folic acid are used for the prevention of megaloblastic anaemia in pregnancy. The low doses of folic acid in these preparations are inadequate for the treatment of megaloblastic anaemias.

Calcium Folate (Leucovorin calcium)

Injection, 3 mg/ml, 7.5mg/ml, 10mg/ml

Tablet, 15mgasFolinic acid

Indications: treatment of megaloblastic anemias when folate is deficient as in infancy, sprue, pregnancy, and nutritional deficiency when oral folate therapy is not possible.

Cautions, Contraindications, Drug interactions, Side effects and Storage; see section 11; under calcium folinate and folic acid.

Dose and Administration:Adult and Child: *Folate-deficient megaloblastic anemia:* IM: 1 mg/day

Megaloblastic anemia secondary to congenital deficiency of dihydrofolate reductase: IM: 3-6 mg/day.

Cyanocobalamin (Vitamin B₁₂)

Injection, 100 mcg/ml, 1000 mcg/ml in 1 ml ampoule.

Indications: Treatment of pernicious anemia; vitamin B₁₂ deficiency due to dietary deficiencies or malabsorption diseases, inadequate secretion of intrinsic factor, and inadequate utilization of B₁₂ (eg, during neoplastic treatment); increased B₁₂ requirements due to pregnancy, thyrotoxicosis, hemorrhage, malignancy, liver or kidney disease

Cautions: I.M route used to treat pernicious anemia; Vitamin B₁₂ deficiency for > 3 months results in irreversible degenerative CNS lesions.

Drug interactions: ethanol, chloramphenicol, cholestyramine, cimetidine, colchicine, neomycin, potassium.

Contraindications: Hypersensitivity to cyanocobalamin, cobalt, or any component of the formulation.

Side effects: headache, anxiety, dizziness, pain, nervousness, hypoesthesia, itching, sore throat, nausea, vomiting, dyspepsia, diarrhea, weakness, back pain, arthritis, myalgia, paresthesia, abnormal gait, dyspnea, rhinitis.

Dose and Administration: *Anemias: IM or deep SC:*

Pernicious anemia, congenital: **Adult:** 100 mcg/day for 6 - 7 days; if improvement, administer same dose on alternate days for 7 doses; then every 3 - 4 days for 2 - 3 weeks; once hematologic values have returned to normal, maintenance

dosage: 100 mcg/month.**Child:** 30 - 50 mcg/day for 2 or more weeks (to a total dose of 1000 - 5000 mcg), Then follow with 100 mcg/month as maintenance dosage.**Vitamin B12 deficiency:****Adult:** Initial: 30 mcg/day for 5 - 10 days; maintenance: 100 - 200 mcg/month.**Child:***Neurologic signs:* 100 mcg/day for 10 - 15 days (total dose of 1-1.5 mg), then once or twice weekly for several months.*Hematologic signs:* 10 - 50 mcg/day for 5 - 10 days, followed by 100 - 250 mcg/dose every 2 - 4 weeks.

Storage: store at room temperature, protect from light.

Epoetin alfa and beta

Injection, epoetin alfa, 2000 units/ml

Epoetin alfa prefilled syringe, 1000 units/ml, 2000 units/ml, 3000 units/ml, 4000 units/ml, 10,000 units/ml.

Epoetin beta powder for injection, 500 units/vial; 1000 units/vial; 2000 units/vial; 3000 units/vial; 4000 units/vial, 5000 units/vial; 6000 units/vial, 10,000 units/vial.

Epoetin beta powder for injection (multi dose injection), 50,000 units/vial, 100,000 units/vial

Indications: Treatment of anemia due to concurrent myelosuppressive chemotherapy in patients with cancer (nonmyeloid malignancies) receiving chemotherapy (palliative intent) for a planned minimum of 2 additional months of chemotherapy; treatment of anemia due to chronic kidney disease (including patients on dialysis and not on dialysis) to decrease the need for RBC transfusion; treatment of anemia associated with HIV (zidovudine) therapy when endogenous erythropoietin levels ≤ 500 mUnits/mL; reduction of allogeneic RBC transfusion for elective, noncardiac, nonvascular surgery when perioperative hemoglobin is >10 to ≤ 13 g/dL and there is a high risk for blood loss

Cautions: hypertension, ischaemic vascular disease, seizures, myeloid malignancy, untreated iron deficiency.

Contraindications: Hypersensitivity to epoetin or any component of the formulation; uncontrolled hypertension; pure red cell aplasia (due to epoetin or other epoetin protein drugs); multidose vials contain benzyl alcohol and are contraindicated in neonates, infants, pregnant women, and nursing women

Side effects: clotting of vascular access and dialysers; hypertension, headache, seizures, flu-like symptoms and skin rash.

Dose and Administration: Anemia associated with chronic kidney disease: Individualize dosing and use the lowest dose necessary to reduce the need for RBC transfusions. *Chronic kidney disease patients ON dialysis* (I.V. route is preferred for hemodialysis patients; initiate treatment when hemoglobin is <10 g/dL; reduce dose or interrupt treatment if hemoglobin approaches or exceeds 11 g/dL): I.V., SubQ: Initial dose: 50-100 units/kg 3 times/week. *Chronic kidney disease patients NOT on dialysis* (consider initiating treatment when hemoglobin is <10 g/dL; use only if rate of hemoglobin decline would likely result in RBC transfusion and desire is to reduce risk of alloimmunization or other RBC transfusion-related risks; reduce dose or interrupt treatment if hemoglobin exceeds 10 g/dL): I.V., SubQ: Initial dose: 50-100 units/kg 3 times/week. *Dosage adjustments for chronic kidney disease patients (either on dialysis or not on dialysis):* If hemoglobin does not increase by >1 g/dL after 4 weeks: Increase dose by 25%; do not increase the dose more frequently than once every 4 weeks. If hemoglobin increases >1 g/dL in any 2-week period: Reduce dose by $\geq 25\%$; dose reductions can occur more frequently than once every 4 weeks; avoid frequent dosage adjustments.

Inadequate or lack of response over a 12-week escalation period: Further increases are unlikely to improve response and may increase risks; use the minimum effective dose that will maintain a Hgb level sufficient to avoid RBC transfusions and evaluate patient for other causes of anemia. Discontinue therapy if responsiveness does not improve.

Anemia due to chemotherapy in cancer patients: Initiate treatment only if hemoglobin <10 g/dL and anticipated duration of myelosuppressive chemotherapy is ≥ 2 months. Titrate dosage to use the minimum effective dose that will maintain a hemoglobin level sufficient to avoid red blood cell transfusions. Discontinue erythropoietin following completion of chemotherapy. SubQ: Initial dose: 150 units/kg 3 times/week or 40,000 units once weekly until completion of chemotherapy.

Dosage adjustments: If hemoglobin does not increase by >1 g/dL **and** remains below 10 g/dL after initial 4 weeks: Increase to 300 units/kg 3 times/week or 60,000 units weekly; discontinue after 8 weeks of treatment if RBC transfusions are still required or there is no hemoglobin response.

If hemoglobin exceeds a level needed to avoid red blood cell transfusion: Withhold dose; resume treatment with a 25% dose reduction when hemoglobin approaches a level where transfusions may be required.

If hemoglobin increases >1 g/dL in any 2-week period **or** hemoglobin reaches a level sufficient to avoid red blood cell transfusion: Reduce dose by 25%.

Anemia due to zidovudine in HIV-infected patients: Titrate dosage to use the minimum effective dose that will maintain a hemoglobin level sufficient to avoid red blood cell transfusions. Hemoglobin levels should not exceed 12 g/dL.

Serum erythropoietin levels ≤ 500 mUnits/mL and zidovudine doses ≤ 4200 mg/week): I.V., SubQ: Initial: 100 units/kg 3

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times/week; if hemoglobin does not increase after 8 weeks, increase dose by ~50-100 units/kg at 4-8 week intervals until hemoglobin reaches a level sufficient to avoid RBC transfusion; maximum dose: 300 units/kg. Withhold dose if hemoglobin exceeds 12 g/dL, may resume treatment with a 25% dose reduction once hemoglobin <11 g/dL. Discontinue if hemoglobin increase is not achieved with 300 units/kg for 8 weeks.

Surgery patients (perioperative hemoglobin should be >10 g/dL and ≤13 g/dL; DVT prophylactic anticoagulation is recommended): SubQ: Initial dose:

300 units/kg/day beginning 10 days before surgery, on the day of surgery, and for 4 days after surgery **or**

600 units/kg once weekly for 4 doses, given 21-, 14-, and 7 days before surgery, and on the day of surgery

Symptomatic anemia associated with myelodysplastic syndrome (unlabeled use): SubQ: 40,000-60,000 units 1-3 times/week (NCCN MDS guidelines v.2.2011)

Storage: store in refrigerator and should not be frozen.

Ferrous Salt

Capsule

Drop

Tablet (enteric coated)

Indications: Prevention and treatment of iron-deficiency anemias

Cautions: hepatitis or hepatic function impairment, kidney diseases, intestinal tract inflammatory conditions (e.g. peptic ulcer, or colitis), or alcoholism. Caution patients about toxic effects of accidental overdose. *Especially in children.*

Drug interactions: acetohydroxamic acid, dimercaprol, etidronate (avoid using iron supplements with in two hours of

etidronate), fluoroquinolones (it should be taken at least two hours before or two hours after iron supplements), tetracycline, chloramphenicol, antacids, calcium (carbonate or phosphate).

Side effects: abdominal discomfort, vomiting, diarrhoea or dark stools may occur commonly, large doses may have irritant and corrosive effects of the gastrointestinal mucosa and necrosis and perforation may occur. Iron drops may temporarily stain the teeth.

Dose and Administration: *Orally.* Iron drops may be placed well back on the tongue followed with water. It is best given on an empty stomach but may be given with or after meals to lessen gastrointestinal irritation. Treatment may be continued for 3-6months, and not longer except in patients with continued bleeding, or repeated pregnancies.*Prophylactic:* **Adult:** 300mg once daily.**Child:** 5mg/kg of body weight once daily or, 150 – 300mg once daily.

*Treatment:***Adult:** 300mg every 12 hours, gradually increased up to 300mg every 6-8 hours daily as needed and tolerated.**Child:** 10mg/kg of body weight every 8 hours daily. Or 6-12 years 300mg every 12 hours daily.1-5 years -120mg every 8 hours daily. Under 1year – 60mg every 8 hours daily.

Storage: At room temperature, in a tight container. Protect from light and freezing.

Ferrous salt + Folic Acid*●

Capsule

Tablet

Indications: Prevention of iron and folic acid deficiencies in pregnancy.

*Any Ferrous salt containing elemental Iron of accepted therapeutic value

Cautions: low doses of folic acid in the combination preparations above are inadequate for treatment of megaloblastic anaemia;

Side effects: see ferrous salts

Dose and Administration: *Prevention of iron and folic acid deficiencies in pregnancy:* Oral: **Adult** the equivalent of about 100mg elemental iron with 350 - 400 micrograms folic acid daily throughout pregnancy.

Fluoxymesterone

Tablet, 2mg, 10mg

Indications: Replacement of endogenous testicular hormone; in females, palliative treatment of breast cancer.

Caution: liver disease, heart disease, kidney disease, allergies, enlarged prostate. Stimulation of erythropoiesis, angioneurotic edema.

Contraindications: Males with carcinoma of the breast or the prostate (known or suspected); women who are or may become pregnant. Pregnancy or breast-feeding.

Side effects: headache, indigestion, oily skin, acne, anxiety, and sleeplessness. Males may experience breast tenderness, change in sex drive, impotence or problems with erections. Females may experience deepening of the voice, change in sex drive, irregular menstruation or enlargement of the clitoris. Vomiting, swelling of the ankles or feet, unusual weight gains, yellowing of the eyes/skin.

Dose and Administration: Hypogonadism (Males): Oral: 5-20 mg/day. Delayed puberty (Males): Oral: 2.5-20 mg/day for 4-6 months. Inoperable breast carcinoma (Females): Oral: 10-40 mg/day in divided doses for 1-3 months

Storage: store at room temperature

Folinic acid, see calcium folinate too

Tablet, 15 mg

Indications:

1. Folinic acid is used to counteract the folate-antagonist action of methotrexate and thus speed recovery from methotrexate-induced mucositis or myelosuppression (*'folinic acid rescue'*).
2. Folinic acid is also used in the management of methotrexate overdose, together with other measures to maintain fluid and electrolyte balance, and to manage possible renal failure.
3. Treatment of megaloblastic anemia when folic acid deficiency is present (this mainly occurs in infants, during pregnancy, in malabsorption syndromes, liver diseases, sprue and malnutrition). When treating megaloblastic anaemias, the results are comparable to those obtained with folic acid. Following an overdose of folic acid antagonists, Calcium folinate performs considerably better than folic acid because the folic acid antagonists inhibit the metabolism of folic acid into folinic acid, but have no effect on the folinic acid.
4. Adjunct to fluorouracil in colorectal cancer. When folinic acid and fluorouracil are used together in metastatic colorectal cancer the response-rate improves compared to that with fluorouracil alone. In combination with fluorouracil to treat cancers such as; colon and rectal, head and neck, esophageal, and other cancers of the gastrointestinal tract.
5. *Folinic acid does not counteract the antibacterial activity of folate antagonists such as trimethoprim. where folates provides differential rescue of the host but not the parasite.*

Caution: avoid simultaneous administration with methotrexate; not indicated for pernicious anaemia or other megaloblastic anaemias caused by vitamin B₁₂ deficiency. Haematological

remissions may occur, while the neurological manifestations remain progressive. Simultaneous therapy with a folic acid antagonist and Calcium Leucovorin is not recommended because the effect of the folic acid antagonist is either reduced or completely inhibited

Contraindications: it is improper therapy for pernicious anaemia and other megaloblastic anaemias secondary to the lack of Vitamin B₁₂. If used in these conditions, haematological remission may occur, but neurological manifestations are likely to progress. *Intrathecal injection*; not known to be harmful during pregnancy, benefit outweighs risk; breast-feeding: presence in breast milk during breast feeding unknown but benefit outweighs risk.

Drug Interactions: Folic acid in large amounts may folates possibly reduce plasma concentration of and counteract the antiepileptic effect of phenobarbital, phenytoin and primidone, and increase the frequency of seizures. High oral, intravenous or intramuscular doses may reduce the efficacy of intrathecally administered methotrexate. Calcium folinate may enhance the toxicity of fluorouracil. Raltitrexed (is chemically similar to folic acid and is in the class of chemotherapy drugs called folate antimetabolites) avoidance concomitant administration with folates advised.

Side effects: rarely pyrexia after parenteral use; insomnia, agitation, and depression after high doses. Allergic sensitisation, including anaphylactoid reactions and urticarial. Nausea and vomiting with very high. Seizures and/or syncope have been reported rarely in cancer patients.

Dose and Administration: Calcium folinate may be given orally or parenterally by intravenous infusion or by intramuscular injection **but should not be administered**

intrathecally. *Suspected methotrexate overdose (Rescue therapy following methotrexate over dose)*, by intravenous injection or by intravenous infusion (at a maximum rate of 160 mg/minute), initial dose equal to or exceeding dose of methotrexate. It is given orally or parenterally to overcome the toxic effects of methotrexate or other DHF reductase inhibitors. *Prevention of methotrexate-induced adverse effects*, usually started 12 to 24 hours after start of methotrexate infusion; by intramuscular injection or by intravenous injection or by intravenous infusion, 15 mg, repeated every 6 hours for 24 hours (may be continued by mouth). *Metabolic disorders leading to folate deficiency*, by mouth or by intravenous infusion: Child up to 18 years 15 mg once daily; larger doses may be required in older children. *Prevention of megaloblastic anaemia associated with pyrimethamine and sulfadiazine treatment of congenital toxoplasmosis*, by mouth: Neonate 5 mg 3 times a week (increased up to 20 mg 3 times a week if neutropenic); Child 1 month to 1 year 10 mg 3 times a week. *Treatment of Folate Deficiency (Megaloblastic anaemia)*, by mouth: Child up to 12 years 250 microgram/kg once daily; Child 12–18 years 5 to 15 mg once daily. *The length of time therapy must be continued depends on the underlying disease. It is customary to continue therapy for about 4 months, when all folate-deficient red cells will have been eliminated and replaced by new folate-replete populations.* *Adjunct to fluorouracil in colorectal cancer*, consult product literature.

Note: Before large doses of folic acid are given, cobalamin deficiency must be excluded and, if present, corrected, otherwise cobalamin neuropathy may develop, despite a response of the anemia of cobalamin deficiency to folate therapy.

Note 2: Particular care should be taken when treating elderly or debilitated colorectal cancer patients with Calcium Leucovorin/5-

fluorouracil, as these patients may be at increased risk of severe toxicity, particularly severe gastrointestinal toxicity.

Note 3: Excessive amounts of calcium folinate may nullify the chemotherapeutic effect of folic acid antagonists.

Storage: room temperature, 15-25°C

Iron Complex

Injection, 50mg/ml in 2ml ampoule (Dextran, Sorbitol) Iron dextran injection is a sterile colloidal solution of ferric hydroxide and dextrans of weight average molecular weight between 5000 and 7000 or a complex of ferric hydroxide with dextran containing 5% (50 mg/mL) of iron. Iron sorbitol injection is a sterile Colloidal solution of a complex of iron, Sorbitol and citric acid, stabilized with dextrin and Sorbitol.

Indications: used for iron-deficiency anaemia

Cautions: oral iron not to be given until 5 days after last injection. Anaphylactic reactions can occur with parenteral iron and a test dose is recommended before *each* dose; the patient should be carefully observed for 60 minutes after the first test dose and for 15 minutes after subsequent test doses (subsequent test doses not necessary for intramuscular administration). Facilities for cardiopulmonary resuscitation must be available; risk of allergic reactions increased in immune or inflammatory conditions.

Contraindications: history of allergic disorders including asthma, and eczema; infection; active rheumatoid arthritis, Hepatic impairment (avoid in severe impairment), Renal impairment (avoid in acute renal failure), Pregnancy (avoid in first trimester); child under 14 years

Side effects: *less commonly* nausea, vomiting, abdominal pain, flushing, dyspnoea, anaphylactic reactions (see Anaphylaxis above), numbness, cramps, blurred vision, pruritus, and rash; *rarely* diarrhoea, chest pain, hypotension, angioedema,

arrhythmias, tachycardia, dizziness, restlessness, fatigue, seizures, tremor, impaired consciousness, myalgia, arthralgia, sweating, and injection-site reactions; *very rarely* hypertension, palpitation, headache, paraesthesia, haemolysis, and transient deafness

Dose and Administration: By deep intramuscular injection into the gluteal muscle or by slow intravenous injection or by intravenous infusion, calculated according to body-weight and iron deficit, consult product literature and.

Iron gluconate + Manganese gluconate + copper gluconate

Oral solution, 5mg+1.33mg+0.77mg

Indications: For treatment of anemia related to pregnancy during the post partum period or lactation and in association with parasitic infection.

Iron sucrose

Injection, 100mg/5ml

Indication: Treatment of iron-deficiency anemia in chronic kidney disease (CKD), including nondialysis-dependent and dialysis-dependent patients

Contraindication: Hypersensitivity to iron sucrose or any component of the formulation

Dose and Administration:Iron-deficiency anemia in CKD:I.V.:Hemodialysis-dependent patient: 100 mg administered during consecutive dialysis sessions to a cumulative total dose of 1000 mg (10 doses); may repeat treatment if clinically indicated.Peritoneal dialysis-dependent patient: Two infusions of 300 mg administered 14 days apart, followed by a single 400 mg infusion 14 days later (total cumulative dose of 1000 mg in 3 divided doses); may repeat treatment if clinically indicated.Nondialysis-dependent patient: 200 mg administered on 5 different occasions within a 14-day

period (total cumulative dose: 1000 mg in 14-day period); may repeat treatment if clinically indicated. Note: Dosage has also been administered as 2 infusions of 500 mg on day 1 and day 14. Cancer-/chemotherapy-associated anemia (*unlabeled use*): I.V.: 200 mg I.V. infusion (maximum: 300 mg/infusion) over 1 hour every 2-3 weeks or 200 mg slow I.V. injection over 2-5 minutes every 1-4 weeks. Total cumulative dose: 1000 mg. Test doses (25 mg slow I.V. push) are recommended in patients with a history of hypersensitivity to any I.V. iron preparation (eg, dextran) or those with other drug allergies.

Storage: Store intact vials at controlled room temperature of 20°C to 25°C. Do not freeze. Iron sucrose is stable for 7 days at room temperature or under refrigeration when undiluted in a plastic syringe or following dilution in normal saline in a plastic syringe (2-10 mg/mL) or I.V. bag (1-2 mg/mL).

Oxymetholone

Tablet, 2.5mg, 5mg, and 10mg

Indication: Treatment of anemias caused by deficient red cell production.

Caution: liver impairment.

Contraindication: Hypersensitivity to oxymetholone or any component of the formulation; breast cancer in men; breast cancer in women with hypercalcemia; prostate cancer; severe hepatic dysfunction; nephrosis or nephrotic phase of nephritis; pregnancy or use in women who may become pregnant

Side effects: liver disturbances and jaundice.

Dose and Administration: Oral: 1-5 mg/kg/day once daily; usual effective dose: 1-2 mg/kg/day; give for a minimum trial of 3-6 months because response may be delayed

Storage: store at room temperature.

12.5. Blood Substitutes and Plasma Expanders

Dextrans (Dextran 70 and Dextran 40) and polygeline are macromolecular substances which are metabolized slowly; they may be used at the outset to expand and maintain blood volume in shock arising from conditions such as burns or septicemia. Plasma substitutes may be used as an immediate short - term measure to treat haemorrhage until blood is available.

They are rarely needed when shock is due to sodium and water depletion because, in these circumstances, the shock responds to water and electrolyte repletion.

Plasma substitutes should not be used to maintain plasma volume in conditions such as burns or peritonitis where there is loss of plasma protein, water and electrolytes over periods of several days or weeks. In these situations, plasma or plasma protein fractions containing large amounts of albumin should be given.

Dextran 70 by intravenous infusion is used predominantly for volume expansion. Dextran 40 intravenous infusion is used in an attempt to improve peripheral blood flow in ischaemic disease of the limbs. Dextrans 40 and 70 have also been used in the prophylaxis of thromboembolism but are now rarely used for this purpose.

Dextrans may interfere with blood group cross-matching or biochemical measurements and these should be carried out before infusion is begun.

Cautions: plasma substitutes should be used with caution in patients with cardiac disease or renal impairment; urine output should be monitored. Care should be taken to avoid haematocrit concentration from falling below 25 - 30% and the patient should be monitored for hypersensitivity reactions.

Side effects: Hypersensitivity reactions may occur including, rarely, severe anaphylactic reaction. Transient increase in bleeding time may occur.

Albumin, Salt-free

Solution, 20 % in 100 ml

Indications: Plasma volume expansion and maintenance of cardiac output in the treatment of certain types of shock or impending shock; may be useful for burn patients, ARDS, and cardiopulmonary bypass; other uses considered by some investigators (but not proven) are retroperitoneal surgery, peritonitis, and ascites; unless the condition responsible for hypoproteinemia can be corrected, albumin can provide only symptomatic relief or supportive treatment

Cautions: hepatic or renal failure.

Drug interactions: ACE inhibitors.

Contraindications: Hypersensitivity to albumin or any component of the formulation; patients with severe anemia or cardiac failure.

Side effects: edema, hyper/hypotension, hypervolemia, tachycardia, chills, fever, headache, pruritus, rash, urticaria, nausea, vomiting, bronchospasm, pulmonary edema, anaphylaxis.

Dose and Administration: *IV:Adult: Note: Use 5% solution in hypovolemic patients or intravascularly-depleted patients. Use 25% solution in patients in whom fluid and sodium intake is restricted. Usual dose: 25 g; initial dose may be repeated in 15-30 minutes if response is inadequate; no more than 250 g should be administered within 48 hours.* **Hypovolemia:** 5% albumin: 0.5-1 g/kg/dose; repeat as needed. **Note:** May be considered after inadequate response to crystalloid therapy and when nonprotein colloids are contraindicated. The volume administered and the speed of infusion should be adapted to individual response.

Large-volume paracentesis (>5 L) (unlabeled use): 25% albumin: 5-8 g for every liter removed (Garcia-Compeán, 1993; Moore, 2003) or 50 g total for paracentesis >5 L (ATS, 2004). **Note:** Administer soon after the procedure to avoid postprocedural complications (eg, hypovolemia, hyponatremia, renal impairment).

Spontaneous bacterial peritonitis (SBP) in patients with cirrhosis (unlabeled use): 25% albumin: Initial: 1.5 g/kg, followed by 1 g/kg on day 3 (in conjunction with appropriate antimicrobial therapy) (ATS, 2004; Sort, 1999). **Note:** Clinical trial employed albumin 20%; however, the difference in concentration compared with 25% albumin is deemed to be clinically inconsequential.

Child:Hypovolemia: I.V.: 0.5-1 g/kg/dose (10-20 mL/kg/dose of albumin 5%); maximum dose: 6 g/kg/day.

Storage: store at a temperature $\leq 30^{\circ}\text{C}$; do not freeze.

Dextran (MW 40, 000)

Solution, 10% w/v in 5% Dextrose; 500ml

Indications: Blood volume expander used in treatment of shock or impending shock when blood or blood products are not available; also used as a priming fluid in pump oxygenators during cardiopulmonary bypass and for prophylaxis of venous thrombosis and pulmonary embolism in surgical procedures associated with a high risk of thromboembolic complications

Cautions: see notes above; can interfere with some laboratory tests (see also above); correct dehydration beforehand, give adequate fluids during therapy and, where possible, monitor central venous pressure; pregnancy.

Contraindications: Hypersensitivity to dextran or any component of the formulation; marked hemostatic defects (eg, thrombocytopenia, hypofibrinogenemia) of all types including

those caused by medications (eg, heparin, warfarin); marked cardiac decompensation; renal disease with severe oliguria or anuria

Side effects: see notes above

Dose and Administrations:Volume expansion/shock: I.V.: Dextran 40: Infuse 500-1000 mL (~10 mL/kg) as rapidly as possible (maximum: 20 mL/kg/day for first 24 hours; 10 mL/kg/day thereafter); therapy should not be continued beyond 5 days.

Pump prime: Dextran40: varies with the volume of the pump oxygenator; generally, the solution is added in a dose of 10-20 mL/kg (or 1-2 g/kg); usual maximum total dose: 20 mL/kg (or 2 g/kg).

Postoperative prophylaxis of venous thrombosis/pulmonary embolism (Dextran 40): Begin during surgical procedure and give 500-1000 mL (~10 mL/kg); an additional 50 g (500 mL) should be administered every 2-3 days during the period of risk (up to 2 weeks postoperatively); usual maximum infusion rate for nonemergency use: 4 mL/minute

Dextran (MW 70,000)

Solution, 6% w/v in 5% dextrose; 500ml

Indications: Blood volume expander used in treatment of shock or impending shock when blood or blood products are not available; also used as a priming fluid in pump oxygenators during cardiopulmonary bypass and for prophylaxis of venous thrombosis and pulmonary embolism in surgical procedures associated with a high risk of thromboembolic complications

Cautions: see notes above; can interfere with some laboratory tests (see also above); where possible, monitor central venous pressure; pregnancy.

Contraindication: Hypersensitivity to dextran or any component of the formulation; marked hemostatic defects (eg, thrombocytopenia, hypofibrinogenemia) of all types including those caused by medications (eg, heparin, warfarin); marked cardiac decompensation; renal disease with severe oliguria or anuria

Side effects: see notes above

Dose and Administrations: *IV infusion:* after moderate to severe haemorrhage or in the shock phase of burn injury (initially 48 hours), 500 - 1000ml rapidly initially followed by 500ml later if necessary (see also notes above); total dosage should not exceed 20ml/kg during initial 24 hours: C total dosage should be not exceed 20ml/kg.

Hydroxyethyl Starch

Large Volume Parenteral, 6%w/v of, 500ml

Indications: blood volume expander used in treatment of hypovolemia; adjunct in leukapheresis to improve harvesting and increase the yield of granulocytes by centrifugation.

Cautions: caution in patients with severe bleeding disorders, cardiac disease, liver disease, or renal impairment; urine output should be monitored. Care should be taken to avoid haematocrit concentration from falling below 25–30% and the patient should be monitored for hypersensitivity reactions.

Contraindications: Hypersensitivity to hydroxyethyl starch or any component of the formulation; renal failure with oliguria or anuria (not related to hypovolemia); any fluid overload condition (eg, pulmonary edema, congestive heart failure); pre-existing coagulation or bleeding disorders

Side-effects: Hypersensitivity reactions may occur including, rarely, severe anaphylactic reactions. Transient increase in bleeding time may occur.

Dose and Administration: *intravenous infusion only*; total volume and rate of infusion are dependent on the clinical situation and the individual patient; should be individualized according to the duration and extent of hypovolemia & administered in accordance with accepted clinical practices for fluid and electrolyte management. The initial 10 - 20 ml is to be infused slowly, keeping the patient under close observation (due to possible anaphylactoid reactions). Intravenous infusion, hetastarch (weight average molecular weight 450 000) 6% in sodium chloride intravenous infusion 0.9%; Dose by intravenous infusion, 500–1000 mL; usual daily max. 1500 mL (see notes above)

Children: The dosage in children should be adapted to the individual patient colloid needs, taking into account the disease state, as well as the hemodynamic and hydration status.

Storage: do not freeze

Isoplasma

Solution, 500 ml.

Indications: Used for plasma volume expansion in the treatment of certain types of shock, including shock resulting from burns, crushing injuries, abdominal emergencies, or any other cause where there is a predominant loss of plasma fluids and not RBCs.

Cautions and Sideeffects: See note above

Plasma Antihæmophilic (Human)

Solution, 50 ml, 100 ml, 250 ml

Indications: management of hemophilia A for patients in whom a deficiency in factor VIII has been demonstrated; treatment of spontaneous bleeding in patients with severe von Willebrand disease and in mild and moderate von Willebrand

disease where desmopressin is known or suspected to be inadequate.

Cautions: hypersensitivity to any component of the formulation.

Side effects: acute hemolytic anemia, allergic reactions, blurred vision, chest tightness, chills, edema, fever, headache, hyperfibrinogenemia, increased bleeding tendency, itching, lethargy, nausea, tachycardia.

Dose and Administration: Adult and Child: *I.V.:individualize dosage based on coagulation studies performed prior to treatment and at regular intervals during treatment:* 1AHF unit is the activity present in 1 ml of normal pooled human plasma; dosage should be adjusted to actual vial size currently stocked in the pharmacy.

Storage: store under refrigeration, and avoid freezing

Polygeline + Na⁺ + K⁺ + Ca⁺⁺ + Cl⁻

Solution, 35g + 145 mmol + 5.1 mmol + 6.25 mmol + 145mmol/1000ml

Indications: correction of low blood volume

Cautions: blood samples for cross-matching should be taken before infusion; haemorrhagic diathesis; congestive heart failure, renal impairment, hypertension, oesophageal varices.

Contraindications: severe congestive heart failure; renal failure.

Side effects: urticarial and other hypersensitivity reactions - rarely severe anaphylactoid reactions.

Dose and Administrations: *Correction of low blood volume:IV infusion:* initially 500 - 1000ml of a 3.5% solution.

13. MEDICINES for CORRECTING WATER, ELECTROLYTE and ACID-BASE DISTURBANCES

Electrolytes are used to correct disturbances in fluid and electrolyte homeostasis or acid-base balance and to re-establish osmotic equilibrium of specific ions.

13.1. Oral Electrolytes

Ammonium Chloride

Tablet, 500mg

Indications: Ammonium chloride may be used as a systemic acidifying agent for the treatment of metabolic alkalosis or to acidify the urine. Ammonium salts are no longer used as diuretics, but are sometimes used to maintain an acid pH of urine. This may be useful as an adjunct in treating urinary tract infections or for increasing urinary excretion of drugs after an overdose.

Other conditions that have been treated with ammonium chloride include hypochloremia with severe metabolic alkalosis, Meniere's disease, and premenstrual syndrome.

Cautions: Ammonia toxicity may occur; observe constantly for signs and symptoms of toxicity (pallor, sweating, retching, irregular breathing, bradycardia, cardiac arrhythmias, local and general twitching, tonic convulsions and coma)

Side effects: ammonium salts are irritant to the gastric mucosa and may produce nausea and vomiting.

Dose and Administration: The usual dose is one gram three times daily for up to 6 days. To maintain an acidic pH of the urine, ammonium chloride 1 to 2 grams is administered every 4 to 6 hours for no longer than six days. For forced acid diuresis to aid in the excretion of basic drugs, such as amphetamines, 4 grams every two hours may be given.

Storage: store in airtight containers.

Calcium

Tablet (ionizable), 500 mg, 1g (eff.).

Indications: used as calcium supplementation in pregnant and lactating women and in growing children, latent tetany, rickets and osteomalacia (additional to specific therapy). Prevention of pre-and postmenopausal bone demineralisation, osteoporosis, as supportive treatment in allergic conditions

Cautions: calcium salts should be used cautiously if at all, in patients with sarcoidosis, renal or cardiac disease, and in patients receiving cardiac glycosides.

Check urinary calcium excretion in patients with mild hypercalciuria impaired renal function or a history of urinary concrements; reduce dosage or discontinue therapy if necessary. Avoid high doses of Vitamin D.

Drug interactions: oral tetracycline or fluoride (avoid concomitant use within 3 hours); cardiac glycosides; calcium channel blockers; phenytoin; gallium nitrate; Etidronate, cellulose sodium phosphate, thiazide.

Contraindications: hypersensitivity to the drug, hypercalcaemia, severe hypercalcium, severe renal failure, sarcoidosis, and renal calculi.

Side effects: hypotension (dizziness), flushing and /or sensation of warmth or heat, irregular heart beat. Nausea or vomiting, gastrointestinal irritation & constipations, skin redness, rash, pain, or burning at injection site, sweating.

Dose and Administration:*Hypocalcaemia (prophylaxis):*
Oral: amount based on normal daily-recommended intakes:

Persons	Milligram
Adolescent and adult males/females	800 - 1200
Pregnant females and Breast-feeding	1200
Birth to 3 years of age	400 – 800
4 to 10 years of age	800

Hypocalcaemia (treatment): Treatment dose is individualized by prescriber based on severity of deficiency.

Storage: store at room temperature in a tight container or original foil packaging.

Calcium Folate

Tablet, 5mg, 15mg, 25mg

Indications: Antidote for folic acid antagonists (methotrexate, trimethoprim, pyrimethamine) and rescue therapy following high-dose methotrexate; in combination with fluorouracil in the treatment of colon cancer; treatment of megaloblastic anemias when folate is deficient as in infancy, sprue, pregnancy, and nutritional deficiency when oral folate therapy is not possible. Adjunctive cofactor therapy in methanol toxicity; prevention of pyrimethamine hematologic toxicity in HIV-positive patients.

Cautions, Contraindications, Drug interactions, Side effects and Storage; see section 10. under calcium folinate.

Dose and Administration: Adult: Treatment of weak folic acid antagonist overdose (eg, trimethoprim, pyrimethamine): Oral: 5-15 mg/day. High-dose methotrexate-rescue dose: Initial: Oral, I.M., I.V.: 15 mg ($\sim 10 \text{ mg/m}^2$); start 24 hours after beginning methotrexate infusion; continue every 6 hours for 10 doses, until methotrexate level is <0.05 micromole/L. Adjust dose as follows: Normal methotrexate elimination: Oral, I.M., I.V.: 15 mg every 6 hours.

Delayed early methotrexate elimination: I.V.: 150 mg every 3 hours until methotrexate level is <1 micromole/L, then 15 mg every 3 hours until methotrexate level is <0.05 micromole/L

Calcium Glubionate + Calcium Galacto gluconate

Syrup, 28.75 g+ 5.9 g/100ml

Indications, Cautions, Drug interactions, Contraindications; see under calcium gluconate.

Calcium Gluconate

Syrup, 4gm/15ml

Tablet, 500mg

Indications: as a source of calcium ion for treating calcium depletion occurring in conditions such as chronic hypoparathyroidism, pseudo-hypoparathyroidism, osteomalacia, rickets, chronic renal failure, and hypocalcaemia secondary to the administration of anticonvulsant medications. It is also used as a dietary supplemental therapy for persons who may not get enough calcium in their regular diet.

Cautions: dehydration or electrolyte imbalance, diarrhoea, chronic gastrointestinal malabsorption, history of renal calculi, chronic renal function impairment.

Drug interactions: calcitonin, calcium channel blocking agents such as verapamil, calcium or magnesium containing medications, estrogens, milk and milk products phenytoin, oral tetracyclines, vitamin D.

Contraindications: Primary or secondary hypercalcemia, hypercalciuria or calcium renal calculi, sarcoidosis.

Side effects: acute hypercalcemic syndrome (drowsiness, continuing nausea, and vomiting, weakness), calcific renal calculi.

Dose and Administration:Adult: *Antihypocalcemic or Nutritional supplement:Oral:* 8.8 - 16.5gm (800 - 1500 mg of calcium ion) a day, in divided doses.**Child:** *Antihypocalcemic: Oral:* 500-720mg (45-65mg of calcium ion) per kg of body weight a day, in divided doses.

Storage: at room temperature in a well-closed container.

Calcium Lactate

Tablet, 300mg

Indications: as a source of calcium ion for treating calcium depletion.

Cautions, Contraindication, Drug Interaction, Side effects; see under calcium gluconate.

Dose and Administration:Adult:*Adults, Females/Males:* recommended dietary allowance (RDA):19-50 years: 1000 mg/day \geq 51 years, females: 1200 mg/day. 51-70 years, males: 1000 mg/day. Females: Pregnancy/Lactating: Requirements are the same as in nonpregnant or nonlactating females

Child: 1-6 months: Adequate intake: 200 mg/day; 7-12 months: Adequate intake: 260 mg/day; 1-3 years: RDA: 700 mg/day; 4-8 years: RDA: 1000 mg/day; 9-18 years: RDA: 1300 mg/day.

Note: Drink a full glass of water.

Storage: at room temperature in a tight container.

Magnesium Chloride

Tablet, 400mg, 800mg

Injection, 50ml/vial

Indications:correction and prevention of hypomagnesemia

Dose and Administration:Adult: 54-483 mg/day in divided doses; *refer to product labeling.* The RDA of magnesium is 4.5mg/kg which is a total daily allowance of 350-400mg for adult men and 280-300mg for adult women. During pregnancy

the RDA is 300mg and during lactation the RDA is 355mg. *Injection: I.V:Adult:* 8-24mEq/day; **Children:** 2-10 mEq/day. The usual recommended pediatric maintenance intake of magnesium ranges from 0.2-0.6 mEq/kg/day. The dose of magnesium may also be based on the caloric intake; on that basis, 3-10mEq/day of magnesium is needed; maximum maintenance dose: 8-16 mEq/day

Oral Rehydration Salts (ORS)

Powder, each sachet for 1litre contains, see table below

Indications: For the prevention and treatment of mild to moderate dehydration, particularly dehydration from acute diarrhea of any cause, in all age group.

Cautions and Side effects: See notes on section 1.6.

Note: Severe dehydration should be treated with intravenous fluids (Lactated ringer's injection).

Electrolyte	Gram/Liter	Electrolyte	mmol/l
Sodium chloride	2.6	Sodium	75
Glucose Anhydrous	13.5	Glucose Anhydrous	75
Potassium Chloride	1.5	Potassium	20
Trisodium Citrate Dehydrate	2.9	Citrate	10
		Chloride	65
		Total osmolality	245

Dose and Administration: *Orally (by cup and spoon in young children):* To be dissolved in sufficient water to produce 1 litre. Do not boil the prepared solution. Discard any remaining solution after 24 hours.

Prevention of dehydration: In diarrhoea without signs of dehydration, after each loose stool give Less than 2 years, 50 - 100ml; 2 - 10 year, 100 - 200ml.

13. Medicines For Correcting Water Electrolyte And Acid-Base Disturbances

*Treatment of diarrhea:*In diarrhoea with moderate dehydration:75ml of ORS solution per Kg of body weight in 4—6 hours. Repeat if dehydration persists.

See table below.

Note: The Table below shows the approximate amount of ORS solution to be given. Use the patients age only when the weight is not known. During rehydration therapy, continue breast-feeding the infants. In Infants under 6 months of age who are not breastfeed, also give 100 – 200ml of clean water. In dehydrated children with pneumonia, without concurrent diarrhoea, give half the amounts of ORS shown in the Table below.

Oral Rehydration Salt dose by Age and weight:

Age	<4 month	4 -11 month	12-23 month	2 - 4 year	5–14 year	15 year or older
Weight (Kg.)	<5	5-7.9	8 -10.9	11–15.9	16-29.9	30+
Amount (ml)	200-400	400-600	600-800	800-1200	1200-2200	2200-4000

Note: puffy eyelids indicate excess. It should be discontinued until it disappears.

Storage: at room temperature. In a dry place out of direct sunlight. In high humidity, the ORS may lump or become hard. If the powder is white, even if it is hard, the ORS has deteriorated and it should not be used.

Potassium chloride

Tablet, 300mg, 500mg, 600mg, 750mg, and 1gm

Indications: for treatment of potassium depletion

Cautions: in elderly, mild to moderate renal impairment (close monitoring required), intestinal stricture, and history of peptic ulcer; see also interactions.

Drug interactions: special hazard if given with drugs liable to raise plasma potassium concentration such as potassium-sparing

diuretics, angiotension converting enzyme inhibitors, or cyclosporins.

Contraindications: severe renal impairment, plasma potassium concentrations above 5 m mol/liter.

Side effects: nausea, vomiting (severe symptoms may indicate obstruction), oesophageal or small bowel ulceration.

Dose and Administration:*Adult:*for prevention of hypokalaemia: Oral: 2-4gm daily by mouth in patients taking normal diet. Smaller doses must be used if there is renal insufficiency (common in the elderly) otherwise there is danger of hyperkalaemia.

Storage: at room temperature.

Sodium Bicarbonate

Tablet, 500 mg

Indications: Management of metabolic acidosis; gastric hyperacidity; as an alkalinization agent for the urine; treatment of hyperkalemia; management of overdose of certain drugs, including tricyclic antidepressants and aspirin

Cautions: the drug should be administered with extreme caution to patients with heart failure, oedema, renal impairment, hypertension, or aldosteronism and elderly, avoid prolonged use. Sodium bicarbonate should be used during pregnancy only when clearly needed.

Contraindications: metabolic or respiratory alkalosis, in patients with hypocalcemia in whom alkalosis may induce tetany, in patients with excessive chloride loss from vomiting or continuous GI suctioning, and in patients at risk of developing diuretic-induced hypochloremic alkalosis. The drug should not be used orally as an antidote in the treatment of acute ingestion of strong mineral acids.

Side effects: stomach cramps, belching, and flatulence, alkalosis on prolonged use.

Dose and Administration: 3 g in water every 2 hours until urinary PH exceeds 7; maintenance of alkaline urine 5-10 g daily.

Storage: in tightly closed containers at room temperature.

Sodium Chloride

Tablet, 650 mg, 1 g

Indications: used for the treatment of extracellular volume depletion and in the prevention or treatment of deficiencies of sodium and chloride ions and in the prevention of muscle cramps and heat prostration resulting from excessive perspiration during exposure to high temperature.

Cautions: hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function or pre-eclampsia; in patients receiving corticosteroids or corticotropin, particular caution is necessary in geriatric or post operative patients.

Contraindications: in patients with conditions in which administration of sodium and chloride is detrimental.

Side effects: administration of large doses may give rise to sodium accumulation and oedema, nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduced salivation and lachrymation, sweating, fever, tachycardia, hypertension, renal failure.

Dose and Administration: A suggested oral replacement dose of sodium chloride is about 1 to 2 g (approximately 17 to 34 mmol of sodium) three times daily depending on individual needs either with food or as a solution; doses of up to 12 g daily may be necessary in severe cases.

13.2. Parenteral Electrolyte

Solutions of electrolytes are given intravenously, to meet normal fluid and electrolyte requirements or to replenish substantial deficits or continuing losses, when the patient is nauseated or vomiting and is unable to take adequate amounts by mouth. Sodium, potassium, chloride, magnesium, phosphate, and water depletion can occur singly and in combination with or without disturbances of acid - base balance.

Calcium Chloride

Injection, 10% (100mg/ml),

13.6mEq Calcium in 10ml, 5mmol of calcium in 10ml, 5mmol of calcium & Ions in 5ml

Indications: Cardiac resuscitation when epinephrine fails to improve myocardial contractions, cardiac disturbances of hyperkalemia, hypocalcemia, or calcium channel blocking agent toxicity; emergent treatment of hypocalcemic tetany, treatment of hypermagnesemia.

Contraindications: In ventricular fibrillation during cardiac resuscitation, hypercalcemia, and in patients with risk of digitalis toxicity, renal or cardiac disease; not recommended in treatment of asystole and electromechanical dissociation; patients with suspected digoxin toxicity.

Cautions: Digitalized patients, respiratory failure, or acidosis

Drug interactions: Thiazide diuretics, digoxin, calcium channel blockers (eg. verapamil)

Side effects: Bradycardia, cardiac calcemia, hypercalciuria, hypotension, lethargy, mania, muscle weakness, syncope, tissue necrosis, vasodilation, ventricular fibrillation.

Dose and Administration: Calcium chloride has 3 times more elemental calcium than calcium gluconate. One gram of calcium chloride is equal to 270mg of elemental calcium; one

gram of calcium gluconate is equal to 90mg of elemental calcium. Dosages are expressed in terms of the Calcium chloride salt based on a solution concentration of 100mg/ml(10%) containing 1.4mEq (27.3mg/ml) elemental calcium.*Cardiac arrest in the presence of hyperkalemia, magnesium toxicity, or calcium antagonist toxicity: IV: **Infant and children:** 20mg/kg; may repeat in 10 minutes if necessary. **Adolescents and adults:** 2-4mg/kg, repeat in 10 minutes if necessary.**Hypocalcemia: IV:**Children:** 2.7-5mg/kg/dose every 4-6 hours.*Alternative pediatric dosing: **Infants and Children:** 10-20mg/kg/dose, repeat every 4-6 hours if needed. **Adults:** 500mg to 1g/dose repeated every 4-6 hours if needed.*Hypocalcemic tetany: IV:**Neonates:** Divided doses totaling approximately 170mg/kg/24 hours. **Infants and children:** 10mg/kg over 5-10 minutes; may repeat after 6-8 hours or follow with an infusion with a maximum dose of 200mg/kg/day; alternatively, higher doses of 35-50mg/kg/dose repeated every 6-8 hours have been used.***Adults:** 1g over 10-30 minutes; may repeat after 6 hours.*Hypocalcemia secondary to citrated blood transfusion: IV:**Neonates, Infant and children:** Give 32mg (0.45mEq elemental calcium) for each 100ml citrated blood infused.***Adult:** 200-500mg per 500ml of citrated blood (infused into another vein).

Calcium gluconate (levulinate)

Injection, 10% in 10ml ampoule

Indications: in the treatment of hypocalcaemia in conditions that require a rapid increase in serum calcium - ion concentration, such as neonatal hypocalcaemia tetany; tetany due to parathyroid deficiency.

It is also indicated to decrease or reverse the cardiac depressant effect of hyperkalemia on electrocardiographic (ECG) function,

and as an aid in the treatment of CNS depression due to over dosage of magnesium sulfate.

Cautions: cardiac function impairment, ventricular fibrillation during cardiac resuscitation, renal function impairment, diarrhoea.

Drug interactions: calcitonin, verapamil, calcium and magnesium containing medications, digitalis glycoside, magnesium sulfate, milk and milk products, phenytoin, oral tetracyclines, vitamin D.

Contraindications: digitalis toxicity, primary or secondary hypercalcemia, hypercalciuria, calcium renal calculi, sarcoidosis.

Side effects: hypotension (dizziness), flushing and/or sensation of warmth or heat, irregular heartbeat; nausea or vomiting, skin redness, rash, pain, or burning at injection site, sweating, tingling sensation.

Dose and Administration:**Adult:***Antihypocalcemic or Electrolyte replenisher: IV:* 970mg (94.7mg of calcium ion), administered slowly at a rate not to exceed 5ml (47.5mg of calcium ion) a minute. The dosage may be repeated, if necessary, until tetany is controlled.*Antihyperkalemic:IV:* 1 to 2 grams (94.7 to 189 mg of calcium ion), administered slowly at a rate not to exceed 5ml a minute, the dosage being titrated and adjusted by constant monitoring of ECG changes during administration.*Antihypermagnesemic:IV:* 1 to 2gms, administered at a rate not to exceed 5ml a minute.**Child:***Antihypocalcemic: IV:* 200-500mg (19.5-48.8mg of calcium ion) as a single dose, administered slowly at a rate not to exceed 5ml (47.5mg of calcium ion) a minute, repeated if necessary until tetany is controlled.

Storage: at room temperature, protect from freezing.

Dextrose

Injection, 5% in 500ml, 1000ml; 10% in 500ml, 1000ml; 40% in 20ml, 50% in 50ml

Indications: for the treatment of hypoglycemia due to insulin excess or other causes.

Cautions: caution in patients with diabetes mellitus or with carbohydrate intolerance for any reason.

Contraindication: anuria.

Side effects: rapid administration may cause local pain; hyperglycemia and glycosuria, which if undetected and untreated can lead to dehydration, coma, and death.

Dose and Administration: The clear solution is given slowly *by intravenous* route. *For the treatment of hypoglycemia:* **Adult and child:** 20 to 40ml Dextrose 40%; may be repeated in severe cases.

Storage: at room temperature.

Dextrose in Normal Saline

Injection, 5% in 500ml, 1000ml; 10% in 500ml, 1000ml

Indications: In states of sodium depletion like vomiting and diarrhoea due to gastroenteritis, Diabetic keto acidosis, Paralytic ileus, salt losing bowel disease, Renal salt wasting diseases.

Cautions: In volume overload states.

Dose and Administration: Depending on the volume of fluid lost and clinical parameters. Monitor the patient during administration to prevent volume overload.

Hdroxyethyl starch

Large Volume Parenteral, 6% w/v of 500ml

A starch composed of more than 90% of amylopectin that has been etherified with hydroxyethyl groups; the terms tetrastarch, pentastarch, and hetastarch reflect the degree of etherification

Indications: low blood volume

Cautions, Contraindications, Side effects, Dose and administrations and Storages see section 11.4 under Hydroxyethyl starch

Lactated potassium saline injection (Darrow's solution)

Injection solution, each 1000 ml contains K^+ 35mEq + Na^+ 121 mEq+Cl 103 mEq+ lactate 53 mEq in 500 ml, 1000 ml

Injection solution (half strength) – each 1000 ml contains; K^+ 17.5 meq+ Na^+ 60.5 mEq+Cl 51.5 meq + Lactate 26.5 mEq in 500 ml, 1000 ml

Indications: It is a mixture of potassium chloride, sodium chloride and sodium lactate; used in fluid therapy to repair a potassium deficit.

Lactated Ringer's injection (Hartmann's solution)

Injectable solution, each 1000ml contains; K^+ 5.4meq + Na^+ 130.7meq+ Ca^{++} 3.6meq+Cl 111.5meq+Lactate 28.2meq in 500ml, 1000ml

Indications: for replacement of electrolytes and water losses in severe dehydration.

Contraindications: severe liver and renal damage.

Dose and administration: *slow intravenous: Adult and Older*

Child: 100ml/kg of body weight within 4 hours, immediately until radial pulse is easily felt. **Infant:** 30ml/kg of body weight within 1 hour followed by 40ml/kg of body weight within the next 2 hours; followed by Oral ORS 40ml/kg of body weight within the next 3 hours.

Note: If condition worsens, the rate of administration and the amount of fluid may need to be increased. After the first 6 hours, begin breast-feeding, or for nonbreastfeed infants give 100 – 200ml clean water before continuing ORS therapy. After rehydration is complete, feeding should start immediately.

Storage: at room temperature.

Peritoneal dialysis fluid No 1

Injectable solution, each 1000ml contains;

Na⁺ 130.0-140mmol + Ca⁺⁺ 1.5-2.0mmol +Mg⁺⁺ 0.5-0.75mmol +HCO₃⁻ (as acetate/lactate) 35-45mmol +Cl⁻ 90.0-102mmol +Dextrose 15g in 1000ml, 2000ml

Indications: It is indicated for a single daily exchange for the long (8 to 16 hour) for the management of End-Stage Renal Disease or indicated for patients in acute or chronic renal failure when nondialytic medical therapy is judged to be inadequate. It may also be indicated in the treatment of certain fluid and electrolyte disturbances, and for patients intoxicated with certain poisons and drugs. However, for many substances other methods of detoxification have been reported to be more effective than peritoneal dialysis.

Cautions: in patients with a number of abdominal conditions including disruption of the peritoneal membrane or diaphragm by surgery or trauma, extensive adhesions, bowel distention, undiagnosed abdominal disease, abdominal wall infection, hernias or burns, fecal fistula or colostomy, tense ascites, obesity, and large polycystic kidneys, recent aortic graft replacement and severe pulmonary disease.

Side effects: Fluid imbalances, hypovolemia, hypervolemia, hypertension, hypotension, disequilibrium syndrome and muscle cramping.

Dose and Administration:To avoid the risk of severe dehydration and hypovolemia and to minimize the loss of protein, it is advisable to select the peritoneal dialysis solution with the lowest level of osmolarity consistent with the fluid removal requirements for that exchange.

Peritoneal dialysis fluid No. 2

Injectable solution, each 100ml contains;

Na⁺ 130.0-140mmol + Ca⁺⁺ 1.5-2.0mmol + Mg⁺⁺ 0.5-0.75mmol +HCO₃⁻ (as acetate/lactate) 35 - 45mmol +Cl⁻ 90.0 - 102mmol +Dextrose 45g in 1000ml, 2000ml

See under peritoneal dialysis fluid No 1

Potassium chloride

Injection, 150mg/ml in 10ml ampoule

Indications: treatment of potassium depletion or hypokalaemia, with or without metabolic alkalosis, in chronic digitalis intoxication, and in patients with hypokalaemia familiar periodic paralysis; see also oral potassium supplements, section 11.1.

Cautions: for intravenous infusion the concentration of solution should not usually exceed 3.2g (43mmol)/litre; specialist advice and ECG monitoring in difficult cases.

Drug interactions: potassium sparing diuretics, angiotension converting enzyme inhibitors cyclosporins, digitalis glycoside, parenteral calcium salts, laxatives.

Contraindications: hyperkalemia.

Side effects: rapid infusion toxic to heart; see section 11.1

Dose and Administration: *IV infusion Note:Injectable potassium chloride products, in strengths of 1.5mEq and 2mEq per ml must be diluted prior to IV administration. Direct patient injection of potassium concentrate may be instantaneously fatal. However, injectable potassium chloride products in strengths of 0.1 and 0.4mEq per ml are intended for use with a calibrated infusion device and do not require dilution.*

Adult:Antihypokalemic or electrolyte replenisher:IV infusion: the dose and rate of infusion to be determined by the individual requirements of each patient, up to 400mEq of potassium a day (usually not more than 3mEq per kg of body weight). The

response of the patient, as determined by the measurement of serum potassium concentration and the electrocardiogram following the initial 40 to 60mEq infusion, should indicate the subsequent infusion rate required.

Child: *Antihypokalemic or Electrolyte replenisher: IV infusion:* up to 3mEq of potassium per kg of body weight or 40mEq per square meter of body surface area a day. Volume of administered fluids must be adjusted to body size.

Storage: at room temperature, protect from freezing.

Ringer's injection

Injectable solution, each 1000ml contains:

Na^+ 147mEq + K^+ 4mEq + Ca^{++} 45mEq + Cl^- 155.5mEq in 300ml, 500ml, 1000ml

Sodium Bicarbonate

Injection (concentrated), 7.5 % (40 meq/50ml) in 50 ml ampoule; 8.4% (50meq/50ml)

Indications: for the treatment of acute metabolic acidosis, and relief of discomfort in mild urinary tract infections.

Cautions: in acute metabolic acidosis – the manufacturers warn that avoid excessive IV administration or avoid rapid injection (10 ml /minute) of hypertonic sodium bicarbonate solutions in neonates and children younger than 2 years of age; and see also notes under sodium bicarbonate (oral).

Contraindications: see under sodium bicarbonate (oral).

Side effects: chemical cellulitis because of their alkalinity, subsequently resulting in tissue necrosis, ulceration, and/or sloughing at the site of injection; and see also notes under sodium bicarbonate (oral)

Note: The above side effect is caused due to inadvertent extravasation of hypertonic solutions of sodium bicarbonate and this can be treated by

elevating the affected area, applying warm compresses to the site, and locally injecting lidocaine or hyaluronidase.

Dose and Administration: *By slow intravenous injection, a strong solution (up to 8.4 %), or by continuous intravenous infusion, a weaker solution (usually 1.26 %), an amount appropriate to the body base deficit.*

Storage: at room temperature & freezing should be avoided.

Sodium chloride

Injection, 235mg/ml, 0.9% (Normal saline) in 10ml, 20ml, 500ml, 1000ml; 3% in 500ml

Injection, 30%-30mg in 10ml

Indications: used for extracellular fluid replacement and in the management of metabolic alkalosis in the presence of fluid loss and mild sodium depletion. Hypertonic (3%, 5%) sodium chloride injection is used in the management of severe sodium chloride depletion when rapid electrolyte restoration is essential.

Cautions: see section 11.1

Contraindications: in patients with conditions in which administration of sodium and chloride is detrimental. Sodium chloride 3% and 5% injections are also contraindicated in the presence of increased, normal, or only slightly decreased serum electrolyte concentrations.

Side effects: venous thrombosis or phlebitis, extravasation, hypervolemia, hypernatremia (on excessive administration); see also section 11.1

Dose and Administration:Adult: *IV infusion* - 1 liter of 0.9% sodium chloride injection daily or 1-2 L of 0.45% sodium chloride injection daily. The usual initial IV dose of 3 or 5% sodium chloride injection is 100ml given over a 1-hour period,

before additional amounts are administered. It should not exceed 100ml/hour.

Storage: at room temperature, protect from freezing.

Sodium lactate

Injection Na⁺ 16.7mEq + Lactate 16.7mEq in 100ml

Indications: It is primarily indicated, after dilution, as a source of bicarbonate for prevention or control of mild to moderate metabolic acidosis in patients with restricted oral intake whose oxidative processes are not seriously impaired. It is neither intended nor effective for correcting severe acidosis states which require immediate restoration of plasma bicarbonate levels. Sodium lactate has no advantage over sodium bicarbonate and may be detrimental in the management of lactic acidosis. It should not be used in conditions in which lactate levels are increased (e.g., shock, congestive heart failure, respiratory alkalosis) or in which utilization of lactate is diminished (e.g., anoxia, beriberi). Therefore, it is not use for the treatment of lactic acidosis.

Contraindications: It is contraindicated in patients suffering from hypernatremia or fluid retention.

Cautions: Congestive heart failure, sodium-retaining states, other edematous, over hydration, pulmonary edema, severe renal insufficiency, in patients with oliguria or anuria. Caution must be exercised in the administration of parenteral fluids, especially those containing sodium ions, to patients receiving corticosteroids or corticotrophin, Pregnancy and breast feeding mother.

Dose and Administration:Sodium Lactate Injection is administered intravenously only after addition to a larger volume of fluid. The amount of sodium ion and lactate ion to be added to larger volume intravenous fluids should be determined

in accordance with the electrolyte requirements of each individual patient.

13.3. Enteral Nutrition

Enteral nutrition includes feeding by mouth, by nasogastric or nasoenteric tube, or directly into a gastrostomy or other enterostomy. It may be supplemental, if normal food intake is possible but inadequate, or total. Individual patients vary in their requirements according to age, size, and metabolic state, but a diet supplying 2000 to 3000 kcal of energy and 10-15g of nitrogen (as 60 to 90 g of protein) in 2 to 3 litres of fluid is fairly typical; because absorption from the gastrointestinal tract is incomplete requirements are higher than by parenteral route. Preparations containing whole protein (often derived from milk or soya) are generally preferred. Although preferred to parenteral nutrition, enteral feeding is not without complications. Patients may be at risk of oesophagitis, aspiration, and regurgitation as a result of the tube insertion; other potential problems include diarrhea, nausea and vomiting, gastric retention, hyperglycaemia, fluid and electrolyte disturbances, and microbial contamination of the feed regimen.

- 1. Calcium Caseinate**
- 2. Soya-based non-milk preparations**

14. VITAMINS

Vitamins are used for the prevention and treatment of specific deficiency states or when the diet is known to be inadequate. Large doses of vitamins (megavitamin therapy) have been proposed for a variety of disorders, but adequate evidence of their value is lacking. Excessive intakes of most water - soluble vitamins have little effects due to their rapid excretion in urine, but excessive intakes of fat - soluble vitamins accumulate in the body and are potentially dangerous. Vitamin A (Retinol) is a fat - soluble substance stored in body organs, principally the liver.

Deficiency of Vitamin A (Retinol) is associated with ocular defects (particularly xerophthalmia) and an increased susceptibility to infections particularly measles and diarrhoea. Despite initial epidemiological evidence suggesting that vitamin A or carotene may have a protective effect against some epithelial cancers, the claims have not been substantiated. Massive overdose can cause rough skin, dry hair, an enlarged liver, and a raised erythrocyte sedimentation rate and raised serum calcium and serum alkaline phosphatase concentrations.

In view of evidence suggesting that high levels of vitamin A may cause birth defects women who are (or may become) pregnant are advised not to take vitamin A supplements (including tablets and fish liver oil drops), except on the advice of a doctor or an antenatal clinic; nor should they eat liver or products such as liver pate or liver sausage.

Vitamin B is composed of widely differing substances which are, for convenience, classed as 'vitamin B complex'. Thiamine (Vitamin B1) is used orally for deficiency due to inadequate dietary intake, severe deficiency may result in 'beriberi'. Thiamine is given by intravenous injection in doses of up

to 300mg daily (parenteral preparations may contain several B group vitamins) as initial treatment in severe deficiency states. Potentially severe allergic reactions may occur after parenteral administration; facilities for resuscitation should be immediately available. Pyridoxine (Vitamin B6) deficiency is rare as the vitamin is widely distributed in foods, but deficiency may occur during isoniazid therapy and is characterized by peripheral neuritis. High dose are given in some metabolic disorders, such as hyperoxaluria.

Nicotinic acid inhibits the synthesis of cholesterol and triglyceride and is used in some hyperlipidaemias. Nicotinic acid and nicotinamide are used to prevent and treat nicotinic acid deficiency (pellagra). Nicotinamide is generally preferred as it does not cause vasodilation.

Folic acid is essential for the synthesis of DNA and certain proteins. Deficiency of folic acid or vitamin B₁₂ is associated with megaloblastic anaemia. Folic acid should not be used in undiagnosed megaloblastic anaemia unless Vitamin B₁₂ is administered concurrently, otherwise neuropathy may be precipitated.

Supplementation with folic acid 400 micrograms daily is recommended for women of child - bearing potential in order to reduce the risk of serious neural tube defects in their offspring.

Ascorbic acid (Vitamin c) is used for the prevention and treatment of scurvy. Claims that ascorbic acid is of value in the treatment of common colds are unsubstantiated.

The term Vitamin D covers a range of compounds including ergocalciferol (Vitamin D₂) and colecalciferol (Vitamin D₃). These two compounds are equipotent and either can be used to prevent and treat rickets.

Simple deficiency of Vitamin D occurs in those who have an inadequate dietary intake or who fail to produce enough colecalfiferol (Vitamin D₃) in their skin from the precursor 7 - dehydrocholesterol in response to ultraviolet light.

Children with dark skin must continue vitamin D prophylaxis for up to 24 months because of their inability to produce enough vitamin D₃ in their skin. Dark skin with a high melanin content must be exposed to daylight longer than light skin in order to obtain the same synthesis of vitamin D₃. Vitamin D is also used in deficiency states caused by intestinal malabsorption or chronic liver disease and for the hypocalcaemia of hypoparathyroidism.

Vitamin K is necessary for the production of blood clotting factors (see sec. 10.1)

14.1. Vitamins, single

Alfacalcidol (1ahydroxycholecalciferol)

Capsule, 0.25mcg

Capsule(s/g), 1mcg

Vitamin D requires hydroxylation by the kidney to its active form, therefore the hydroxylated derivatives alfacalcidol or calcitriol should be prescribed if patients with severe renal impairment require vitamin D therapy.

Indications: see notes above.

Cautions: monitor plasma-calcium concentration in patients receiving high doses and in renal impairment; pregnancy; breast-feeding; nephrolithiasis

Contra indications: hypercalcaemia; metastatic calcification

Side effects: symptoms of overdosage include anorexia, lassitude, nausea and vomiting, diarrhoea, constipation, weight loss, polyuria, sweating, headache, thirst, vertigo, and raised

concentrations of calcium and phosphate in plasma and urine; also rarely nephrocalcinosis, pruritus, rash, and urticaria

Dose and Administration: *Oral: Adult and Child over 20 kg*, initially 1 microgram daily (elderly 500 nanograms), adjusted to avoid hypercalcaemia; maintenance, usually 0.25–1 microgram daily; **Neonate and Preterm Neonate:** initially 50–100 nanograms/kg daily, **child under 20 kg** initially 50 nanograms/kg daily

Ascorbic Acid (Vitamin C)

Drops, 200mg/ml

Injection, 50mg/ml in 2ml ampoule, 100mg/ml in 5ml ampoule, 200mg/ml

Tablet, 100mg, 500mg, 1gm

Indications: for prophylaxis and treatment of vitamin C (ascorbic acid) deficiency states which lead to scurvy.

Cautions: caution should be necessary not to take large amount during pregnancy. Importance of not taking more than the RDA should also be considered. Caution is required in those with sensitivity to ascorbic acid.

Drug interactions: cellulose sodium phosphate, deferoxamine, disulfiram and vitamin B12 (with large doses of vitamin C).

Side effect: dizziness or faintness, kidney stones (oxalate)

Dose and Administration: Adult: *Dietary supplement: Oral:* 50 to 100mg a day. *Treatment of deficiency: Oral, IV or IM:* 100 to 250mg one or three times a day. **Child:** *Dietary supplement:* Infants and Children up to 4 years of age: *Oral:* 20 to 50mg a day. *Treatment of deficiency: Oral, IV or IM:* 100 to 300mg a day in divided doses.

Storage: at room temperature in a tight, light resistant container.

Calciferol (Ergocalciferol/Vitamin D₂)

Injection, 300,000-units/ml in 2 ml ampoule

Oral solution, 20,000-units/ml, 400,000 units/ml

Tablet (strong), 1.25 mg (50,000units)

Indications: used in the treatment of chronic hypocalcemia, hypophosphatemia, rickets and osteodystrophy associated with various medical conditions including chronic renal failure, familial hypophosphatemia, and hypoparathyroidism (post surgical or idiopathic or pseudohypoparathyroidism); for prevention and treatment of vitamin D deficiency states; and to treat anticonvulsant induced rickets & osteomalacia.

Note: Ergocalciferol may not be the preferred agent in the treatment of familial hypophosphatemia or hypoparathyroidism because the large doses needed are associated with a risk of overdose and hypercalcemia, and ergocalciferol not usually preferred in patients with renal failure since these patients have impaired ability to synthesize calcitriol from colesterciferol and ergocalciferol.

Cautions: ergocalciferol should be administered with extreme caution, if at all, to patients with impaired renal function and with extreme caution in patients with heart disease, renal stones, or arteriosclerosis; large doses of Vitamin D analogs should not be administered to nursing women; take care to ensure correct dose in infants and pregnant.

Drug interactions: antacids (magnesium containing), in high doses of calcium containing preparations and diuretics (thiazide), vitamin D analogs.

Contraindications: hypercalcemia, hypervitaminosis D, Renal Osteodystrophy with hyperphosphatemia, metastatic calcification, hypersensitivity to effects of Vitamin D.

Side effects: symptoms of over dosage include anorexia, lassitude, nausea and vomiting, diarrhoea, weight loss, polyuria, sweating, headache, thirst, vertigo, and raised concentrations of calcium and phosphate in plasma and urine.

Dose and Administrations:*Ergocalciferol injection*

Adult:*Deficiency (prophylaxis or treatment): Intravenous infusion*, as part of total parenteral nutrition solutions, the specific amount determined by individual patient need. *Malabsorption: IM:* 10,000 units per day. **Child:** see adult dose. *Ergocalciferol oral solution* **Adult:** *Deficiency (prophylaxis): Oral:* amount based on normal daily-recommended intakes: **Person**

	Microgram	Units
Adolescent and adult	5-10	200 – 400
Pregnant and breast feeding	10	400

Deficiency (treatment): Treatment dose is individualized by prescriber based on severity or deficiency: *Vitamin D – resistant rickets: Oral:* 12,000 to 500,000 units per day.

Vitamin D – dependent rickets: Oral: 10,000 to 60,000 units per day (up to 500,000 units/day). *Osteomalacia due to prolonged use of anticonvulsants: Oral:* 1000 to 4000 units per day. *Familial hypo phosphatemia: Oral:* 50,000 to 100,000 units per day. *Hypoparathyroidism: Oral:* 50,000 to 150,000 units per day. **Child:***Deficiency (prophylaxis):* Oral amount based on normal daily-recommended intakes.

Persons	Microgram Units	
Birth to 3 years of age	7.5 – 10	300 - 400
4 to 10 years of age	10	400

Deficiency (treatment): Treatment dose is individualized by prescriber based on severity of deficiency. *Vitamin D-dependent rickets: Oral:* 3000 to 10,000 units per day (up to 50,000 units/day). *Osteomalacia due to prolonged use of anticonvulsants: Oral:* 1000 units per day.

Hypoparathyroidism: Oral: 50,000 to 200,000 units per day. *Ergocalciferol tablets: Adult:* see Ergocalciferol oral solution; **Child:** see Ergocalciferol oral solution
Storage: in tight, light - resistant containers at a room temperature.

Cholecalciferol (Vitamin D₃)

Capsule, 250mcg

Injection (oily), 300,000 IU/ml

Indications, Cautions, Side effects, Drug interactions, Dose and Administration; see under ergocalciferol.

Cyanocobalamine (vitamin B₁₂)

Injection, 100mcg/ml, 1000mcg/ml in 1ml ampoule

See section 11.3 under Cyanocobalamine (vitamin B₁₂)

Folic Acid

Injection, 5 mg/ml in 1 ml ampoule

Tablet, 200 mcg, 1 mg, 5 mg

Indications: for prevention and treatment of folic acid deficiency states, including megaloblastic anemia and in anemias of nutritional origin, pregnancy, infancy, or childhood; folic acid is being used in the diagnosis of folate deficiency

Cautions: women receiving antiepileptic therapy need counseling before starting folic acid.

Drug interactions: cyanocobalamin; agents causing folic acid deficiency with long term use (phenytoin, oral contraceptives, isoniazid, NSAIDs in high doses and glucocorticosteroids); antifolate agents (trimethoprim, pyrimethamine and methotrexate)

Contraindications: should never be given without vitamin B₁₂ in undiagnosed megaloblastic anaemia or other vitamin B₁₂

deficiency states because risk of precipitating subacute combined degeneration of the spinal cord; folate-dependent malignant disease, folic acid injection that contains benzyl alcohol as a preservative should not be used in new born and immature infants.

Side effects: allergic reaction, specifically; bronchospasm; erythema; fever; general malaise; skin rash; or itching.

Dose and Administrations: Folic acid Injection: Adult: *Deficiency (prophylaxis): IV infusion*, as part of total parenteral nutrition solutions, the specific amount determined by individual patients need. *Deficiency (treatment): IM, IV, or deep SC:* 250 mcg (0.25 mg) to 1 mg a day until a hematologic response occurs. *Diagnostic aid (folate deficiency): IM:* 100 to 200 mcg (0.1 to 0.2 mg) a day for ten days plus low dietary folic acid and Vitamin B₁₂. **Child:** See usual adult dose.

Folic acid Tablets: *Deficiency (prophylaxis): Oral:* amount based on normal daily-Recommended intakes:

Persons	Microgram
Adult males	150 – 400
Adult females	150 – 400
Pregnant females	400 - 800
Breast feeding females	260 – 800
Birth to 3 years of age	25
4 to 6 years of age	75 – 400
7 to 10 years of age	100 – 400

Diagnostic aid (folate deficiency): Oral: 100 to 200 mcg (0.1 to 0.2 mg) a day for ten days plus low dietary folic acid and vitamin B₁₂. *Deficiency (treatment):* treatment dose is individualized by prescriber based on severity of deficiency.

Storage: at room temperature in a well-closed container.

Mecobalamine

Tablet, 500mcg

Indications: management of peripheral neuropathies such as diabetic neuropathies which are associated with damaged nerve fibers leading to symptoms like tingling, numbness and pain.

Contraindications: Hypersensitivity to mecobalamin.

Cautions: should not be used for more than one month unless it is effective.

The prolonged use of larger doses of mecobalamin is not recommended for patients whose occupation requires the handling of mercury or mercury compounds.

Side effects: anorexia, nausea, vomiting and diarrhea, rash.

Dose and Administration: Adult: Oral: 3 tablets (1500mcg) daily divided into three doses. The doses may be adjusted depending on the patients age and symptoms

Storage: store at a temperature below 25°C, protect from light and moisture

Menadiol Sodium Diphosphate

Injection, 10mg /ml

Tablet, 10 mg

Indications: in the prevention and treatment of hypoprothrombinemia secondary to factors limiting absorption or synthesis of Vitamin K.

Cautions: the drug should not be used in neonates; in patients with hepatic function impairment, G6PD deficiency and vitamin E deficiency.

Drug interactions: anticoagulants (coumarin or indandione – derivative), hemolytics

Contraindications: neonates and infants, late pregnancy

Side effects: anaphylaxis, cyanosis, dizziness, hypotension, profuse sweating, rapid and weak pulse, and in newborns,

hemolytic anemia and liver toxicity, which may progress to kernicterus.

Dose and Administration: *Oral dosage forms* **Adult:**

Hypoprothrombinemia secondary to obstructive jaundice and biliary fistulas: Oral: 5 mg/day. Hypoprothrombinemia anemia secondary to the administration of antibacterials or salicylate: Oral: 5 to 10 mg per day. **Child:** Vitamin (prothrombogenic); or Antidote (to drug-induced hypoprothrombinemia): Oral: 5 to 10 mg per day, parenteral dosage forms.

Adult: Nutritional supplement (Vitamin), prothrombogenic; or Antidote (to drug-induced hypoprothrombinemia): IM or SC: 5 to 15 mg one or two times a day.

Storage: in a light resistant container at room temperature; especially menadiol sodium bicarbonate injection should be protected from freezing.

Nicotinamide

Injection, 5 mg/ml, 100 mg/ml in 1 ml ampoule

Tablet, 100 mg

Indications: nicotinamide and nicotinic acid (niacin) are used to prevent niacin deficiency and to treat pellagra. Niacin (but not nicotinamide) is also indicated in the treatment of hyperlipidemia.

Cautions: blood glucose concentration should be monitored periodically and also liver function should be determined periodically in patients receiving long-term niacin or nicotinamide therapy. Large doses of niacin or nicotinamide should be administered with caution to patients with gallbladder disease or a history of jaundice or liver disease, diabetes mellitus, gout, peptic ulcer, or allergy, in women who are or may become pregnant unless the possible benefits outweigh the potential risks to the fetus.

Drug interactions: niacin reportedly potentiates the hypotensive effect of ganglionic blocking drugs.

Contraindications: niacin and nicotinamide are contraindicated in patients with, active peptic ulcer, or hypersensitivity to the drugs. Niacin is also contraindicated in patients with arterial hemorrhaging or severe hypotension

Side effects: anaphylactic reaction with injection only, hepatotoxicity or cholestasis with high doses of extended – release niacin.

Dose and Administration: *Oral:Deficiency (prophylaxis):* *Oral:* amount based on normal daily- Recommended intakes:

Persons	Milligram
Adolescent and adult males	15 – 20
Adolescent and adult females	13 – 15
Pregnant females	17
Breast feeding females	20
Birth to 3 years of age	5-9
4 to 6 years of age	12
7 to 10 years of age	13

Deficiency (treatment): Treatment dose is individualized by prescriber based on severity of deficiency.

Parenteral:Deficiency (prophylaxis):IV infusion: as part of total parenteral nutrition solutions, the specific amount determined by individual patient need. *Deficiency (treatment):Adult:IM:* 50 to 100 mg five to more times a day; *IV (slow):* 25 to 100 mg 2 or more times a day. **Child:IV (slow):** up to 300 mg a day

Storage: at room temperature in a tight container.

Nicotinic Acid

Injection, 50 mg/ml in 1 ml ampoule

Tablet, 50 mg

Indications, Cautions, Side effects, Drug interactions, Contraindications, see notes under nicotinamide

Dose and Administrations: *Oral: Adult: Antihyperlipidemic:*

Initial: *Oral:* 1 gram three times a day, the dosage being increased in increments of 500 mg a day every two to four weeks as needed. Maintenance: *Oral:* 1 to 2 grams three times a day. *Parentral:* see under nicotinamide

Storage: at room temperature in a well closed container. Protect from freezing.

Phytomenadione (Vitamin K₁)

Injection, 1mg/0.5ml 10mg/ml in 1ml ampoule.

Indications: prothrombogenic nutritional supplement, it is also used for treatment and prevention of various coagulation disorders including hypoprothrombinemia, or as an antidote to drug induced hypoprothrombinemia; see also section 10.1

Cautions, Drug interactions, Side effect; see section 10.1 under phytomenadione

Dose and Administration: *SC or IM,* it should not be given repeatedly to patients with severe liver disease, once the response to the initial dose is unsatisfactory.

Adult: Nutritional supplement (Vitamins), prothrombogenic or Antidote (to drug-induced hypoprothrombinemia): 2.5 to 10mg (up to 25mg), may be repeated after 6-8 hours if necessary.

Child: Nutritional supplement (vitamin), prothrombogenic or Antidote (to drug-induced hypoprothrombinemia), Treatment of hypoprothrombinemia: **Infants:** *IM or Sc:* 1-2 mg. **Child:** *IM or Sc:* 5-10mg.

Storage: at room temperature, protect from light and freezing.

Pyridoxine Hydrochloride (Vitamin B₆)

Injection, 50mg/ml in 2ml ampoule, 150mg/ml

Tablet, 40mg, 50mg, 100mg, 300mg.

Indications: for prevention and treatment of pyridoxine deficiency states that may occur as a result of inadequate nutrition or intestinal malabsorption.

It is also used as antidote in cyclosporin poisoning and to terminate seizures and prevent neuropathy associated with isoniazid poisoning.

Cautions: sensitive to pyridoxine.

Drug interactions: levodopa, cycloserine, isoniazid, penicillamines, hydralazine.

Side effects: sensory neuropathy in prolonged use

Dose and Administration:**Adult:***Deficiency states: Oral: 20-50mg up to 3 times daily isoniazid neuropathy, prophylaxis 10mg daily, therapeutic - 50mg three times daily. Idiopathic sideroblastic anaemia: Oral: 100-400mg daily in divided doses. Nutritional supplement - Dietary supplement: Oral: 10-20mg per day for three weeks followed by 2 to 5mg per day (in a multivitamin preparation) for several weeks. Drug Induced deficiency: Prevention: Oral: 10-50mg per day for penicillamine or 100-300mg per day for cycloserine, hydralazine, or isoniazid. Treatment: Oral: 50 to 100mg per day as needed to prevent relapse; IM or IV, 50 to 200mg per day for three weeks, followed by 25 to 100mg per day as needed. Child: Dietary supplement: Oral: 2.5 to 10mg per day for three weeks, followed by 2 to 5mg per day (in a multivitamin preparation) for several weeks.*

Storage: at room temperature, protect from light and from freezing.

Thiamine Hydrochloride (Vitamin B₁)

Injection, 50mg/ml in 2ml ampoule

Tablet, 5mg, 10mg, 100mg, 300mg

Indications: for prevention and treatment of thiamine deficiency states that may occur as a result of inadequate nutrition or intestinal malabsorption. It is used for temporary metabolic correction of genetic enzyme deficiency diseases such as subacute necrotizing encephalomyelopathy (SNE, Leigh's disease), maple syrup urine disease (branched-chain aminoacidopathy), and lactic acidosis associated with pyruvate carboxylase deficiency and hyperalaninemia.

Cautions: patients sensitive to thiamine and in those with Wernicke's encephalopathy.

Side effects: anaphylactic reaction (coughing, difficulty in swallowing; hives; itching of the skin, swelling of face, lips or eyelids, or wheezing or difficulty in breathing).

Dose and Administration: Adult: Nutritional supplement (Vitamin) Beriberi (initial in mild or maintenance following severe): Oral: 5 to 10mg three times a day (in a multivitamin preparation).

Beriberi (critical illness): IM or slow IV, 5-100mg three times a day followed by maintenance oral administration. Treatment of deficiency: Oral: 1-10mg three times a day until improvement occurs, followed by recommended dietary allowance.

Child: Nutritional supplement (Vitamin) Beriberi (mild): Infants: Oral: 10mg per day. Beriberi (critical illness): IM or slow IV: 10-25mg per day. Treatment of deficiency: Oral: 10 to 50mg per day in divided doses. Dietary supplement: **Infants:** Oral: 300 to 500mcg (0.3-0.5mg) per day. **Child:** Oral: 500mcg (0.5mg) to 1mg per day.

Storage: at room temperature in a tight, light-resistant container. Protect from light and freezing.

Vitamin A

Capsule, 25,000 IU, 50,000 IU, 100,000 IU

Oral solution, 150,000 IU/ml (concentrated), 50,000 IU/ml

Tablet, 50,000 IU, 100,000 IU 200,000 IU

Injection, under 200,000 IU/ml

Indications: for prevention or treatment of vitamin A deficiency states, causing keratomalacia, xerophthalmia and nyctalopia (night blindness). This may occur as a result of inadequate nutrition or intestinal malabsorption.

Note: Vitamin A is not useful for treatment of dry or wrinkled skin, eye problems, or prevention or treatment of infections not related to vitamin A deficiency.

Cautions: high doses exceeding 6000 units are not recommended during pregnancy, caution is recommended in young children taking high doses of vitamin A; long-term vitamin A use in the elderly may increase the risk of vitamin A overload; in patients with chronic renal failure, chronic alcoholism, cirrhosis, hepatic disease and viral hepatitis.

Drug interactions: calcium supplements, isotretinoin, tetracycline, vitamin E, cholestyramine, colestipol, mineral oil, oral neomycin.

Contraindications: hypervitaminosis A

Side effects: symptoms of acute overdose - bleeding from gums or sore mouth; bulging soft spot on head-in babies, confusion or unusual excitement; diarrhoea, dizziness, or drowsiness, double vision, severe headache, severe irritability, peeling of skin, especially on lips and palms; severe vomiting

Dose and Administration:Adult:Deficiency:*Oral:* 30,000 RE (100,000units) a day for 3 days followed by 7500 to 15,000 RE (25,000 to 50,000 unit) a day for 14 days. *With xerophthalmia:* *Oral:* 7500 to15, 000 RE (25,000 to 50,000 units) a day.

Note: RE=Retinol Equivalent; one RE = one mcg of Retinol = 3.33 units of vitamin A.

- *IM, Intravenous infusion*, as a part of total parenteral nutrition solution, the specific amount determined by individual patient need.
- *IM* 15,000 to 30,000 RE (50,000-100,000 units) a day for three days, followed by 15,000 RE (50,000 units) a day for two weeks.

Child: Deficiency Infants less than 1 year: *Oral*: 3000 RE (10,000 units) per kg per day for 5 days followed by 2250 - 4500 RE (7500 to 15,000 units) per day for 10 days; *IM*, 1500 - 3000 RE (500-10,000 units) a day for ten days; in severe deficiency - *IM*, 2250 to 4500 RE (7500 to 15,000 units) a day for ten days.

Children 1-8 years of age: *Oral*: 3000 RE (10,000 units) per kg per day for 5 days followed by 5100 to 10,500 RE (17,000 to 35,000 units) a day for 10 days.

With xerophthalmia: *Oral*: 1500 RE (5000 units) per kg of body weight for five days, then in combination with intramuscular Vitamin A (7500 RE or 25,000 units per kg of body weight a day) until recovery occurs.

IM: 1500-4500 RE (5000-15,000 units) a day for ten days; in severe deficiency – *IM*: 5250 to 10,500 RE (17,500-35,000 units) a day for ten days.

Storage: at room temperature in a tight, light-resistant container. Protect from light and freezing.

Vitamin E (Tocopherol)

Injection, 50mg/ml in 20ml ampoule

Tablet, 100mg; 100mg (Chewable)

Capsule, 200mg, 400mg

Soft gelatin capsule, 400mg

Indications: Dietary supplement

Cautions: predisposition to thrombosis; increased risk of necrotising enterocolitis in neonate weighing less than 1.5 kg.

Interactions: warfarine, tipranavir

Contraindications: hypersensitivity to Vitamin E or any component of the formulation.

Side effects: diarrhoea and abdominal pain with doses more than 1 g daily

Dose and Administration: Recommended daily allowance (RDA): Premature infants \leq 3 months: 17mg

Infants (adequate intake; *RDA not established*): \leq 6 months: 4mg; 7 – 12 months: 6mg; Children: 1-3 years: 6mg; upper limit of intake should not exceed 200mg/day; 4-8 years: 7mg; upper limit of intake should not exceed 300 mg/day; 9-13 years: 11mg; upper limit of intake should not exceed 600 mg/day; 14-18 years: 15mg; upper limit of intake should not exceed 800 mg/day; Adult: 15mg; upper limit of intake should not exceed 1000 mg/day; Vitamine E deficiency: Child (with malabsorption syndrome): 1 unit/kg/day of water miscible vitamin E (to raise plasma tocopherol concentrations to the normal range within 2 months and to maintain normal plasma concentrations); Adult: 60-75 units/day; Prevention of Vitamin E deficiency: Adult: 30 units/day

Storage: protect from light

14.2. Vitamins, Combinations

Vitamin A + D

Capsule, 4,000 IU + 400IU; see notes above

14.2.1. Vitamin B complex preparations*

The most important B group vitamins appear to be thiamine (vitamin B1), riboflavin (vitamin B2), pyridoxine (vitamin B6), Pantothenic acid (vitamin B5), nicotinic acid/nicotinamide

(niacin, vitamin B3, niacinamide), cyanocobalamin (vitamin B12) and folic acid/folate.

Indications: supplement for use in the wasting syndrome in chronic renal failure, uremia, impaired metabolic functions of the kidney, dialysis; labeled for OTC use as a dietary supplement.

Dose and Administration: *Oral: Adult: Dietary supplement:* One tablet daily. *Renal patients:* One tablet or capsule daily between meals; takes after treatment if on dialysis.

14.2.2. Multivitamin preparations*

14.2.3. Multivitamin with minerals and/or extracts*

* Any combinations proven to be therapeutically effective can be acceptable

15. ANTIHISTAMINES and ANTIALLERGICS

15.1. Antihistamines

Antihistamines diminish or abolish the main actions of histamine in the body by competitive, reversible blockade of histamine receptor sites on tissues; they do not inactivate histamine or prevent its synthesis or release. Histamine H₁ receptors are responsible for vasodilatation, increased capillary permeability, flare and itch reactions in the skin, and to some extent for contractions of smooth muscle in the bronchi and gastro-intestinal tract.

Antihistamines are used for the symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis, and conjunctivitis. Antihistamines are generally considered to be ineffective in asthma. They should not be used to control transfusion reactions caused by ABO incompatibility.

Antihistamines are widely used, often with a decongestant, in compound preparations for the symptomatic treatment of coughs and the common cold.

Antihistamines are also used to control the pruritus associated with skin disorders such as atopic eczema. Some antihistamines, including promethazine, are used for their sedative effects; antihistamines such as cyproheptadine may be of value in the prophylaxis of migraine, particularly in children.

Side effects: The most common side effects of the older antihistamines is sedation, varying from slight drowsiness to deep sleep, and including lassitude, dizziness, and in coordination, sedative effects, when they occur, may diminish after a few days of treatment.

Paradoxical CNS stimulation may occur especially in children, with insomnia, nervousness, euphoria, irritability, tremors and rarely nightmares, hallucinations, and convulsions. In high doses CNS stimulation may be attributed to

antimuscarinic activity. Extrapyramidal symptoms may develop with phenothiazine derivatives and have been reported with some other antihistamines.

Older antihistamines possess antimuscarinic properties and may produce similar adverse effects to atropine. In addition headache, psychomotor impairment, gastro intestinal disturbances such as nausea, vomiting, diarrhoea, or epigastric pain have occurred with antihistamines.

Other side effects of antihistamines include palpitations and arrhythmias, hypotension, hypersensitivity reactions (including bronchospasm, angioedema, and anaphylaxis, rashes and photosensitivity reactions), extrapyramidal effects, dizziness, confusion, depression, sleep disturbances, tremor, convulsions, blood disorders, and liver dysfunction.

Caution and Contraindications: Antihistamines should not be given to premature infants or neonates: this group of patients has an increased susceptibility to antimuscarinic effects. Phenothiazine antihistamines should be avoided in young children because of the potential risk of central and obstructive apnoea and reduced arousal. Recommendations range from avoidance in children under 1 year of age to children under 2 years. Elderly patients are also more susceptible to many adverse effects of antihistamines, including antimuscarinic effects, sedation, and hypotension. Sedating antihistamines have significant antimuscarinic activity and they should therefore be used with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma, and pyloroduodenal obstruction. Caution may be required in epilepsy. Children and the elderly are more susceptible to side-effects. Many antihistamines should be avoided in acute porphyria but some are thought to be safe.

Hepatic impairment: Sedating antihistamines should be avoided in severe liver disease—increased risk of coma.**Pregnancy:** Most manufacturers of antihistamines advise avoiding their use during pregnancy; however, there is no evidence of teratogenicity except for hydroxyzine where toxicity has been reported with high doses in *animal* studies. The use of sedating antihistamines in the latter part of the third trimester may cause adverse effects in neonates such as irritability, paradoxical excitability, and tremor.

Breast-feeding: Most antihistamines are present in breast milk in varying amounts; although not known to be harmful; most manufacturers advise avoiding their use in mothers who are breast-feeding.

Many antihistamines may cause drowsiness; so patients should not drive or operate machinery. Because of their antimuscarinic properties antihistamines should be used with care in conditions such as closed angle glaucoma, urinary retention prostatic hyperplasia, or pyloroduodenal obstruction. Other adverse effects of antihistamines suggest caution in patients with epilepsy, severe cardiovascular disorders, or, for phenothiazines, in those with liver disorders.

Drug interactions: Antihistamines may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, opioid analgesias, anxiolytic sedatives, and neuroleptics. MAOIs may enhance the antimuscarinic effects of antihistamines, and antihistamines have an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and tricyclic antidepressants. Antihistamines could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.

Budesonide

Nasal Spray, 32mcg, 64mcg

Indications: management of symptoms of seasonal or perennial rhinitis.

Contraindications: hypersensitivity to Budesonide or any component of the formulation.

Dose and Administration: Nasal inhalation: Children ≥ 6 years and Adults: 64mcg/day as a single 32mcg spray in each nostril. Some patients who do not achieve adequate control may benefit from increased dosage. A reduced dosage may be effective after initial control is achieved. Maximum dose: Children < 12 years: 128mcg/day; Adult: 256mcg/day.

Storage: store with valve up at 20°C to 25°C and protect from light.

Cetirizine

Oral solution, 1mg/ml

Tablet, 5mg, 10mg

Indications: symptomatic relief of hypersensitivity reactions including rhinitis and chronic urticaria.

Cautions and Drug interactions; see notes above

Contraindications: see notes above; also pregnancy and breast-feeding

Side effects: see notes above, incidence of sedation and antimuscarinic effect is low

Dose and Administration: *Oral:* Adult and Child over 6 years: 10mg daily or 5mg twice daily; Child 2 - 6 years: *hay fever*, 5mg daily or 2.5mg twice daily.

Storage: store in a well - closed container at room temperature.

Chlorpheniramine Maleate

Syrup, 2mg/5ml

Tablet, 2mg, 4mg, 6mg

Indications: symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylactic reactions.

Cautions: see notes above; also pregnancy and breast-feeding.

Drug interactions, Contraindications: see notes above.

Side effects: see notes above; also exfoliative dermatitis and tinnitus reported; injections may cause transient hypotension or CNS stimulation and may be irritant.

Dose and Administration: *Oral:* Adult: 4 mg every 4-6 hours, maximum 24 mg daily; Child: *Less than 1 year old not recommended.* 1-2 years 1mg twice daily; 2-5 years 1mg every 4-6 hours, maximum 6 mg daily; 6-12 years 2 mg every 4-6 hours, maximum 12 mg daily.

Storage: at room temperature in a tight, light-resistant container.

Cyproheptadine Hydrochloride

Syrup, 2mg/5ml

Tablet, 4mg, 10mg

Indications: symptomatic relief of allergy such as hay fever, urticaria migraine.

Cautions, Drug interactions and Side effects; see notes above

Contraindications: see notes above; also breast-feeding

Dose and Administration: *Oral:Allergy:* Adult: 4 mg 3-4 times daily; usual range 4 - 20mg daily, max, 32 mg daily; Child under 2 years not recommended, 2-6 years, 2mg 2-3 times daily, maximum 16 mg daily. *Migraine:* 4 mg with a further 4 mg after 30 minutes if necessary; maintenance, 4 mg every 4 - 6 hours.

Desloratadine

Tablet, 5mg

Syrup, 0.5mg/ml

Indications: relief of nasal and non-nasal symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR); treatment of chronic idiopathic urticaria (CIU)

Contraindications: hypersensitivity to desloratadine, loratadine or any component of the formulation.

Cautions: pregnancy, breastfeeding

Side effects: headache, fatigue, somnolence, dizziness, xerostomia, nausea, dyspepsia, myalgia, pharyngitis.

Drug interactions: erythromycin, ketoconazole

Dose and Administration: Child 6-11 months: 1 mg once daily; 12 months to 5 years: 1.25mg once daily; 6-11 years: 2.5mg once daily; Children \geq 12 years and adult: 5mg once daily.

Storage: store at room temperature.

Dexchlorpheniramine Maleate

Tablet, 2mg, 4mg, 6mg

Indications: Treatment of perennial and seasonal allergic rhinitis; vasomotor rhinitis; allergic conjunctivitis due to inhalant allergens and foods; mild, uncomplicated allergic skin manifestations of urticaria and angioedema; amelioration of allergic reactions to blood or plasma; dermatographism; adjunctive anaphylactic therapy.

Cautions: Use in the children and elderly (approximately 60 years and above), narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, Bladder neck obstruction, History of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension.

Drug interactions: Alcohol, CNS depressants (hypnotics, sedatives, tranquilizers, etc.), MAOIs.

Contraindications: Treatment of lower respiratory tract symptoms; MAO inhibitor therapy; any component of the product or other antihistamines of similar chemical structure.

Antihistamines also are contraindicated in newborn or premature infants, and breast-feeding mothers.

Side effects: Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and the throat, hemolytic anemia, thrombocytopenia, agranulocytosis, hemolytic anemia, thrombocytopenia, agranulocytosis, sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesias, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions, epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation, urinary frequency, difficult urination, urinary retention, early menses, thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

Dose and Administration: Adults and Children 12 year of age and older: Oral tablets: 4 or 6 mg at bedtime orevery 8 to 10 hours.Children 6 to 12 yr of age: oraltablets: 4 mg/ day, preferably at bedtime.Children 2 to 5 yr of age: oralsyrup: 0.5 mg (¼ teaspoonful) every 4 to 6 hours.*Note: Advice patient to swallow tablets whole and not to crush, chew, or break the tablet.*

Dexchlorpheniramine Maleate+ Betamethasone

Tablet, 2mg+0.25mg

Indications: It is recommended in the treatment of difficult cases of respiratory, dermatologic and ocular allergies, as well as ocular inflammatory disorders, where adjunctive systemic corticosteroid therapy is indicated.

Cautions, Drug interactions and Side effects: See individual medicine

Contraindications: It is contraindicated in patients with systemic fungal infections, newborn and premature infants, and

patients receiving MAO inhibitor therapy and in those who have shown hypersensitivity to any component of the products or medicines of similar chemical structures.

Dose and Administration: The recommended initial dose for adults and children over 12 years is 1 to 2 tablets two times daily, after meals and at bedtime. The dose is not to exceed 8 tablets per day. *In younger children dosage should be adjusted according to the severity of the condition and the response of the patient, rather than by age or body weight.* Children 6 to 12 years the recommended dose are 1 tablet twice a day. If an additional daily dose is required, it should be taken preferable at bedtime. The dose is not to exceed 4 tablets a day.

Diphenhydramine Hydrochloride

Capsule, 25mg, 50mg

Elixir, 12.5mg/5ml

Injection, 50ml in 1ml ampoule

Indications: symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis and conjunctivitis and in pruritic skin disorders; other indications also for motion sickness and in control of parkinsonism and drug induced extrapyramidal disorders; short term management of insomnia.

Cautions, Drug interaction, Contraindications, Side effects; see notes above.

Does and Administration: *Oral:* Adult: 25 to 50 mg every four to six hours as needed. Child: Up to 6 years of age, 6.25 to 12.5 mg every four to six hours; 6 to 12 years of age, 12.5 to 25 mg every four to six hours, not to exceed 150mg per day. *Parenteral dosage form:* Adult: *IM or IV:* 10 to 50 mg. Child: *IM:* 1.25 mg per kg of body weight or 37.5 mg per square meter of body surface four times a day not to exceed 300 mg per day. *Note: premature and full-term neonates use is not recommended.*

Storage: at room temperature, in tight and light-resistant containers. Protect from freezing.

Fexofenadine

Tablet: 120mg, 180mg

Indications: management of allergic rhinitis and chronic idiopathic urticaria.

Cautions: sleep disorder, insomnia or paroniria, nausea, dyspepsia, back pain, throat irritation

Contraindications: other antihistamines or decongestants fruits (grape, orange, apple) juice.

Drug interaction: Antacids containing aluminum and magnesium

Storage: store at room temperature

Levocetizine

Tablet, 5mg

Indications, Cautions, Drug interactions, Side effects and storage; see under cetizine.

Dose and Administration:Adult: *Allergic rhinitis and Urticaria:Oral:* 5mg once daily (at night). Child: over 12 years, as for adults. Safety and efficacy not established in children under 12 years.

Loratadine

Syrup, 5mg/5ml

Tablet, 10mg

Indications: symptomatic relief of allergy such as hay fever, urticaria.

Cautions, Drug interactions: see notes above

Contraindications: see notes above, also pregnancy and breast-feeding

Side effects: see notes above; incidence of sedation and antimuscarinic effect is low.

Dose and Administrations:*Oral:* Adult and Child over 6 years: 10mg daily; Child 2 - 5 years: 5mg daily.

Storage: store in airtight containers, protect from light.

Loratadine+ Pseudoephedrine

Tablet, 5mg+120mg

Indications:temporarily relieves these symptoms due to hay fever or other upper respiratory allergies (runny nose, sneezing, itchy, watery eyes, itching of the nose or throat).Temporarily relieves nasal congestion due to the common cold, hay fever or other respiratory allergies. Reduces swelling of nasal passages.Temporarily relieves sinus congestion and pressure. Temporarily restores freer breathing through the nose

Cautions: heart disease, thyroid disease, high blood pressure, diabetes, trouble urinating due to an enlarged prostate gland, liver or kidney disease.

Drug interactions: Bromocriptine, ergot alkaloids,MAOIs, medicines for allergies, colds, breathing difficulties, procarbazine, stimulant medicines for attention disorders, weight loss, or to stay awake, digoxin, efavirenz, linezolid, medicines for depression like amitriptyline, nortriptyline, medicines for heart disease or blood pressure like atenolol, clonidine, doxazosin, mecamlamine, methyl dopa, reserpine, St. John's wort, theophylline, tizanidine, yohimbine.

Contraindications: if you have ever had an allergic reaction to this product or any of its ingredients. If you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug.

Side effects: Cough, dry mouth, headache, loss of appetite, nausea

Dose and Administration: Adults and children 12 years and over: 1 tablet daily with a full glass of water; not more than 1 tablet in 24 hours.

Note: do not divide, crush, chew or dissolve the tablet

Storage: Store at room temperature between and protect from moisture and light.

Pheniramine Aminosalicylate

Tablet, 50mg, 75mg

Indications: symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis and conjunctivitis, and in pruritic skin disorders; prevention and control of motion sickness.

Cautions, Drug interactions, Contraindications and Side effects; see notes above.

Dose and Administration: *Oral:* 25 to 50 mg two or three times a day

Storage: Protect from light.

Promethazine Hydrochloride

Elixir, 5 mg/5ml

Injection, 25 mg/ml in 1 ml and 2 ml ampoules

Suppository, 25 mg, 50 mg

Tablet, 10 mg, 25 mg

Indications: symptomatic relief of allergy such as hay fever, urticaria, premedication; emergency treatment of anaphylactic reactions; sedation; motion sickness

Cautions: see notes above; also pregnancy and breast-feeding.

Contraindications, Drug interactions; see notes above

Side effects: see notes above; intramuscular injection may be painful.

Dose and Administration: Adult:*Oral:* 5-12.5 mg three times a day before meals and at bed time, or 25 mg at bed time as needed.*IM or IV:* 25mg; may be repeated within two hour if necessary. *Rectal:* 25mg; may be repeated in two hours if necessary. Child (Children 2 years of age and over):*Oral:* 125mcg per kg of body weight every four to six hours, or 500 mcg (0.5mg) at bed time as needed, or 5 to 12.5mg three times a day or 25mg at bed time as needed.*IM:* 125mcg (0.125mg) per kg of body weight every four to six hours or 500 mcg (0.5mg) per kg of body weight at bed time as needed, or 6.25-12.5mg three times a day or 25mg at bed time as needed.

Storage: Tablet and Injectables - store at room temperature in a tight and light resistant container. Suppository - store between 2^oc and 8^oc in a tight, light resistant container.

Terfenadine

Syrup, 30 mg/5ml

Tablet, 60 mg

Indications: symptomatic relief of allergy such as allergic rhinitis, urticaria

Cautions: see notes above; also pregnancy and breast-feeding

Contraindications: see notes above; avoid grapefruit juice (may inhibit metabolism of terfenadine)

Drug interactions: see notes above

Side effects: see notes above; incidence of sedation and antimuscarinic effects low; erythema multiform and galactorrhoea reported; ventricular arrhythmias (including torsades de pointes) have followed excessive dosage.

Dose and Administration:*Allergic rhinitis and conjunctivitis:* Adult and child over 50 kg: *Oral:* 60 mg daily increased if

necessary to 120 mg daily in single or 2 divided doses. *Allergic skin disorders:* Adult and Child over 50 kg: *Oral:* 120 mg daily in single or 2 divided doses.

Triprolidine Hydrochlorides

Elixir, 2mg/5ml

Tablet, 2.5 mg, 10 mg

Indications: symptomatic relief of hypersensitivity reactions including urticaria, rhinitis and conjunctivitis and in pruritic skin disorders

Cautions, Drug interactions, Contraindications, Side effects; see notes above

Dose and Administration:Adult: 2.5 to 5 mg three times daily

Storage: in airtight containers, protect from light.

15.2. Medicines used in Allergic Emergencies

Anaphylactic shock and conditions such as angioedema are medical emergencies that can result in cardiovascular collapse and/or death. They require prompt treatment of possible laryngeal edema, bronchospasm or hypertension. Atopic individuals are particularly susceptible. Insect bites and certain foods including eggs, fish, peanuts and nuts are also a risk for sensitized persons. Therapeutic substances particularly associated with anaphylaxis include blood products, vaccines, hyposensitizing (allergen) preparations, antibiotics (especially penicillins), iron injections, heparin, and neuromuscular blocking medicines. Acetyl salicylic acid and other NSAIDs may cause bronchoconstriction in leukotriene-sensitive patients. In the case of medicine allergy, anaphylaxis is more likely to occur after parenteral administration. Resuscitation facilities should always be available when injecting a medicine associated with a risk of anaphylactic reactions.

First line treatment of a severe allergic reaction includes administering epinephrine (adrenaline), keeping the airway open (with assisted respiration if necessary) and restoring blood pressure. Epinephrine (adrenaline) should immediately be given by intramuscular injection to produce vasoconstriction and bronchodilation and injections should be repeated every 10 minutes until blood pressure and pulse have stabilized. If there is cardiovascular shock with inadequate circulation, epinephrine (adrenaline) must be given cautiously by slow intravenous injection of a dilute solution. An intravenous corticosteroid e.g. hydrocortisone (as sodium succinate) in a dose of 100 - 300 mg is of secondary value in the initial management of anaphylactic shock because the onset of action is delayed for several hours, but should be given to prevent further deterioration in severely affected patients.

Adrenaline (Epinephrine)

Injection, 0.1 % in 1 ml ampoule

Indications: emergency treatment of acute anaphylaxis; angioedema; cardiopulmonary resuscitation; see also section 2.5 and 3.2 for other uses of Adrenaline

Cautions: hyperthyroidism, diabetes mellitus, heart disease, hypertension, arrhythmias, cerebro-vascular disease, angle-closure glaucoma, second stage of labor, elderly patients.

Side effects: anxiety, tremor, tachycardia, arrhythmias, headache, cold extremities; also hypertension (risk of cerebral hemorrhage) and pulmonary edema (on excessive dosage or extreme sensitivity) nausea, vomiting, sweating, weakness, dizziness, and hyperglycemia also reported

Dose and Administrations: Caution: Different dilutions of epinephrine injection are used for different routes of administration. *IM or SC injections* use 1:1000 epinephrine

injection. *Slow IV injection* use 1:10 000 epinephrine injection. This route should be reserved for severely ill patients when there is doubt about the adequacy of circulation and absorption from the intramuscular site.

Hydrocortisone

Injection (sodium succinate), 50 mg/ml

Indications: used for life-threatening shock only after less toxic therapies have proven ineffective.

Cautions: pregnancy and in children; in patients with hypothyroidism or cirrhosis, psychosis, hypertension, congestive heart failure, diverticulitis, HIV, herpes simplex, oral herpetic lesions, renal function impairment or disease, tuberculosis, diabetes mellitus.

Drug interactions: alcohol, acetaminophen, non-steroidal anti-inflammatory drugs, parenteral amphoterecin B, atropine, oral antidiabetic agents or insulin, digitalis glycoside, diuretics, isoniazid.

Contraindications: known hypersensitivity to any of corticosteroids, recent surgery, osteoporosis, scleroderma, Cushing's syndrome.

Side effects: immunosuppression, muscle pain or weakness, delayed wound healing, edema, hypertension, cataract, diabetes mellitus, nausea, vomiting, anorexia, headache, vertigo, insomnia, restlessness, acne, impaired wound healing, increased sweating, hirsutism.

Dose and Administration: Adult: *for life threatening shock:* IV-massive dose 50 mg/kg initially and repeated in 4 hours and/or every 24 hours if needed, or 0.5-2g IV initially and repeated at 2 to 6 hours intervals as required.

Storage: at room temperature.

Promethazine Hydrochloride

Injection, 0.1% in 1ml ampoule,

1:1000 1mg/ml

Indications: Symptomatic relief of allergy such as hay fever and urticaria; emergency treatment of anaphylactic reactions.

Cautions: see section 1.4 under promethazine HCl; also avoid extravasation with IV injection; severe coronary artery disease, hepatic and renal dysfunction.

Contra-indications: see section 1.4 under promethazine HCl

Drugs interaction and Side-effects: See section 1.4 under promethazine HCl

Dose and administration: By deep intramuscular injection, 25–50 mg; max. 100 mg; child 5–10 years 6.25–12.5 mg. By slow intravenous injection in emergencies, 25–50 mg as a solution containing 2.5 mg/ml in water for injections; maximum 100 mg.

Storage: prior to dilution, store at room temperature; protect from light. Solutions in NS or D₅W are stable for 24 hours at room temperature.

16. OPHTHALMIC AGENTS

16.1. Antiglaucoma

16.1.1. Beta -adrenergic Antagonists

Topical application of a beta-blocker to the eye reduces intra-ocular pressure effectively in chronic simple glaucoma, probably by reducing the rate of production of aqueous humour. Administration by mouth also reduces intra-ocular pressure but this route is not used since side effects may be troublesome.

Betaxolol

Solution (eye drop), 0.5 %

Indications: treatment of chronic open-angle glaucoma and ocular hypertension.

Dose and Administration: Adult: Instill one drop twice daily.

Cautions: concurrent use of beta-blockers

Drug interactions: amiodarone, ciprofloxacin, ketoconazole, norfloxacin, chlorpromazine, fluoxetine, quinine, ritonavir, phenobarbital.

Contraindications: hypersensitivity to the drug, sinus bradycardia, overt cardiac failure, cardiogenic shock, pregnancy (2nd and 3rd trimester).

Side effects: bradycardia, breast abscess, cataracts, cystitis, diabetes melitus, gout, heart block, hypertension, hypothyroidism.

Storage: store at room temperature

Levobunolol

Solution (eye drop), 0.5%

Indications: treatment of chronic open-angle glaucoma or ocular hypertension

Dose and Administration: Adult: Instill one drop in the affected eye(s) 1-2times/day.

Storage: store at room temperature

Timolol Maleate

Solution (eye drop), 0.25%, 0.5 %

Indications: ocular hypertension; chronic open-angle glaucoma, aphakic glaucoma, some secondary glaucoma.

Cautions: older people; angle-closure glaucoma.

Drug interactions: acetazolamide, alcohol, epinephrine, lidocaine, nifedipine, prazosin, procainamide, quinidine, verapamil, thiopental, reserpine, metformin, hydralazine.

Contraindications: uncontrolled heart failure, bradycardia, heart block; asthma, obstructive airways disease.

Side effects: stinging, burning, pain, itching, erythema, transient dryness, allergic blepharitis, transient conjunctivitis, keratitis, decreased corneal sensitivity, diplopia, ptosis; systemic effects, particularly on the pulmonary, cardiovascular and central nervous systems, may follow absorption.

Dose and Administration: by *instillation* into the eye, 1 drop twice daily.

Storage: store at room temperature.

16.1.2. Adrenergic Agents

Most adrenergic agonists reduce the pressure in the eyes by reducing how much fluid (aqueous humor) the eyes produce. They also increase the amount of fluid that drains out of the eyes.

Apraclonidine HCL

Eye drops, 0.5%, 1%

Indications: prevention and treatment of post surgical intraocular pressure (IOP) elevation; short-term, adjunctive therapy in patients who require additional reduction of IOP.

Cautions: history of angina, severe coronary insufficiency, recent myocardial infarction, heart failure, cerebrovascular disease, vasovagal attack, chronic renal failure; depression; pregnancy and breast-feeding

Contraindications: history of severe or unstable and uncontrolled cardiovascular disease

Dose and Administration: 1%; control or prevention of postoperative elevation of intraocular pressure after anterior segment laser surgery, apply 1 drop 1 hour before laser procedure then 1 drop immediately after completion of procedure; CHILD not recommended

0.5%; short-term adjunctive treatment of chronic glaucoma in patients not adequately controlled by another drug (see note below), apply 1 drop 3 times daily usually for max. 1 month, CHILD not recommended

Side effects: dry mouth, taste disturbance; hyperaemia, ocular pruritus, discomfort and lacrimation (withdraw if ocular intolerance including oedema of lids and conjunctiva); headache, asthenia, dry nose; lid retraction, conjunctival blanching and mydriasis reported after peri-operative use; since absorption may follow topical application systemic effects (see Clonidine Hydrochloride, section 2.5) may occur. *Note: May not provide additional benefit if patient already using two drugs that suppress the production of aqueous humour.*

Brimonidine

Eye drop, 0.2%

Indications: lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Cautions: severe cardiovascular disease; cerebral or coronary insufficiency, Raynaud's syndrome, postural hypotension, depression, hepatic or renal impairment; pregnancy, breast-feeding; Driving

Dose and Administration: Children ≥ 2 years of age and Adults: Glaucoma: Instill 1 drop in affected eye (s) 3 times/day (approximately every 8 hours)

Side effects: ocular reactions including conjunctival hyperaemia, stinging, pruritus, allergy, and conjunctival folliculosis, visual disturbances, blepharitis, epiphora, corneal erosion, superficial punctuate keratitis, eye pain, discharge, dryness, and irritation, eyelid inflammation, oedema, pruritus conjunctivitis, photophobia; also, hypertension, headache, depression, dry mouth, fatigue, drowsiness; less commonly, taste disturbances, palpitation, dizziness, syncope, rhinitis, nasal dryness.

16.1.3. Parasympathomimetics (miotics)

They act by opening up the inefficient drainage channels in the trabecular meshwork resulting from contraction or spasm of the ciliary muscle.

Pilocarpine hydrochloride

Solution (eye drop), 1-4%

Eye ointment, 1-4%

Indications: chronic open-angle glaucoma; ocular hypertension; emergency treatment of acute angle-closure glaucoma; to antagonize effects of mydriasis and cycloplegia following surgery or ophthalmoscopic examination.

Cautions: retinal disease, conjunctival or corneal damage; monitor intra-ocular pressure in chronic open-angle glaucoma and in long term treatment; cardiac disease, hypertension, asthma, peptic ulceration, urinary - tract obstruction, Parkinson disease, stop treatment if symptoms of systemic toxicity develop.

Do not carry out skilled tasks, for example operating machinery or driving until vision is clear.

Drug interactions: beta-blockers, anticholinergic drugs (atropin).

Contraindications: acute iritis, acute uveitis, anterior uveitis, some forms of secondary glaucoma; acute inflammation of anterior segment; not advisable after angle closure surgery.

Side effects: eye pain, blurred vision, ciliary spasm, lacrimation, myopia, browache; conjunctival vascular congestion, superficial keratitis, vitreous hemorrhage and increased pupillary block have been reported; lens opacities have occurred following prolonged use; rarely systemic effects including hypertension, tachycardia, bronchial spasm, pulmonary oedema, salivation, sweating, nausea, vomiting, and diarrhea.

Dose and Administration:

Chronic open-angle glaucoma: instill into the eye, 1 drop 4 times daily. *Acute angle-closure glaucoma before surgery: by instillation into the eye, 1 drop every 10 minutes for 30-60 minutes, then 1 drop every 1-3 hours until intra-ocular pressure subsides.*

Storage: store at room temperature.

16.1.4. Carbonic Anhydrase Inhibitors

The carbonic anhydrase inhibitors, acetazolamide and dorzolamide, reduce intra-ocular pressure by reducing aqueous humour production. Systemic use also produces weak diuresis.

Acetazolamide

Tablet/capsule, 250 mg

Powder for injection, 125 mg, 500 mg in vial

Indications: reduction of intra-ocular pressure in open-angle glaucoma, secondary glaucoma, and preoperatively in angle-closure glaucoma

Cautions: elderly; pregnancy; breastfeeding; diabetes; pulmonary obstruction; monitor blood count and electrolytes if used for long periods.

May impair ability to perform skilled tasks, for example operating machinery, driving.

Drug interactions: quinidine, procainamide, mexiletine and TCAs, lithium, diuretics and potassium-depleting agents.

Contraindications: hypersensitivity to sulfonamides; chronic angle-closure glaucoma, hypokalaemia, hyponatraemia, hyperchloraemic acidosis; renal and hepatic impairment.

Side effects: nausea, vomiting, diarrhea, taste disturbance; loss of appetite, paraesthesia, flushing, headache, dizziness, fatigue, irritability, depression; thirst, polyuria.

Dose and Administration: Adult: *Primary open-angle: Oral:* 250 mg 1 - 4 times daily or 500 mg sustained release capsule twice daily. *Secondary, acute (closed angle): IV:* initially 250 - 500 mg repeated if necessary in 2 - 4 hours to a maximum of 1g/day.

Child: *Oral:* 8 - 30 mg/kg/day in 3 - 4 divided doses. *IV:* 20-40 mg/kg/24 hours divided every 6 hours, not to exceed 1g/day.

Storage: store at room temperature.

Brinzolamide

Eye Drops, 1 %, 2%

Indications: adjunct to beta-blockers or used alone in raised intra-ocular pressure; in ocular hypertension and in open-angle glaucoma.

Cautions: pregnancy, breast-feeding; closed angle glaucoma, Glaucoma caused by accumulation of pigment particles in the drainage channels of the eye (pigmentary glaucoma), Glaucoma

caused as a result of a disorder of part of the eyeball called the ciliary body (pseudoexfoliative glaucoma), Diabetes; Contact lens wearers; dry eyes; People with conditions that may affect the front layer of the eye (cornea).

Drug interactions: oral carbonic anhydrase inhibitors (e.g. Acetazolamide), other eye medications, clotrimazole, itraconazole, ketoconazole, eritronavir, high dose salicylates

Contra-indications: Known hypersensitivity to brinzolamide or any ingredient in the formulation; Allergy to medicines from the sulphonamide group; renal impairment; hyperchloraemic acidosis; Children under 18 years old.

Side-effects: Inflammation of the eyelids (blepharitis), dry eyes, Eye itching, blurred vision, eye stinging or burning, sensation of something being in the eye, discharge from the eye, headache, abnormal taste, dry mouth. Uncommon side effects: keratitis, conjunctivitis, eyelid swelling, redness or itching, corneal erosion, photophobia, bradycardia, atrial fibrillation, anaemia, sleepiness, diarrhoea, nausea, upper abdominal pain, flatulence, urticaria, Nasal inflammation or dryness, feeling weak or fatigued

Dose and administration: Adult:*ophthalmic*: For glaucoma or ocular hypertension, instill 1 drop of a 1% suspension in the affected eye(s) 3 times daily.

Dorzolamide

Drops, 2 %

Indications: topical treatment of ocular hypertension and open angle glaucoma

Cautions and Side effects: see acetazolamide

In dorzolamide, local effects include bitter taste, burning, stinging or itching of the eye, blurred vision, tearing, conjunctivitis, eyelid inflammation.

Dose and Administration: Adult:*Monotherapy*: Instill 1 drop 3 times daily. Adjunctive therapy with a topical beta-blocker: Instill 1 drop twice daily

Storage: store in light- resistant containers at room temperature

Methazolamide

Tablet, 25 mg, 50 mg, 100 mg

Indications: Adjunctive treatment of open-angle or secondary glaucoma; short-term therapy of narrow-angle glaucoma when delay of surgery is desired

Cautions, Drug interactions, Contraindications and Side effects: see under acetazolamide

Dose and Administration: Adult: *Oral:* 50-100mg 2-3 times/day.

16.1.5. Prostaglandins analogue

They reduce intra-ocular pressure in ocular hypertension or in open-angle glaucoma by increase uveoscleral outflow.

Bimatoprost

Eye drops, 0.003%

Indications: raised intra-ocular pressure in open-angle glaucoma; ocular hypertension

Cautions: Hepatic impairment, renal impairment

Contraindication: Hypersensitivity to bimatoprost or any component of the formulation

Dose and administration: *Open-angle glaucoma or ocular hypertension:* Instill 1 drop into affected eye(s) once daily in the evening; do not exceed once-daily dosing (may decrease IOP-lowering effect.)If used with other topical ophthalmic agents, separate administration by at least 5 minutes.

Side-effects: brown pigmentation particularly in those with mixed-color irides, blepharitis, ocular irritation and pain, conjunctival hyperaemia, transient punctuate epithelial erosion,

skin rash, dry eyes, headache, and photophobia; they may also cause, darkening, thickening and lengthening of eye lashes.

Storage: between 2 to 25⁰c

Latanoprost

Eye drops, 0.005%

Indications: reduction of elevated intraocular pressure in glaucoma and ocular hypertension in patients intolerant or unresponsive to other agents.

Dose and Administration: Adult: Instill 1 drop once daily.

Cautions, Side effects & Contraindication as Bimatoprost

Storage: store at room temperature.

Travoprost

Eye drops, 0.004%

Indications: for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

Cautions: See under bimatoprost

Contraindication: Hypersensitivity to travoprost or any component of the formulation; pregnancy

Dose and Administration: one drop in the affected eye(s) once daily in the evening.

Storage: between 2 to 25⁰c

16.1.6. Hyperosmotic agents

Hyperosmotic agents lower intraocular pressure by creating an osmotic gradient between the blood and the ocular fluids. Glycerol Mannitol and Isosorbide are useful short - term ocular hypotensive drugs, used in the pre-operative treatment of acute closed - angle glaucoma.

Glycerol

Oral solution, 50%, 70%

Indications: used for short-term reduction of vitreous volume and intraocular pressure before and after ophthalmic surgery, and as an adjunct in the management of acute glaucoma.

Cautions: caution in applying glycerol to the cornea.

Side effects: headache, nausea, vomiting, diarrhoea, thirst, dizziness, and mental confusion may occur less frequently. Cardiac arrhythmias have been reported.

Dose and Administration: Adult and Child: *Oral:* 1 to 1.8 g/kg given as a 50 % solution.

Storage: store in airtight container.

Isosorbide

Oral solution, 40% - 50%

Indications: short-term reduction of intraocular pressure, used prior to and after intraocular surgery, interrupt an acute attack of glaucoma.

Cautions: when giving repetitive doses particularly in patients with diseases associated with salt retention; breast feeding.

Contraindications: Well-established anuria, severe dehydration, frank or impending acute pulmonary edema, severe cardiac decompensation, hypersensitivity to any component of this preparation

Side effects: nausea, vomiting, headache, confusion, and disorientation may occur. Occurrences of syncope, gastric discomfort, lethargy, vertigo, thirst, dizziness, hiccups, hypernatremia, hyperosmolarity, irritability, rash and light-headedness have been reported.

Dose and Administration: initial dose of is 1.5 gm/kg body weight (equivalent to 1.5 mL /lb. of body weight). The onset of action is usually within 30 minutes while the maximum effect is expected at 1 to 1 1/2 hours. The useful dose range is 1 to 3 gm/kg body weight and the drug effect will persist up to 5 to 6 hours. Use two to four times a day as indicated.

Storage: Store at 15°-30°C

Mannitol

Injection, 20%, 25%

Indications: reduction of increased intraocular pressure.

Cautions: extravasation causes inflammation and thrombophlebitis.

Dose and Administration: Adult: IV: 1.5-2 g/kg administered as a 20 % or 25% solution over a period of 30-60 minutes.

16.1.7. Combinations

Dorzolamide HCL and timolol maleate in a fixed combination ophthalmic solution is used topically to reduce elevated IOP in patients with open angle glaucoma or ocular hypertension who have not responded adequately to a topical Beta-adrenergic blocking agent. Timolol may be used alone or in conjunction. When used in conjunction with these agents, timolol may have an additive IOP-lowering effect. If timolol is used to reduce IOP in patients with angle closure glaucoma, the drug should not be used alone but in combination with mitotic since timolol has little or no effect on pupil size.

Timolol + Bimatoprost

Eye drops, 0.5% + 0.003%

Indications: see note above

Cautions: Decreased kidney function, Decreased liver function, Closed angle glaucoma, neovascular glaucoma, inflammatory glaucoma, congenital glaucoma, Inflammatory conditions of the eye, disorders of the back of the eye (cornea), dry eyes, People with an artificial lens in (pseudophakia), People with no lens in the eye (aphakia), Closed or blocked retinal vein, diabetic retinopathy, hypoglycaemia, history of severe heart disease, Heart failure, A severe form of angina pectoris, not caused by

exertion (Prinzmetal's angina), Severe disorders of blood circulation, hypotension, hyperthyroidism, Psoriasis, Abnormal muscle weakness (myaesthesia gravis).

Drug Interactions: beta-blockers, eg atenolol; calcium channel blockers, e.g. nifedipine, verapamil, diltiazem, digoxin, medicines for abnormal heart rhythms (antiarrhythmics), e.g. amiodarone.

Contraindications: Hypersensitivity to the active substances or to any of the excipients, asthma or history of asthma, Severe chronic obstructive pulmonary disease (COPD), sinus bradycardia, Serious defect in the heart's electrical message pathways resulting in decreased function of the heart (2nd or 3rd degree heart block), Uncontrolled heart failure, cardiogenic shock, Pregnancy, Breastfeeding, children and adolescents under 18 years of age

Dose and Administration: The recommended dose is one drop in the affected eye(s) once daily, administered in the morning. If more than one topical ophthalmic product is to be used, the different products should be instilled at least 5 minutes apart.

Side effects: Red eye(s), Growth and darkening of eyelashes, Eye irritation including stinging, burning and itching, Sensation of something in the eye(s), Dry eye(s), Eye pain, photophobia, Corneal erosion, Redness, itching or swelling of the eyelid(s), Darkening of the eyelid(s) or skin around the eye(s), Inflammation of the eyelid(s), inflammation of the iris, Eye discharge, Headache, rhinitis, change in colour of the iris, cataracts, Dizziness, slowed or irregular heart rate, changes in blood pressure, shortness of breath, macular oedema

Storage: Store below 25°C. Do not use more than 30 days after opening. Keep bottle tightly closed when not in use.

Timolol + Brimonidine

Eye drops, 0.5% + 2%

Indications: see note above

Cautions, contraindications and side effects: see under Timolol + Bimatoprost

Drug interaction: monoamine oxidase inhibitor (MAOIs), eg the antidepressants phenelzine, tranylcypromine or isocarboxacid (these eye drops should not be started until 14 days after stopping treatment with an MAOI) tricyclic antidepressants, eg amitriptyline, imipramine related antidepressants, eg mianserin, medicines for high blood pressure, see also under Timolol + Bimatoprost

Dose and Administration: instill one drop twice a day (12 hours apart) into the affected eye(s)

Timolol + Brinzolamide

Eye drops, 0.5% + 1%, 2%

Indications: see notes above

Timolol + Dorzolamide

Eye drops, 0.5% + 2%

Indications: inhibitor of human carbonic anhydrase II.

Cautions: pregnancy; lactation

Contraindications: bronchial asthma; history of bronchial asthma; severe chronic obstructive pulmonary disease; sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure; cardiogenic shock; hypersensitivity to any components of the product.

Side effects: burning; stinging; redness of the eye(s); blurred vision; tearing or itching; bitter taste sensation after instillation; shortness of breath; upset stomach

Dose and Administration: instill one drop into the affected eye (s) 2 times daily

Storage: store between 15-25 °c. Discard after 30 days of opening.

Timolol + Latanoprost

Eye drops, 0.5% + 0.005%

Indications: reduction of intraocular pressure (IOP) in patients with open angle glaucoma and ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues.

Contraindications: lactation; also see under Timolol + Dorzolamide

Side effects: eye irritation; eye pain; increased iris pigmentation which may be permanent; bradycardia; arrhythmia; congestive heart failure; bronchospasm and allergic reactions

Dose and Administration: instill one drop into the affected eye (s) once daily.

Storage: store between 2-8 °c. Protect from light, once opened container may be stored at room temperature below 25°c

Timolol + Pilocarpine

Eye drops, 0.5% + 2% - 4%

Indications: see notes above

Timolol + Travoprost

Eye drops, 0.5% + 0.004%

Indications: treatment of open angle glaucoma and raised pressure in the eye (ocular hypertension)

Caution: Closed angle glaucoma; neovascular glaucoma; pigmentary glaucoma; pseudoexfoliative glaucoma; congenital glaucoma; Thyroid eye disease; conjunctivitis; pseudophakia; aphakia; People with a closed or blocked retinal vein; Diabetes; diabetic retinopathy; hypoglycaemia ; History of severe heart disease; Heart failure; A severe form of angina

pectoris, not caused by exertion (Prinzmetal's angina); People with poor blood circulation in the arteries of the extremities, eg hands and feet ; hypotension; hyperthyroidism ; History of allergies; Psoriasis; myaesthesia gravis.

Contraindications: Allergy to other beta-blocker medicines; asthma or history of asthma; severe COPD; allergic rhinitis; People with other breathing problems; sinus bradycardia; 2nd or 3rd degree heart block; Uncontrolled heart failure; cardiogenic shock; corneal dystrophy; Pregnancy; Breastfeeding; allergic to one or any of its ingredients

Side effects: see under Timolol + Latanoprost

Dose and Administration: Adults: instill one drop into the affected eye (s) once daily.

16.2. Mydriatics / Cycloplegics

Both dilation of the pupil (mydriasis) and paralysis of accommodation (cycloplegia) are produced by anticholinergic agents applied topically. These agents are not only used as aids in the examination of the eye and other ophthalmic procedures but also in the management of inflammatory conditions of the eye to treat or prevent the formation of adhesions between the lens and the iris. Atropine is useful in inflammatory conditions involving the iris and uveal tract, and for refraction in children up to about 6 years of age.

Cyclopentolate has a more rapid onset and shorter duration of action than atropine. Systemic toxicity is possible, especially in infants.

Homatropine has weaker effects than atropine; action is more rapid and less prolonged. It may be preferred to atropine for diagnostic purposes but is considered an inadequate cycloplegic in children.

Tropicamide displays action similar to atropine but with more rapid onset and shorter duration. It is considered an inadequate cycloplegic in children.

Hyoscine onset of action is more rapid, duration shorter and it is more toxic than atropine.

Phenylephrine is mainly a direct acting alpha-adrenoceptor stimulant. 2.5-10% solutions produce mydriasis with insignificant effect on accommodation. 10% solutions may have profound effects on the cardiovascular system and should be used with caution. It is mainly indicated for dilatation of the pupil for funduscopy, sometimes in combination with cyclopentolate or tropicamide.

Atropine Sulphate

Solution (eye drops), 0.5 %, 1 %

Eye ointment, 1%

Indication: iritis, uveitis; cycloplegic refraction procedures.

Cautions: may precipitate acute attack of angle-closure glaucoma, particularly in the elderly or long-sighted; risk of systemic effects with eye drops in infants under 3 months - eye ointment preferred. May cause sensitivity to light and blurred vision. Do not carry out skilled tasks, for example operating machinery or driving, until vision is clear.

Contraindication: angle-closure glaucoma.

Side effects: transient stinging and raised intra-ocular pressure; on prolonged administration, local irritation, hyperaemia, edema, conjunctivitis, contact dermatitis; systemic toxicity may occur in the very young and the elderly.

Dose and Administration: by instillation into the eye:

Cycloplegic refraction: **Adult:** 1 drop (1%) twice daily for 1-2 days before procedure or a single application of 1 drop (1%) 1 hour before procedure. **Child:** under 3 months (see cautions), 3

months-1 year (0.1%), 1-5 years (0.1-0.5%), over 5 years (0.5-1%), 1 drop twice daily for 1-3 days before procedure with a further dose given 1 hour before procedure. *Iritis, Uveitis*:**Adult**: instill 1 drop (0.5 or 1%) up to 4 times daily.**Child**: instill 1 drop (0.5 or 1%) up to 3 times daily.

Storage: store at room temperature.

Cyclopentolate Hydrochloride

Solution (eye drops), 0.5 %, 1 %, 2 %

Indications: diagnostic procedures requiring mydriasis and cycloplegia.

Cautions, Contraindications and Side effects; see under atropine sulphate.

Dose and Administration: Instill 1 drop followed by another drop in 5 minutes.

Storage:store at a temperature not exceeding 8°C in airtight containers.

Homatropine Hydrobromide

Solutions (eye drop), 1%, 2%

Indications: mydriasis and cycloplegia; uveitis.

Cautions: see notes above.

Contraindications: angle closure glaucoma.

Side effects: transient stinging and raised intraocular pressure, on prolonged administration, local irritation, hyperaemia, oedema and conjunctivitis may occur: contact dermatitis; systemic toxicity may occur in the very young and the elderly.

Dose and Administration:*For refraction*: instill one drop, repeated if necessary 5 or 10 minutes later.*Uveitis (treatment)*: one or two drops may be installed up to every 3 to 4 hours.

Storage: store in airtight containers. Protect from light.

Hyoscine (scopolamine) Hydrobromide

Solution (eye drop), 0.25 %

Indications: produce cycloplegia and mydriasis; treatment of iridocyclitis. **Cautions,** Drug interactions, **Contraindications,** Side effects and **Storage,**

Dose and Administration: *Refraction:* **Adult:** Instill 1-drop 1 hour before procedure. **Child:** Instill 1 drop twice daily for 2 days before procedure. *Iridocyclitis:* **Adult:** Instill 1 drop up to 4 times /day. **Child:** Instill 1 drop of 0.25 % to eye(s) up to 3 times/day.

Storage: store at room temperature

Phenylephrine

Solution (eye drop), 1 %, 2 %, 2.5 %, 5 %, 10 %.

Indications: mydriasis, diagnostic aid and ophthalmic decongestion

Cautions: The 10% solution should be used with caution in patients with diabetes, hypertension, cardiac disease, severe arteriosclerotic changes or thyrotoxicosis. (A dramatic increase in blood pressure may be produced). It should be avoided in the elderly and neonates.

Drug interactions: beta-blockers and other antihypertensive (reserpine), TCA, MAO inhibitors.

Contraindications: hypersensitivity, hypertension, and ventricular tachycardia.

Side effects: systemic effects include hypertension, subarachnoid haemorrhage, ventricular arrhythmias and myocardial infarction; also trembling, headache, agitation and sweating. Blood pressure changes are most pronounced in the elderly, neonates and patients with orthostatic hypotension. Hypersensitivity reactions such as allergic conjunctivitis or dermatitis may occur. Pigment granules may be released from

the iris into the aqueous; they disappear within 12-24 hours. Rebound miosis the day after administration and subsequent decreased sensitivity to the mydriatic effect may occur in the elderly.

Dose and Administration:Adult: 1 drop of a 10 % solution as required.

Storage: store at controlled room temperature; protect from light and excessive heat.

Tropicamide

Solution (eye drop), 0.5 %, 1 %

Indications: dilatation of the pupil to examine the fundus.

Cautions: patients aged over 60 years and hypermetropic (long-sighted) may precipitate acute angle-closure glaucoma; darkly pigmented iris, more resistant to papillary dilatation – exercise caution to avoid overdosage.

Avoid operating machinery or driving for 1 to 2 hours after mydriasis

Side effects: transient stinging and raised intraocular pressure; on prolonged administration - local irritation, hyperaemia, oedema and conjunctivitis.

Dose and Administration:Adult and **Child:***Ocular instillation:* 1 or 2 drops of 0.5%; 15 - 20 minutes before examination of eye.

Storage: store at room temperature.

Tropicamid + Phenylephrine

Solution (eye drop), 0.5 % + 1 %

Indication: can be used both for diagnostic and therapeutic purpose:*Therapeutic purpose:* Inflammatory conditions of the uveal tract. *Diagnostic purpose:* Retinal photography,

Refractive errors, Fundus examination/photography, Slit lamp examination

Pre-operative use: In order to undergo surgical procedure that requires the visualization of structures behind the iris, such as cataract extraction, vitrectomy and retinal detachment surgery, the pupil must be adequately dilated before surgery.

Cautions: Pregnancy, breast-feeding mother, children

Drug Interaction: MAO inhibitors, tricyclic antidepressants

Contraindications: Hypersensitivity to the medicine and any components of the formulation; narrow angles or narrow angles glaucoma.

Side effects: May cause elevated Intra ocular pressure, stinging on application, dryness of the mouth, blurred vision, tachycardia, photophobia with or without corneal staining, headache, parasympathetic stimulation and allergic reactions.

Dose and administration:*Therapeutic purpose:* 1-2 drops bid-qid or as required.*Diagnostic /Pre-operative purpose:* 1-2 drops in the eye(s) 15-30 minutes prior to the procedure.

Storage: Store in a cool dry place Protect from light.

16.3. Anti-infectives, Ophthalmic

16.3.1. Antibacterials

Acute bacterial infection of the external eye, including acute bacterial conjunctivitis, corneal ulceration, blepharitis, dacryocystitis, and discharging sockets are caused by the pathogens *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. Bacterial infections are generally treated topically with eye drops and eye ointments. Systemic administration is sometimes appropriate in blepharitis. Intra-ocular infection, a variety of routes (intra corneal, intra vitreal and systemic) may be used.

Chloramphenicol has a broad spectrum of activity and is the drug of choice for superficial eye infections.

Gentamicin is a broad-spectrum bactericidal aminoglycoside antibiotic with particular activity against *Pseudomonas aeruginosa*, *Neisseria gonorrhoea* and other bacteria that may be implicated in blepharitis or conjunctivitis.

Tetracycline is a broad spectrum antibiotic with activity against many Gram- positive and Gram-negative bacteria including *N. gonorrhoea*. Ophthalmic tetracycline is used in blepharitis, conjunctivitis, and keratitis produced by susceptible bacteria. Many antibacterial preparations also incorporate a corticosteroid but such mixtures should **not** be used unless a patient is under close specialist supervision. In particular they should not be prescribed for undiagnosed 'red eye' which is sometimes caused by the herpes simplex virus and may be difficult to diagnose.

Administration: Frequency of application depends on the severity of the infection and the potential for irreversible ocular damage; antibacterial eye preparations are usually administered as follows: *Eye drops*, apply 1 drop at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing; *Eye ointment*, apply *either* at night (if eye drops used during the day) *or* 3–4 times daily (if eye ointment used alone).

Chloramphenicol

Eye ointment, 1 %, 5 %

Solution (eye drop), 0.4 %, 0.5 %, 1 %, 5 %

Indications: topical treatment of superficial ocular infections involving the conjunctiva and/or cornea caused by susceptible organisms.

Contraindications: previous allergy or toxic reaction to chloramphenicol

Side effects: hypersensitivity

Dose and Administration: *Ointment topical:* a thin strip (approximately 1cm) to the conjunctiva every three hours; *Eye drops,* 1 drop every one to four hours

Storage: at room temperature in a tight container, protect from freezing.

Ciprofloxacin

Eye ointment, 0.3 %

Solution (eye drop), 0.3%

Indication: superficial bacterial infections, see notes above; corneal ulcers and prophylaxis during otic surgeries such as mastoid surgery

Cautions: if irritation persists or increases, discontinue. Do not touch the dropper, since this may contaminate solution.

Contraindications: Hypersensitivity to quinolone group of antibacterial or any of the Components of the formulation

Dose and administration: *Superficial bacterial infection:* **Adult** and **Child** apply eye drops 4 times daily; in severe infection apply every 2 hours during waking hours for 2 days, then 4 times daily; maximum duration of treatment 21 days. **Adult** and **Child** over 1 year, apply 1.25 cm eye ointment 3 times daily for 2 days, then twice daily for 5 days. *Corneal ulcer:* **Adult** and **Child** apply eye drops throughout day and night, day 1 apply every 15 minutes for 6 hours then every 30 minutes, day 2 apply every hour, days 3–14 apply every 4 hours; maximum duration of treatment 21 days. **Adult** and **Child** over 1 year, apply eye ointment throughout day and night; apply 1.25 cm ointment every 1–2 hours for 2 days, then every 4 hours for next 12 days.

Side effects: local burning and itching; lid margin crusting; hyperaemia; taste disturbances; corneal staining, keratitis, lid

oedema, lacrimation, photophobia, corneal infiltrates; nausea and visual disturbances.

Storage: Store at room temperature

Erythromycin

Eye ointment, 0.5 %

Solution (eye drop), 1%

Indications: topical prophylaxis of neonatal conjunctivitis caused by *Chlamydia trachomatis*. Topical treatment of superficial ocular infections of the conjunctiva and/or cornea caused by susceptible organisms.

Cautions: intolerance to erythromycin.

Side effects: eye irritation.

Dose and Administration: ointment, a thin strip (approximately 1cm six times a day. *Neonatal conjunctivitis/Ophthalmia neonatorum: topical:* to each conjunctiva, a thin strip (approximately 0.5 to 1 cm) of ointment as a single dose following cesarean or vaginal delivery.

Storage: at room temperature. Protect from freezing.

Gentamicin

Solution (eye drop), 0.3 %

Indications: blepharitis; bacterial conjunctivitis; systemic infections.

Cautions: discontinue if purulent discharge; inflammation or exacerbation of pain.

Contraindications: hypersensitivity to aminoglycoside group of antibiotics

Side effects: burning, stinging, itching, dermatitis.

Dose and Administration: *Mild to moderate infection: by instillation into the eye: Adult and Child:* 1 drop every 2 hours, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete. *Severe infection: by*

installation in to the eye: **Adult and Child:** 1 drop every hour, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete.

Moxifloxacin

Solution (eye drop), 0.3%, 5ml

Indication: bacterial conjunctivitis.

Side effects: conjunctivitis, dry eye, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, tearing, visual acuity decreased.

Dose and Administration: Children ≥ 1 year and Adult: Instill 1 drop into affected eye (s) 3 times per day for 7 days.

Storage: store at room temperature

Neomycin Sulphate

Eye ointment 0.5 %, 2 %

Indications: treatment of superficial ocular infections, caused by susceptible organisms

Cautions: sensitive to neomycin.

Side effects: burning or stinging, blurred vision hypersensitivity to neomycin

Dose and Administration: a thin strip (approximately 1cm) every eight to twenty-four hours.

Storage: at room temperature, protect from freezing

Ofloxacin

Solution (eye drop), 0.3%, 5ml

Indications: to treat bacterial infections of the eye

Cautions: pregnancy; breast-feeding

Drug interactions: see quinolone under section 7.1.2

Contraindications: History of hypersensitivity to Ofloxacin, to other quinolone, or to any of the components in this medication

16. Ophthalmic Agents

Side effects: dizziness; nausea; blurred vision; burning; discomfort in the eye, edema, eye pain; redness; stinging; tearing. Systemic effects

Dose and administration: Adults and children > 1 year:
conjunctivitis: instill 1-2 drops in affected eye(s) every 2-4 hours for the first 2 days, then use 4 times/day for additional 5 days.

Corneal ulcer: 1-2 drops every 30 minutes while awake and every 4-6 hours after retiring for the first 2 days; beginning on day 3, instill 1-2 drops every hour while awake for 4-6 additional days; thereafter, 1-2 drops 4 times/day until clinical cure

Storage: store at room temperature

Oxytetracycline Hydrochloride

Eye ointment, 0.5 %

Indications: superficial infections of the eye caused by susceptible bacteria.

Cautions: sensitive to tetracyclines.

Side effect: burning, stinging, increased lacrimation, foreign body sensation.

Dose and Administration: Adult: *topical, in the lower conjunctival sac of the infected eye:* a thin amount of ophthalmic ointment every 6-12 hours daily.

Storage: at room temperature in a collapsible ophthalmic ointment tube, protect from freezing.

Polymyxin B + Bacitracin

Eye ointment, polymyxin B 100,000 units and Bacitracin 500,000 units

Indications: treatment of superficial infections caused by susceptible organisms.

Dose and Administration: Adult and Child: Instil $\frac{1}{2}$ ribbon in the affected eye(s) every 3 - 4 hours for acute infections or 2 -3 times/day for mild to moderate infections for 7 - 10 days.

Rifamycin

Solution (eye drop), 1%

Rifamycin is an antibacterial that has been used in the treatment of infections caused by susceptible organisms such as staphylococci. It is given by local instillation and topical application.

Tetracycline

Eye ointment, 1 %

Solution (eye drop), 1 %

Indications: for the treatment of superficial bacterial infections of the eye (*Purulent conjunctivitis*), trachoma, and for the prophylaxis of gonococcal and nongonococcal ophthalmia neonatorum.

Dose and Administration: *Topical*, to the conjunctiva.

Purulent Conjunctivitis: **Adult and Child:** Apply a thin strip (approximately 1cm) of ointment onto the infected eye every 6 hours daily for 5 days. *Trachoma:* **Adult and Child:** Apply a thin strip of ointment onto each eye twice daily for a minimum of 6 weeks. *Prophylaxis of gonococcal and nongonococcal ophthalmia neonatorum:* Apply a thin strip of ointment onto each of neonates shortly (no later than 1 hour) after delivery.

Storage: at room temperature.

Tobramycin

Solution (eye drop), 0.3 %

Indications: topically used to treat superficial ophthalmic infections caused by susceptible bacteria.

Cautions, Contraindications and Drug interactions; see under section 7.1.2.

Side effects: conjunctival erythema, lid itching, lid swelling.

Dose and Administration: Adult and Child ≥ 2 months: Instill 1 to 2 drops of solution every 4 hours; for severe infections instill 2 drops every 30 - 60 minutes initially, then reduce to less frequent intervals.

Storage: store at 2-30°C.

16.3.2. Antivirals

Herpes simplex virus may cause serious sight-threatening eye infections. Ophthalmologists should treat these conditions. Acyclovir is the drug of choice for all herpes simplex eye infections. It is highly active in vitro against herpes simplex (HSV) types II and I. Penetration through the cornea is sufficient to provide antiviral concentrations in the aqueous humour. With usual doses, clinically significant amounts are not absorbed systemically.

Acyclovir

Eye ointment, 3 %

Indications: used for herpes simplex keratitis.

Side effects: transient stinging which occasionally may follow immediately after application. Acyclovir has caused superficial punctuate keratopathy, but this has healed without apparent sequelae.

Dose and Administration: The ointment should be placed inside the lower conjunctival sac 5 times a day, at about 4 hourly intervals. Treatment should be continued for 14 days, or at least 3 days after healing is complete, whichever is shorter.

Storage: store at room temperature

Gancyclovir

Injection, 500mg in ampoule

Indications: sight-threatening cytomegalovirus infections in immunocompromised patients only; prevention of cytomegalovirus disease during immunosuppressive therapy following organ transplantation; local treatment of CMV retinitis

Cautions: Close monitoring of full blood count (severe deterioration may require correction and possibly treatment interruption); history of cytopenia; potential carcinogen and teratogen; radiotherapy; ensure adequate hydration during intravenous administration; vesicant—infuse into vein with adequate flow preferably using plastic cannula; children (possible risk of long-term carcinogenic or reproductive toxicity);

Drug interactions: didanosine, mycophenolate, probenecid, zidovudine.

Contra indications: Hypersensitivity to ganciclovir, ganciclovir, aciclovir, or valaciclovir; abnormally low haemoglobin, neutrophil, or platelet counts, pregnancy, preast-feeding, renal impairment

Dose and Administration: Adult: By *intravenous infusion*, initially (induction) 5 mg/kg every 12 hours for 14–21 days for treatment or for 7–14 days for prevention; maintenance (for patients at risk of relapse of retinitis) 6 mg/kg daily on 5 days per week *or* 5 mg/kg daily until adequate recovery of immunity; if retinitis progresses initial induction treatment may be repeated;

Child 1month- 18 years : initially (induction) 5mg/kg every 12 hours for 14-25 days, *for treatment* or for 7-14 days for *prevention*; maintainance (for patients at risk of relapse of retinitis), 6mg/kg daily on 5 days per week or 5mg/kg daily

until adequate recovery of immunity; if retinitis progresses initial induction treatment may be repeated.

Side effects: GI upset, taste disturbance, hepatic dysfunction; dyspnoea, chest pain, cough; headache, insomnia, convulsions, dizziness, peripheral neuropathy, depression, anxiety, confusion, abnormal thinking, fatigue, weight loss, anorexia; infection, pyrexia, night sweats; anaemia, leucopenia, thrombocytopenia, pancytopenia, renal impairment; myalgia, arthralgia; macular oedema, retinal detachment, vitreous floaters, eye pain; ear pain; dermatitis, pruritus; injection-site reactions;

Idoxuridine

Solution (eye drop), 0.1 %

Eye ointment, 0.5 %

Indications: keratitis or keratoconjunctivities caused by herpes simplex.

Cautions: do not exceed frequency or duration of treatment, discontinue if no relief within 7 days; concurrent use of a corticosteroid.

Contraindications: pregnancy; concurrent use of an eye preparation containing boric acid.

Side effects: burning, itching, irritation, pain, conjunctivities, oedema, inflammation, photophobia, pruritus, and rarely allergic reactions.

Dose and Administration: *Herpes simplex keratitis:* by *instillation* into the eye, 1 drop every hour during daytime and every 2 hours at night-time, reducing frequency as infection is controlled to 1 drop every 2 hours during daytime and every 4 hours at night-time, then continue for 3 - 5 days after healing is complete; maximum length of treatment 21 days; alternatively, by application to the eye, 1 application of ointment every 4

hours during daytime and once at night time (5 applications), then continue for 3 - 5 days after healing is complete; maximum length of treatment 21 days.

Storage: store at room temperature.

Trifluridine

Solution (eye drop), 1 %

Indications: treatment of herpetic keratitis and infections with stromal involvement.

Cautions: hypersensitivity to trifluridine.

Side effects: transient irritation, itching and oedema; allergic reactions.

Dose and Administration: Instill 1 drop 2 hourly upto a maximum of 9 times daily, until complete reepithelialisation has occurred; then reduce to 4 hourly, continued for a few days.

Storage: store between 2 °C and 8°C.

Vidarabine

Eye ointment, 3%

Solution (eye drop), 3 %, 5ml

Indications: treatment of herpes simplex keratitis and keratoconjunctivitis.

Side effects: irritation and pain of the eye; superficial punctate keratitis, photophobia, lacrimation, and occlusion of the lachrymal duct.

Dose and Administration: applied 5 times daily every 3 hours until corneal re-epithelialisation has occurred, then twice daily for a further 7 days to prevent recurrence.

Storage: store in airtight containers.

16.3.3. Antifungals

Fungal infections of the cornea can cause serious sight-threatening disease. Fungal ulcers are often associated with excessive and prolonged topical corticosteroid use or eye injuries involving vegetative material. The ulcers are indolent and require specialist management. Topical preparations may need to be made by a pharmacist, e.g. miconazole, amphotericin B. Natamycin is topical ophthalmic preparation. Effective concentrations are produced within the corneal stroma, but not in intraocular fluid. Systemic absorption is not expected.

Econazole

Solution (eye drop), 1 %

It has a broad spectrum of activity against *Cryptococcus*, *Aspergillus*, *Curvularia*, *Candida*, *Microsporum*, *Paecilomyces*, and *Trichophyton*. For topical use, a 1% solution in arachis oil or a 10 mg/mL commercial solution (Monistat IV) is well tolerated. Topical use of miconazole may cause surface toxicity after prolonged use

Natamycin

Solution (eye drop), 5 %

Indications: conjunctivitis and fungal blepharitis, fungal keratitis.

Cautions: concurrent application of natamycin and a topical corticosteroid. **Contraindications:** hypersensitivity to the drug.

Side effects: eye irritation, redness, or swelling.

Dose and Administration: Adult: *Fungal keratitis*: Instill 1 drop 1 - 2 hourly, reduced to 6 - 8 times daily after 3 - 4 days, and generally continued for 14 - 21 days. *Fungal blepharitis and Conjunctivitis*: Instillation 4 - 6 times daily may be sufficient.

Note: shake well before use.

Storage: store at room temperature.

16.4. Anti-inflammatories

Non steroidal anti-inflammatory drugs

NSAIDs inhibit prostaglandin synthesis, thereby reducing prostaglandin-mediated intraocular inflammation. NSAIDs eye drops use for the treatment of seasonal allergic conjunctivitis, cystoid and other types of macular oedema and for prophylaxis and treatment of inflammation of the eye following surgery or laser treatment.

Bromofenac

Solution (eye drop), 1 %

Indications: treatment of postoperative inflammation

Cautions: should be used with caution in patients with underlying bleeding tendencies or in those receiving drugs known to prolong bleeding time.

Drug interactions: topical corticosteroids

Contraindications: known hypersensitivity to bromfenac sodium or any ingredient in the formulation

Side effects transient burning or stinging, punctate corneal epithelial erosion

Dose and administration: Adults: instill 1 drop twice daily beginning 24hrs after surgery and continuing for 2 weeks postoperatively.

Storage: store at room temperature

Cyclosporine

Solution (eye drop), 0.05%, 0.2%, 1%, 2%

Indications: Cyclosporine ophthalmic is used to increase tear production in people with dry eye disease.

Contraindications: known hypersensitivity to Cyclosporine

Side effects: burning, itching, stinging, redness, overflow of tears, red eyes, and eye discharge

Dose and administration: instill 1 drop twice a day.

Storage: Store at room temperature

Diclofenac sodium

Eye drop, 0.1%

Indications: for postoperative prophylaxis and treatment of ocular inflammation; for temporary relief of pain and photophobia in corneal refractive surgery; to prevent and treat cystoid macular oedema

Cautions: pregnancy

Contraindications: known hypersensitivity to any components of the product

Side effects: burning and stinging; corneal deposits; corneal edema; lacrimation

Dose and administration: *Cataract Surgery:* apply One drop six hourly beginning 24 hours after surgery for the first 2 weeks of the postoperative period. *Corneal Refractive Surgery:* apply one drop an hour prior to corneal refractive surgery then 15 minutes after the surgery, and then apply one drop 6 hourly for 3 days.

Storage: Store between 15°C to 25°C

Flurbiprofen

Solution (eye drop), 0.03%

Indications: is used primarily to control intra operative miosis during anterior segment surgery, cystoid macular edema, photophobia.

Cautions: epithelial herpes simplex keratitis, hemophilia or other bleeding problems.

Drug interactions: acetylcholine chloride; anticoagulant, coumarin or heparin; epinephrine (ophthalmic).

Contraindications: allergic reaction to **Flurbiprofen** or other systemic or ophthalmic NSAIDs.

Side effects: keratitis, elevated intraocular pressure, corneal edema, chemosis, bleeding in eye; redness in eye.

Dose and Administration: *Miosis inhibition* 1 drop every thirty minutes, beginning two hours prior to surgery. For postoperative treatment of ocular inflammation: 1 drop every four hours for 1-3 weeks

Storage: store at room temperature.

Ketorolac

Solution (eye drop), 0.4%, 0.5%

Indications: prophylaxis and treatment of inflammation following ocular surgery; mild-moderate allergic conjunctivitis

Contraindications: hypersensitivity to ketorolac or other systemic or ophthalmic NSAIDs

Cautions: Patients with known bleeding tendencies or those receiving anticoagulants; pediatric patients <3 years of age

Side effects: transient burning/stinging, headache, conjunctival hyperemia, corneal infiltrates, iritis, ocular edema, superficial keratitis.

Dose and Administration: Child ≥ 3 years and Adults: Allergic conjunctivitis (0.5%): Instill 1 drop six hourly. *Inflammation following cataract extraction (0.5%):* Instill 1 drop six hourly for 2 weeks; beginning 24 hours after surgery. *Pain following corneal refractive surgery (0.4%):* Instill 1 drop six hourly up to 4 days.

Storage: store at room temperature

Suprofen

Solution (eye drop), 1%

16. Ophthalmic Agents

Indications: inhibition of intraoperative miosis.

Cautions: Patients with known bleeding tendencies

Contraindication: epithelial herpes simplex keratitis (dendritic keratitis) and hypersensitive to any component of the medication.

Side effects: burning and stinging, itching and redness; iritis, pain, chemosis, photophobia, irritation, and punctate epithelial staining.

Dose and Administration: instill 1 drop at 3, 2 and 1 hour(s) prior to surgery to prevent intra operative miosis; or Instill 1 drop every 4 hours since the day before surgery.

Storage: Store at room temperature

Anti-histamines

Drugs under this category attach to histamine receptors, preventing the chemical histamine from triggering symptoms of an allergic reaction.

Ketotifen

Solution (eye drop), 0.025%

Indications: seasonal allergic conjunctivitis in adults and children aged three years and older

Cautions: pregnancy

Contraindications: Children under three years of age; known sensitivity or allergy to any ingredient in the formulation

Side effects: Pain and irritation of the eyes; punctate corneal epithelial erosion; dry eyes; photophobia; eyelid disorders;

Dose and Administration: instill one drop, every 8 to 12 hours

Levocabastine

Solution (eye drop), 0.05%

Indications: treatment of mild-moderate allergic conjunctivitis

Caution: pregnancy

Side effect headache, Bad taste, blurred vision, burning or stinging, corneal infiltrates, dry eye, rhinitis, and sinusitis
Dose and Administration: children \geq 12 years and Adults: instill one drop six hourly for 2 weeks.

Antihistamine and Vasoconstrictor

The body produces antibodies to "fight" specific antigens. Antibodies attach to mast cells to release histamine thereby allergic reaction will trigger. Ocular decongestants constrict the superficial conjunctival vessels and somewhat reduce congestion and redness. The transient stinging of the drop may relieve some of the itching. Ocular decongestant/ antihistamine combinations work better than the vasoconstrictors. Unfortunately, these drops do not provide relief for all allergy sufferers with ocular symptoms because not every allergic response is due to histamine.

Antazoline + Naphazoline

Solution (eye drop), 0.025% + 0.5%

Indications: treatment of temporary relief of the signs and symptoms of allergic conjunctivitis

Cautions: pregnancy; breast-feeding

Side effects: eye pain, headache, redness/itching/swelling in or around the eyes

Dose and Administration: *instill* 1 drop every 3-4 hourly

Storage: store at room temperature

Oxymetazoline Hydrochloride

Solution (eye drop), 0.025%, 0.05%

Oxymetazoline Hydrochloride is a direct-acting sympathomimetic agent, which has a vasoconstrictor effect on mucosal blood vessels when applied topically.

Indications: treatment of Short-term relief for mild allergic symptoms.

Cautions: avoid Prolonged or excessive use that may cause rebound congestion and drug-induced rhinitis.

Side effects: occasionally cause local stinging or burning, sneezing, and dryness of the mouth and throat.

Dose and Administration*instill* 1 drop every 4-6 hourly

Tetrahydrozoline Hydrochloride

Solution (eye drop), 0.05 %

Tetrahydrozoline is a sympathomimetic agent with alpha-adrenergic activity.

Indications: treatment of Short-term relief for mild allergic symptoms

Cautions: avoid Prolonged or excessive use

Side effects: occasionally cause local stinging or burning, sneezing, and dryness of the mouth and throat.

Dose and Administration*instill* 1 drop every 4-6 hourly

Mast cell Stabilisers

Mast-cell stabilizers prevent calcium influx across mast-cell membranes, thereby preventing mast-cell degranulation and mediator release. They take days to weeks to reach their peak efficacy. They do not provide immediate relief from allergic symptoms. Cromolyn sodium (Crolom) inhibits neutrophil, eosinophil, and monocyte activation in vitro. Traditional mast-cell stabilizers such as cromolyn sodium, lodoxamide (Alomide), and pemirolast (Alamast) prevent mast-cell degranulation but They are used for allergic, vernal, and atopic conjunctivitis.

Lodoxamide Tromethamine

Solution (eye drop), 0.1%

Indications: for the treatment of vernal keratoconjunctivitis, vernal conjunctivitis, and vernal keratitis

Contraindications: hypersensitivity to any component of the formulation

Side effects burning, stinging, and discomfort upon instillation

Dose and Administration: instill 1 drop six hourly for up to 3 months.

Storage: store at room temperature

Nedocromil Sodium

Solution (eye drop), 2%

It has a mast-cell stabilizing effect as well as H1-antagonism

Indications: for the treatment of *Allergic Conjunctivitis*, vernal conjunctivitis, vernal keratitis and vernal keratoconjunctivitis,

Cautions: breast-feeding

Contraindications: hypersensitivity to any component of the formulation, Children >3 years

Side effects: stinging or burning of the eyes; blurred vision; increased eye redness or itching; Odd taste in the mouth; nasal congestion

Dose and Administration: instill one drop twice daily.

Storage: store at room temperature

Sodium cromoglycate

Solution (eye drop), 2% and 4%

Indications: for the treatment of allergic, vernal, and atopic conjunctivitis

Cautions: breast-feeding

Contraindications: hypersensitivity to any component of the formulation

Side effects: transient burning and stinging; dryness around the eye; edema; watery eyes; dyspnea

Dose and Administration: children > 4 years and Adults: instill one drop six hourly for up to 3 months

Storage store at room temperature

Pemirolast potassium

Solution (eye drop), 0.1%

Indications: for the treatment of allergic, vernal, and atopic conjunctivitis

Cautions: pregnancy

Contraindications: hypersensitivity to any component of the formulation

Side effects: transient burning and stinging; dryness around the eye; watery eyes; dyspnea

Dose and Administration: children > 3 years and Adults: apply one drop four times/ day for up to 3 months

Storage store at room temperature

Combined Antihistamine and mast cell stabilizer

These agents distinguish by their ability to block as well as to stabilize activated mast cells and prevent the release of cytokines

Olopatadine

Solution (eye drop), 0.1%

Indications: for the treatment of allergic, vernal, and atopic conjunctivitis

Cautions: pregnancy; children <3 years of age; do not wear contact lenses if eyes are red

Contraindications: hypersensitivity to Olopatadine hydrochloride or any component of the formulation

Side effects: headache; cold syndrome; nausea; taste perversion; weakness; blurred vision; burning; stinging; dry

eye; foreign body sensation; hyperemia; keratitis; eyelid edema; rhinitis; sinusitis; pharyngitis

Dose and Administration: Adults and children ≥ 3 years: instill 1 drop twice daily

Storage: store at room temperature

Steroids: Corticosteroids

Corticosteroids are very effective at treating ocular allergies and many ocular disorders but they have a more dangerous side-effect profile. They are also prone for abuse. Complications of corticosteroid therapy can be seen with any mode of administration. Therefore, these agents should be used only when the benefits of therapy outweigh the risks of the medications themselves. The dose and duration of therapy must individualize. It is generally preferable to begin therapy with a high dose of corticosteroids (topical or systemic) and taper the dose as the inflammation subsides. If corticosteroid therapy needs for longer than 2–3 weeks, the dosage should taper before discontinuation.

Indications: for the treatment of corticosteroid-responsive allergic conjunctivitis, active inflammation of conjunctiva, cornea, and anterior segment of the globe, prevention or treatment of complications such as treat cystoid macular oedema, therapy for corneal allograft rejection, explosive onset of severe noninfectious posterior uveitis, panuveitis or optic neuritis

Cautions: Long-term use of corticosteroid need close follow-up for glaucoma (open-angle glaucoma) and for other major complications. Corticosteroid therapies, longer than 2–3 weeks, should be tapered before discontinuation. All corticosteroids may exacerbate bacterial, viral, mycobacterial and fungal

diseases of the eye and should be used with caution in these settings.

Contraindications : Patients with ocular fungal diseases ; herpes simplex keratitis; tuberculosis; viral disease; cataracts, open angle glaucoma; diabetes mellitus; hypertension; peptic ulcer or gastro esophageal reflux disease; patients who are immunocompromised (from acquired or congenital causes) and patients with psychiatric conditions are at high risk for corticosteroid-induced exacerbations of their systemic conditions. In these patients, Corticosteroids treatment should be avoid or the last choice.

Side effects: Glaucoma; cataract formation; secondary ocular infections or exacerbations of ocular infections are the most serious ocular side effects. Other ocular side effects include decreased vision, lacrimation, burning, stinging, redness; optic nerve damage, eye pain and ptosis.

Retardation of skeletal maturation and growth, osteoporosis and bone fractures, cushingoid appearance, diabetes, peptic ulcers, myopathy, hypertension, altered mental status, pseudotumor cerebri, and increased mortality from infection Addisonian crisis on withdrawal are more on systemic corticosteroid use.

Dose and Administration: Choice of available corticosteroid agents and dosage regimens remains somewhat empirical. Steroids can be used topically (iritis), intravenously (optic neuritis), intravitreally (endophthalmitis), or in a periocular fashion (uveitis). Topical corticosteroid drops are effective for allergic conjunctivitis, active inflammation of conjunctiva, cornea, and anterior uveitis, beneficial effects on vitritis or macular edema. Systemic corticosteroids use for the treatment of vision-threatening chronic uveitis when topical corticosteroids are insufficient, explosive onset of severe noninfectious posterior uveitis or panuveitis optic neuritis.

Dexamethasone

Solution (eye drop), 0.1%

Indications; contraindications; drug interactions and side effects: see notes above

Dose and Administration : in severe inflammatory conditions instill one drop every hour during day, every 2 hours at night until favorable response is obtained, then taper to 1 drop every 4 hours ;

For mild to moderate inflammation, instill one drop 2-4 times /day.

Storage: store at room temperature

Fluometholone

Solution (eye drop), 1%

Eye ointment, 0.1%

Indications; contraindications; drug interactions and side effects: see notes above

Dose and Administration: *ointment:* apply thin strip ointment one to three times a day. *Eye drop:* In severe inflammation, instill 1 drop every hour during day, every 2 hours at night until favorable response is obtained, then taper to 1 drop every 4 hours.

For mild to moderate inflammation, instill one drop 2-4 times /day.

Storage: store at room temperature

Loteprednol

Solution (eye drop), 0.1%, 0.2%, 0.5%

Indications; contraindications; drug interactions and side effects: see notes above

Dose and Administration: In severe inflammation, instill 1 drop every hour during day, every 2 hours at night until

favorable response is obtained, then taper to 1 drop every 4 hours;

For mild to moderate inflammation, instill one drop 2-4 times /day.

Storage: store at room temperature

Methylprednisolone

Injection, 40mg/ml in 1ml ampoule

Indications: vision-threatening, explosive onset of severe noninfectious posterior uveitis, panuveitis or optic neuritis

Contraindications; drug interactions and side effects: see notes above.

Dose and Administration: methylprednisolone (1 gm/day infused over 1 hour) therapy may be administered for 3 days, followed by oral prednisone starting at 1–2 mg/kg/day, which is tapered in a gradual fashion every 1 to 2 weeks until the disease is quiescent. The lowest possible dose that will control the ocular inflammation and minimize side effects is desired. This dose should be 5–10 mg or less per day.

Prednisolone

Eye drop: 0.25%, 1%

Indications, Contraindications; drug interactions and side effects: see notes above

Dose and Administration: *For mild to moderate inflammation*, instill one drop 2-4 times /day. Therapy for corneal allograft rejection: 1% eye drops every 15 minutes to two hours, which is tapered based on the clinical responses

Storage: store at room temperature

16.5. Anti-infective/Anti-inflammatory combination.

Many antibacterial preparations also incorporate a corticosteroid but such mixtures should not be used unless a patient is under

close specialist supervision. In particular, they should not be prescribed for undiagnosed 'red eye', which is sometimes caused by the herpes simplex virus and may be difficult to diagnose.

Chloramphenicol + Dexamethasone

Solution (eye drop), 0.5% + 0.1%

Indications: treatment of mild to moderate bacterial conjunctivitis and eyelids associated with inflammation; pre and post-operatively for prevention of infection and scarification

Cautions: pregnancy, breast feeding

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: install one to two drops in the affected eye four times daily.

Storage: at room temperature

Flucortolone Pivalante + Chloramphenicol

Solution (eye drop), 0.5% + 0.2%

Indications: treatment of mild to moderate bacterial conjunctivitis and eyelids associated with inflammation; pre and post-operatively for prevention of infection and scarification

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: install one two to four times daily.

Storage: at room temperature

Gentamycine + Betamethasone

Solution (eye drop), 3mg + 1mg/ml

Indications: treatment of mild to moderate bacterial conjunctivitis and eyelids associated with inflammation; pre and post-operatively for prevention of infection and scarification

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: install one to two drops in the affected eye four times daily.

Storage: at room temperature

Gentamycine +Dexamethasone

Solution (eye drop), 0.3% +0.1%

Indications: treatment of mild to moderate bacterial conjunctivitis and eyelids associated with inflammation; pre and post-operatively for prevention of infection and scarification

Cautions: pregnancy, breast feeding

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: install one to two drops in the affected eye four times daily.

Storage: at room temperature

Neomycin + Dexamethasone phosphate

Solution (eye drop), 0.5% + 0.05%; 0.5% + 0.1%

Indications: treatment of mild to moderate bacterial conjunctivitis and eyelids associated with inflammation;

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: instill 1-2 drops up to six times a day

Storage: store at room temperature

Neomycin + Hydrocortisone + Polymixin B Sulphate

Suspension (eye drop), 3.5mg (base) + 10mg +10,000 units (base) in each ml

Indications: steroid-responsive inflammatory condition and bacterial infection or a risk of bacterial infection exists.

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: instill 1-2 drops every 4 to 6 hours

Storage: store at room temperature

Neomycin Sulphate + Polymixin B Sulphate + Dexamethasone

Solution (eye drop), 3.5mg +6000 IU +0.1%

Indications: steroid-responsive inflammatory condition and bacterial infection or a risk of bacterial infection exists.

Drug interactions: see in the individual drug above

Cautions: pregnancy, breast feeding

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: instill 1-2 drops in eye(s) every 4 to 6 hours

Storage: store at room temperature

OxytetracyclineHydrochloride+ Hydrocortisone Acetate + Polymixin B sulphate

Solution (eye drop), 5 mg + 15 mg + 10,000 units in each ml.

Indications: steroid-responsive inflammatory condition and bacterial infection or a risk of bacterial infection exists.

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: instill 1-2 drops in every 4 to 6 hours

Storage: store at room temperature

Tobramycin + Dexamethason

Solution (eye drop), 0.3% +0.1%

Indications: steroid-responsive inflammatory condition and bacterial infection or a risk of bacterial infection exists.

Drug interactions: see in the individual drug above

Contraindications: see in the individual drug above.

Side effects: see in the individual drug above

Dose and Administration: instill 1-2 drops in every 4 to 6 hours

Storage: store at room temperature.

16.6. Anesthetics, Local

Indications: Topical preparations yield corneal and conjunctival anesthesia for comfortable performance of examination techniques, removal of superficial foreign bodies, corneal scraping for bacteriologic studies, for use of contact lenses associated with fundus examination and laser procedures. Local retrobulbar and eyelid blocks yield excellent anesthesia and akinesia for intraocular and orbital surgery.

Cautions: Because topical anesthetics can become drugs of abuse that can eventually lead to chronic pain syndromes and vision loss, they should not be dispensed to patients.

Drug interactions: anti-arrhythmic drugs, MAOIs, clozapine, indometacin, phenelzine

Contraindications: local anesthetics are contraindicated in patients with known hypersensitivity to these drugs, cardiovascular disease, epilepsy, hypertensive crisis, liver disease, renal failure, avoid in the 3rd trimester of pregnancy, If treatment is essential during breast feeding alternative methods of feeding the infant should be considered.

Side effects: Reactions following the administration of local anesthetics are usually toxic and only rarely allergic. A true allergic reaction to a “-caine” medication includes wheezing, urticaria, and respiratory distress. A history of sweating, tachycardia, headache, or hypertension suggests intravascular injection of epinephrine. The toxic manifestations of local anesthetics are generally related to dose. Toxic reactions cause overstimulation of the CNS, which may lead to excitement, restlessness, apprehension, disorientation, tremors, and convulsions (cerebral cortex effects), as well as nausea and vomiting (medulla effects). Cardiac effects initially include tachycardia and hypertension. Ultimately, however, depression of the CNS and the cardiovascular system occurs, which may result in sleepiness and coma (cerebral cortex effects) as well as in irregular respirations, sighing, dyspnea, and respiratory arrest (medulla effects). Cardiac effects of CNS depression are bradycardia and hypotension. Central nervous system stimulation can be counteracted by IV diazepam; respiratory depression calls for ventilatory support.

Benoxinate hydrochloride

Solution (eye drop), 0.4 % topical use

Indications; Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Bupivacaine Hydrochloride

Injection, 0.5 %, 0.75 % in 10 ml ampoule

Indications; Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Cocaine Hydrochloride –topical use

Solution (eye drop), 1%, 2%

Indications: Corneal anesthesia

Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Lidocaine Hydrochloride

Lidocaine (Xylocaine) is an amide local anesthetic used in strengths of 1%, and 2% (with or without epinephrine) for injection. It yields a rapid (5-minute) retrobulbar or eyelid block that lasts 1–2 hours. The topical solution, applied to the conjunctiva with a cotton swab for 1–2 minutes, reduces the discomfort of subconjunctival injections.

Indications; Drug interactions; Contraindications and Side effects: see note above

Dose and administration: the maximum safe dose of the 2% solution for local injection is 15 mL in adults

Storage: store at room temperature

Lidocaine Hydrochloride + Adrenaline

Injection, 1%, 2% +1: 1000 IU

Indications; Drug interactions; Contraindications and Side effects: see note above

Dose and administration: the maximum safe dose of the 2% solution for local injection is 15 mL in adults

Storage: store at room temperature

Marcaine Hydrochloride

Injection, 0.5%

Indications; Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Procaine Hydrochloride

Injection 2 % in 2 ml vial

Indications; Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Propanocaine Hydrochloride

Solution (eye drop), 0.5 %

Injection, 2 %

Indications; Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature

Tetracaine Hydrochloride

Solution (eye drop), 0.5 %

Indications: short-acting local anesthesia of cornea and conjunctiva.

Drug interactions; Contraindications and Side effects: see note above

Storage: store at room temperature.

16.7. Diagnostics and Miscellaneous Agents

Artificial tear (Carboxyl methyl Cellulose + Hydroxypropyl Methyl Cellulose)

Ointment, Drops

Acetylcholine Chloride

Powder for injection (intra-ocular), 100 mg

Indications: produces complete miosis in cataract surgery, keratoplasty, iridectomy and other anterior segment surgery where rapid miosis is required.

Cautions: If miosis is to be obtained quickly anatomical hindrances to miosis, such as anterior or posterior synechiae, must be released, prior to administration. During cataract surgery, use only after delivery of the lens. Aqueous solutions of acetylcholine chloride are unstable. Prepare solution immediately before use. Do not use solution, which is not clear and colorless. Discard any solution that has not been used.

Drug interactions: tacrine, flubiprofen and suprofen

Contraindications: hypersensitivity to acetylcholine chloride, acute iritis and acute inflammatory disease of the anterior chamber

Side effect Infrequent cases of corneal edema, corneal clouding, and corneal decompensation have been reported with the use of intraocular acetylcholine. Adverse reactions have been reported rarely, which are indicative of systemic absorption. These include bradycardia, hypotension, flushing, breathing difficulties and sweating.

Dose and Administration: Adult: Intraocular: 0.5 - 2 ml of 1 % injection (5 to 220 mg) instilled into anterior chamber before or after securing one or more sutures.

Storage: store at room temperature.

Acetylcysteine + Hypermellose

Eye drop, 5% + 0.35%

Indications: relief of severe dry eye symptoms associated with syndromes related to excess mucous production

Ahmed Valve

Indications: drainage device commonly used in the treatment of recalcitrant glaucoma

Complications: can include shallow anterior chamber, hypotony, suprachoroidal hemorrhage, and blockage of the tube by blood, fibrin, or iris Long-term complications include tube

erosion through the conjunctiva, valve migration, corneal decompensation, tube–cornea touch, and retinal detachment

Alphachymotrypsin

Powder for injection, 300 units

Indications: intra-capsular cataract extraction, to have Chemical dissolution of the zonular fibers to reduced the number and severity of complications. Proteolytic enzyme that has been used in ophthalmology for the dissection of the zonule of the lens, thus facilitating and reducing trauma of the eye. For this purpose a solution of chymotrypsin in a sterile diluent such as sodium chloride 0.9% has been injected to irrigate the posterior chamber.

Baerveldts Valve

Indication: Glaucoma drainage devices (Baerveldts Valve) are used for patients with refractory glaucoma or complicated glaucoma, such as uveitic glaucoma, neovascular glaucoma, and pediatric and developmental glaucoma. It is designed to divert aqueous humor from the anterior chamber to an external reservoir.

Bevacizumab

Injection, 4mg/ml vial

Indications: to reduce Macular oedema occurs in diabetes mellitus; retinal vein occlusion or other macular diseases. It has valuable effect in various neovascular and edematous retinal conditions

Cautions: Do not mix with dextrose-containing solutions. Heart disease, stork, or bleeding disorder,

Drug interaction: Anthracyclines, any drugs or supplements that interfere with blood clotting can raise the risk of bleeding during treatment with Bevacizumab. These include vitamin E;

NSAIDs such as aspirin, ibuprofen and naproxen and many others; warfarin; clopidogrel

Contra indications: hypersensitive to Bevacizumab, murine products, or any component of the formulation and pregnancy and breast-feeding.

Side effects: cataract formation, glaucoma, bleeding, hypotony, damage to the retina or cornea, endophthalmitis

Dose and administration: Under direct visualization in indirect ophthalmoscopy, through the pars plana at 3.75 mm posterior to the limbus, inject 1.25mg Bevacizumab into the mid-vitreous cavity as slowly as possible. After the injection, you have to check patient's intraocular pressure, the retina status or for vitreous hemorrhage.

Storage: store vials at 2°C to 8°C. Protect from light; do not freeze.

Biological Glue Tubes

Indications: Tissue adhesive is one of the alternatives to conventional suturing and has some added advantages. Use of the Biological glue is simple, safe, cost and effective.

Contraindications: Jagged or stellate lacerations; Bites, punctures or crush wounds; contaminated wounds; mucosal surfaces or high-moisture areas

Side effects: anaphylaxis, interference with tissue repair, bleeding diathesis.

Dose and Administration: After cleansing, approximate edges of the wound manually and evenly. Squeeze the glue gently on its applicator to apply the edges of the wound at least three layers should be applied to ensure optimal strength to the wound closure. The wound should not be touched until the adhesive dries completely. Fanning or blowing on the wound will not

speed up polymerization. Excess adhesive can simply be wiped away with dry gauze if done immediately.

C3F8 Gas Injection

100ml, 500ml, 1lit, 2lit, 5lit. Bottle

Indications: for the treatment of sub macular hemorrhage due to age-related macular degeneration; to close macular holes; for Vitrectomy (retinal disorder surgery) and useful for flattening a detached retina and keeping it attached while healing occurs

Cautions: It is unsafe to fly in a plane while gas remains in the eye.

Contraindications: Gas injection is also used. It is frequently necessary to maintain a certain head position following surgery when gas is used.

Complications: include progression of cataracts and elevated eye pressure (glaucoma). Vision in a gas-filled eye is usually rather poor until at least 50% of the gas is absorbed.

Express Tube

Glaucoma Filtration tube

Indication: use in glaucoma patients to reduce intraocular pressure where medical and conventional surgical treatments have failed

Caution: it should not be used if sterility or performance is compromised.

Contraindications: Presence of ocular disease such as uveitis, ocular infection, severe dry eye, severe blepharitis.

Fluorescein sodium

Solution (eye drop), 0.25%, 0.4%

Eye paper (sterile strip)

Injection (IV), 0.5%, 2.5%, 5 %, 10% in 10 ml ampoule

Indications: demonstrates defects of corneal epithelium, diagnostic aid in ophthalmic angiography.

Cautions: transient blurring of vision - advice patient not to operate machinery or drive until vision is clear. Care must be taken to avoid extravasations during injection as the high pH of fluorescein solution can result in severe local tissue damage.

Contraindications: avoid use with soft contact lenses; in known patient with hypersensitivity to fluorescein sodium or any other ingredients in this product.

Side effects: Irritating to eyes May cause skin and respiratory tract irritation. Prior to use the injection form, perform intradermal skin test; have epinephrine 1:1000, an antihistamine, and oxygen available

Dose and Administration:*Strips:* moisten strip with sterile water. Place moistened strip at the fornix into the lower cul-de-sac close to the punctum. For best results, patient should close lid tightly over strip until desired amount of staining is obtained. Patient should blink several times after application.

Injection:Adult: 500 - 750 mg injected rapidly into antecubital vein.**Child:** 3.5 mg/lb (7.5 mg/kg) injected rapidly into antecubital vein.

Storage: Store at 2° - 25°C; Donot Freeze

5-Flurouracil

Injection, 50mg/ml, 250mg, 500mg vial

Hydroxypropyl Methyl Cellulose (Hypromellose)

Solution (eye drop), 0.3%, 0.5%, 1%, 2.5%

Injection, 2% vial

Indications: it is used as a surgical aid in certain eye surgeries, such as cataract removal and lens implantation procedures. It helps maintain the shape of the eye during surgery as well as protect the tissues of the eye from damage due to surgical

instruments and as a vehicle for eye drops and as artificial tears and contact lens solution

Side effects: Blurred vision, decreased vision, Pain in the eye, redness of the white part of the eye or inside of the eyelid, sensitivity of the eye to light, lacrimation or throbbing eye pain

Lisseman Green

Solution (eye drop), 1%

Indications: Evaluation of tear deficiency states and detection of various epithelial lesions.

Mitomycin C

Powder for injection, 2mg vial

Indications: antimetabolite used during the initial stages of a trabeculectomy to prevent excessive postoperative scarring.

Molteno Valve

Indication: It is Glaucoma Drainage Devices for surgical Implants for the treatment of Glaucoma

Perfluorocarbon liquids

Injection, 5ml, 10ml vial

Indications: facilitate surgery in conditions like proliferative vitreoretinopathy, giant retinal tears, and drainage of suprachoroidal hemorrhages, diabetic traction, retinal detachments with a rhegmatogenous component, dislocated crystalline or intraocular lenses, and retinal detachment associated with choroidal coloboma.

Polyvinyl Chloride

Solution (eye drop), 0.1%, 0.5%, 1%

Indication: For use as a lubricant to prevent further Irritation or to relieve dryness of the eye(s)

Cautions: Stop use and ask a doctor if you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours.

Dose and Administration: Instill 1 or 2 drops in the affected eye(s) as needed

Store: at 20⁰ to 25°C; away from heat; Protect from freezing. Keep tightly closed.

Povidone Iodine Solution

Eye drop, 1%, 5%, 10% bottle

Povidone-iodine is readily available worldwide, either as a powder or as a 10% solution. Depending on the type of application, for ophthalmic use, the solution must be diluted to the appropriate strength. The diluents may be a balanced salt solution or other appropriate diluents. In the appropriate concentration, it is not toxic to the eye as are other iodine bearing compounds

Indication: disinfect the eyes and surrounding skin before ophthalmic surgery and intraocular injections.

Cautions: pregnancy, breast feeding, pediatric patients, patients with thyroid disorders, renal dysfunction

Contraindications: Hypersensitivity to iodine or to any of the excipients

Side effects: the medication the eye turns brown for a few minutes proving that it has been applied

Ranibizumab

Injection, 10mg/ml vial

Indications: treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to diabetic macular oedema (DME), visual impairment due to macular oedema

secondary to retinal vein occlusion (branch RVO or central RVO).

Cautions: monitor intra-ocular pressure, the perfusion of the optic nerve head and for signs of ocular infection, pregnancy

Drug interactions: anti-VEGF (vascular endothelial growth factor) agents (systemic or ocular).

Contraindications: Hypersensitivity to the active substance or to any of the excipients, active or suspected ocular or periocular infections, active severe intraocular inflammation

Side effects: Dry eye; eye discomfort; feeling of something in the eye; eye or eyelid swelling; eye pain, pressure, redness, bleeding, or discharge, headache; increased tears; nausea; nose or throat irritation; seeing floaters or spots, allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue); chest, jaw, or left arm pain

Dose and Administration:*intravitreal***Adult:** Initially 0.5 mg once a month for 3 months into the affected eye, There after monitor visual acuity once a month; if Necessary subsequent doses may be given at least 1 Month apart. Antimicrobial eye drops should be administered into the affected eye for 3 days before and 3 days after each injection.

Storage: Store in the refrigerator between 2-8⁰c, Protect from Sunlight.

Rose benegal

Solution (eye drops), 1%

Indication: For use as a diagnostic agent when superficial corneal or conjunctival tissue change is suspected, especially in dry eyes. Unlike fluorescein, which stains epithelial defects, rose bengal will stain damaged cells and give a clearer indication of the extent of damage. It is irritating to the eyes.

Storage: Store at room temperature

Silicon oil

Injection, 1000CSK, 5000CSK vials

Indications: Used in eye operations, retinal surgery for substituting the vitreous fluid.

Side effects: Silicone oil injection may induce multiple complications, including cataract, glaucoma, and keratopathy, raised intraocular pressure, band keratopathy

Sodium Hyaluronate

Solution (eye drop), 0.1%

Injection, 1%, 1.3%, 1.4%, 2%, 3% vials

Indications: assist in the extraction of cataracts, the implantation of intraocular lenses, corneal transplants, glaucoma filtration, retinal attachment and in the treatment of dry eyes

Cautions: Monitor intraocular pressure, Pregnancy

Side effects: Transient rise in intraocular pressure
Synthetic Tissue Graft Pericardium, Cornea, Sclera

Trypan Blue

Injection, 0.01%, 0.25%, 0.5%

Indications: as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

Storage: Store between 15-25°C. Protect from direct sunlight.

17. EAR, NOSE and THROAT PREPARATIONS

17.1. Nasal and Oropharyngeal, Preparations

Symptoms of nasal congestion associated with vasomotor rhinitis and the common cold can be relieved by the short-term use (usually not longer than 7 days) of decongestant nasal drops and sprays. These all contain sympathomimetic drugs which exert their effect by vasoconstriction of the mucosal blood vessels which in turn reduces oedema of the nasal mucosa. They are of limited value because they can give rise to rebound congestion (rhinitis medicamentosa) on withdrawal, due to a secondary vasodilatation with a subsequent temporary increase in nasal congestion.

Ephedrine nasal drop is the safest sympathomimetic preparation and can give relief for several hours. The more potent sympathomimetic drugs xylometazoline and oxymetazoline are more likely to cause a rebound effect. All of these preparations may cause a hypertensive crisis if used during treatment with a monoamine oxidase inhibitor.

Mild cases of allergic rhinitis are controlled by topical nasal corticosteroids or oral antihistamines; systemic nasal decongestants are of doubtful value. Antazoline is often used with a vasoconstrictor such as naphazoline for the treatment of rhinitis.

Inhalations of warm moist air are useful in the treatment of symptoms of acute infective conditions, and the use of compounds containing volatile substances such as menthol and eucalyptus may encourage their use.

Mouthwashes have a mechanical cleansing action and freshen the mouth. Providone - Iodine mouthwash is useful for mucosal infections but does not inhibit plaque accumulation. It should

not be used for periods longer than 14 days because a significant amount of iodine is absorbed.

There is no convincing evidence that antiseptic lozenges and sprays have a beneficial action and they sometimes irritate and cause sore tongue and sore lips. Some of these preparations also contain local anesthetics which relieve pain but may cause sensitization. The throat lozenges are Amyl-metacresol + Dichlorobenzyl Alcohol and Dequalinium Chloride.

The most common cause of a sore throat is a viral infection which does not benefit from anti-infective treatment. Fungal mouth infections such as candida albicans which are sometimes associated with the use of broad-spectrum antibiotics or of cytotoxics; withdrawing the causative drug may lead to rapid resolution. Otherwise, an antifungal drug may be effective. Of the antifungal drugs used for mouth infections, miconazole and nystatin are not absorbed from the gastro-intestinal tract and are used by local application in the mouth. Miconazole occupies an intermediate position since it is used by local application in the mouth but is also absorbed to the extent that potential interactions need to be considered.

Acyclovir Cream

Cream, 5% 2gm

Indications: to treat cold sores (fever blisters; blisters that are caused by herpes simplex virus) on the face or lips

Cautions: indiscriminate use of topical acyclovir may result in the emergence of resistance. Do not apply acyclovir cream to any unaffected skin, or to genital herpes sores.

Contraindications: allergy to one or any of the ingredients; allergy to valaciclovir; herpes simplex virus infections of the eye.

Dose and Administration: *topical:* **Adult:** 5 times per day for 4 days. Therapy should be initiated as early as possible following onset of signs and symptoms (i.e. during the prodrome or when lesions appear).

Side effects: burning or stinging, dry or cracked lips, flakiness or dryness of skin, itching, difficulty to breathe, tightness in the chest, dizziness.

Storage: store at room temperature

Adrenaline

Inhalation, 1mg/2.5cc normal saline solution

Indications: acute breathing problems; to open breathing passages and make breathing easier.

Cautions: heart disease, heart rhythm problems, chest pain (angina), diabetes, high blood pressure, thyroid disease, a history of strokes, seizures, drug allergies, pregnancy

Drug interactions: anti-hypertensives, beta-blockers (e.g., propranolol), anti-diabetics, anti-depressants

Contraindications: allergy to adrenaline, cardiac arrhythmias, angle closure glaucoma

Dose and Administration: inhaled into the lungs using special breathing equipment

Side effects: Tremor, nervousness, shakiness, headache, nausea, heartburn, lightheadedness, sleeping difficulty, unusual taste in mouth, hoarseness or dry throat may occur the first several days; rash, rapid heartbeats, chest pain, dizziness, coughing, breathing trouble

Storage: Store in a cool area protected from light.

Amyl Meta-cresol + Dichlorobenzyl Alcohol

Lozenges, 0.6 mg + 1.2 mg

See notes above

Antazoline + Naphazoline

Solution (nose drop), 0.5 % + 0.025 %

Indication: allergic rhinitis

See notes above

Beclomethasone Dipropionate

Nasal spray (aerosol), 50 mcg/dose

Indications: prophylaxis and treatment of seasonal (intermittent) and non-seasonal (persistent) allergic rhinitis. Sometimes useful in non-allergic (vasomotor) rhinitis.

Cautions: systemic infections or ocular herpes simplex

Contraindications: status asthmaticus

Side effects: agitation, depression, dizziness, angioedema, rash, urticaria, burning, sneezing, nasal stuffiness, nose bleedings, cough, wheezing.

Dose and Administration: Adult: 100 mcg (2 sprays) into each nostril twice daily, or 50 mcg into each nostril 3-4 times daily.

Storage: store at room temperature. Do not store near heat or open flame.

Chlorhexidine Gluconate

Oral Solution, 0.12%

Indications: used along with regular tooth brushing/flossing to treat gingivitis.

Caution: do not swallow the medicine and instruct not to eat for 2-3 hours after treatment

Contraindications: allergy to chlorhexidine gluconate or other formula ingredients

Side effects: Tooth/tongue staining, increased tartar, mouth/throat irritation, and change in taste of food/drinks; Oral irritation and local allergy-type symptoms.

Dose and Administration: Adult:*Treatment of gingivitis: oral prophylaxis:* floss and brush teeth, completely rinse toothpaste from mouth. Wash with 15ml chlorhexidine undiluted for 30 seconds and expectorate. Repeat twice daily (morning and evening)

Storage: Store at room temperature away from light and moisture.*Note: Chlorhexidine gluconate may be incompatible with some ingredients in toothpaste; leave an interval of at least 30 minutes between using mouthwash and toothpaste*

Clotrimazole

Troches, 10mg ;Drops, 100ml ;Spray, 100ml;Mouth paint, 1%

Indications: treatment and prophylaxis of oropharyngeal candidiasis in immunocompromised patients that may be induced by chemotherapy, radiotherapy, or steroid therapy.

Cautions: pregnancy, lactation, liver disease; children less than 3 years of age (for clotrimazole troches), avoid contact with eye.

Drug interactions: polyene antimycotics like Amphotericin B, nystatin, and natamycin.

Contraindications: known hypersensitivity to the drug or any of the ingredients.

Side effects: Nausea, vomiting, unpleasant mouth sensations and pruritus

Dose and Administration: Adult and children > 3 years:*Troches: Prophylaxis:* 10 mg troches dissolved 3 times/day for the duration of chemotherapy or until steroids are reduced to maintenance level. *Treatment:* Slowly dissolve in the mouth (15-30 minutes), one troche five times a day for fourteen consecutive days. *Mouth paint:* 10-20 drops gently applied to mouth, preferably with cotton bud, 3-4 times a day. All lesions in the mouth must be covered.

Storage: Store in a cool, dry place

Dequalinium chloride

Lozenge, 0.25 ml See notes above

Ephedrine Sulphate

Solution (Nose drop), 1 %

Indication: nasal congestion

Cautions: avoid excessive or prolonged use, caution in infants less than 3 months (no good evidence of value - if irritation occurs might narrow nasal passage)

Drug interactions: anesthetics, antibacterial, antidepressants, antihypertensives, Beta-blockers, dopaminergics.

Side effects: local irritation, nausea, headache; after excessive use tolerance with diminished effect; rebound congestion; cardiovascular effects also reported.

Dose and Administration: Instill 1 - 2 drops into each nostril up to 3 or 4 times daily.

Fluticasone Furoate

Nasal Spray, 27.5mcg

Indications: treatment of symptoms of seasonal and perennial allergic rhinitis in adults and children ≥ 2 years. **Cautions:** pregnancy, breast feeding; Epistaxis, nasal ulceration, Candida albicans infection, nasal septal perforation, impaired wound healing. Monitor patients periodically for signs of adverse effects on the nasal mucosa.

Drug interactions: Potent inhibitors of cytochrome P450 3A4 (CYP 3A4), Co-administration of ritonavir

Contraindications: patients with recent nasal ulcers, nasal surgery, or nasal trauma; hypersensitivity to the medicines and any component of the formulation.

Side effect: headache, epistaxis, pharyngolaryngeal pain, nasal ulceration, back pain, pyrexia, and cough.

Dose and administration: intranasal use only. Usual starting dosages: Adults and adolescents ≥ 12 years: is 110 mcg once daily administered as 2 sprays (27.5 14 mcg/spray) in each nostril. Children 2-11 years: 55 mcg once daily administered as 1 spray (27.5mcg/spray) in each nostril.

Gentian Violet

Solution, 1 %

Indications: candidal infections of the mouth and throat (thrush).

Cautions: avoid swallowing of the solution. Infants should be turned face downward after application to minimize the amount of drug ingested.

Side effects: Irritation or sensitivity reactions or ulceration of mucosal membranes may occur. Esophagitis, laryngitis, or trachitis may result from swallowing the solution.

Dose and Administration: Topical, to the oral mucous membranes. It should be painted only on individual lesions with cotton. Adult and Child: every 8 – 12 hours daily for 3 years.

Storage: at room temperature, in tight containers

Hexetidine [☞]

Solution, 0.1 %

Indications: for local infection and/or hygiene

Side effects: allergic contact dermatitis and alterations in taste and smell local irritation

Dose and Administration: Rinse with 15-30ml, undiluted, for 30 seconds twice daily.

Hexidine

Oral Solution, 0.1gm/100ml, 0.2%

[☞] Any mouth wash and antiseptic preparations are also acceptable

Indications: Prevention of plaque in absence of brushing, prevention and treatment of gingivitis, treatment of oral thrush and oral ulcers, aid in treatment of mouth and throat infections.

Dose and Administration: Rinse with 15-30ml, undiluted, for 30 seconds twice daily.

Hydrogen peroxide

Solution, 1.5%, 3%

Indications: antiseptic and deodorant mouthwash. By its effervescence, it may liberate debris from inaccessible cavities and aid in proper cleansing of the buccal cavity.

Dose and Administration: dilute 3% to 1.5% before use as a mouthwash. (Some 3% hydrogen peroxide with an equal amount of water added will give 1.5% hydrogen peroxide)

Menthol + Eucalyptus oil + Light Magnesium carbonate

Inhalation, 2 % + 10 % + 7 %

Indications: for relief of nasal obstruction in acute rhinitis or sinusitis and to promote warm moist air inspiration in bronchitis.

Cautions: boiling water should not be used for the preparation.

Dose and Administration: add one teaspoonful to a pint of hot, not boiling, water and inhale the vapour.

Miconazole

Oral Gel, 25 mg/ml

Indications: oral fungal infections

Cautions: pregnancy, avoid in porphyria

Drug interactions: anticoagulants, sulphonylureas, phenytoin, cisapride, and cyclosporin.

Side effects: mild gastrointestinal disturbances

Dose and Administration: Adult: Place 5 – 10 ml in the mouth after food and retain near lesions 4 times daily.

child under 2 years: 2.5 ml twice daily, 2 – 6 years 5 ml twice daily, over 6 years : 5 ml 4 times daily.

** Localized lesions smear small amounts of gel on affected area with clean finger*

Storage: Store at room temperature protected from light

Mometasone furoate

Intranasal spray, 0.05%

Indications: treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children ≥ 2 years of age; prevention of nasal symptoms associated with seasonal allergic rhinitis ≥ 12 years of age and adults; treatment of nasal polyps in adults.

Cautions: should be avoided in the presence of untreated nasal infections, and also after nasal surgery (until healing has occurred); also be avoided in pulmonary tuberculosis. Systemic absorption may follow nasal administration particularly if high doses are used or if treatment is prolonged. The height of children receiving prolonged treatment should be monitored; if growth is slowed, referral to a paediatrician should be considered.

Side effects: nasal dryness, irritation of nose and throat, epistaxis, nasal ulceration, headache, smell and taste disturbances, hyperactivity, sleep disturbances, anxiety, depression, and aggression particularly in children, hypersensitivity reactions, including bronchospasm.

Dose and Administration: Nasal spray: Allergic rhinitis: Adult and Child ≥ 12 years: 2 sprays in each nostril daily; when used for the prevention of allergic rhinitis, treatment should begin 2-4 weeks prior to pollen season. Child 2-11 years: 1 spray in each nostril daily.

Nasal polyps: Adult: 2 sprays in each nostril twice daily; 2 sprays once daily may be effective in some patients.

Storage: store at room temperature and protect from light.

Nystatin

Pastilles, 100,000 units

Suspension, 100,000 units/ml

Oral gel, 1000,000 IU/gm, tube- 50gm

Cream, 100,000 IU/gm, Tube- 50gm

Indications: oral and perioral fungal infections

Contraindications: hypersensitivity to the drug or any ingredient in the respective formulation.

Side effects: nausea, vomiting, and diarrhoea, oral irritation and sensitization reported

Dose and Administration: 100,000 units 4 times daily after food. Usually for 7 days (continued for 48 hours after lesions have resolved). Nystatin 100,000 units up to four times daily may be given to neonates. *Immuno suppressed patients may require higher doses (e.g 500,000 units 4 times daily). The formulation should be kept in contact with the affected area for as long as possible and patients should avoid taking food or drink earlier than one hour after a dose.*

Storage: nystatin deteriorates on exposure to heat, light, moisture, or air. Nystatin oral suspension should be stored in tight, light resistant containers at room temperature; freezing of the oral suspension should be avoided.

Oxymetazoline Hydrochloride

Nasal solution 0.05 %

Indications: nasal congestion associated with acute or chronic rhinitis, common cold, upper respiratory allergies, and otitic barotraumas

Cautions, contraindications, side effects see under section OP. 404 Vasoconstrictors, Oxymetazoline Hydrochloride

Dose and Administration: adults and children greater than 6 years of age: 2-3 drops every 12 hours usually in the morning or evening.

Phenylephrine

Solution (Nose drops), 0.25%, 0.5%, 1%

Indications: symptomatic relief of nasal and Eustachian tube congestion

Cautions: breast-feeding women and children

Side effects: prolonged use will cause increase in running nose with chronic nasal mucosa swelling. Burning, dryness, or stinging of nasal mucosa may occur rarely.

Dose and Administration: Intranasal, Avoid prolonged use, and avoid using more medications than the amount recommended. Rinse dropper with hot water and dry with clean tissue after using. Adult and Child over 12 year: 1-2 drops every four hours of 0.25% to 0.5% solution as needed. 2 or 3 drops of the 1% solution into each nostril every 3-4 hours as necessary. Child 6-12 years: 2-3 drops or 0.25% solution into each nostril every 3-4 hours as necessary.

Storage: at room temperature. In a tight and light resistant container.

Povidone - Iodine

Solution, 1 %

Indications: for oral hygiene

Cautions: caution should be taken during pregnancy and breast feeding

Contraindications: avoid regular use in patients with thyroid disorders and receiving lithium therapy.

Side effects: idiosyncratic mucosal irritation and hypersensitivity reactions may interfere with thyroid function tests and with tests for occult blood.

Dose and Administration: Mouth wash or gargle.

Adult and Child over 6 years, up to 10ml undiluted or diluted with an equal quantity of warm water for 30 seconds up to 4 times daily for 14 days.

Pseudoephedrine Hydrochloride

Syrup, 30 mg/ml

Indications: symptomatic relief or nasal congestion

Cautions, Side effects, Drug interactions; see under ephedrine sulphate

Dose and Administrations:Orally: Adult: 60mg, 3 - 4 times daily, children 2 to 5 years, 15 mg 3 times daily; 6 to 12 years, 30 mg 3 times daily.

Pseudoephedrine + Loratadine

Tablet, 120 mg + 5 mg

Indications: temporary relief of symptoms of seasonal allergic rhinitis, other upper respiratory allergies, or the common cold

Cautions, Side effects, Drug interactions: see individual drugs

Dose and Administration: 1 tablet every 12 hours.

Saline Solution

Solution, 0.09%

A saline solution is a salt-water solution. The sterile solution is typically used for nasal irrigation, flush wounds and skin abrasions. It will not burn or sting when applied.

Sodium Chromoglycate

Aqueous Nasal Spray, 4% (5.2mg/spray)

Nasal Spray, 2%

Nasal drop, 2%

Indications: prophylaxis and treatment of allergic rhinitis

Drug interactions: Methacholine

Contraindications: Hypersensitivity to the medicines and any component of the formulation.

Dosage and administration: Adult and children: 4%, 1 spray into each nostril 2–4 times daily

2%, 1 spray into each nostril 4–6 times daily

Side-effects: local irritation; rarely transient bronchospasm

Storage: Store below 30°C, in the original container, in dry place

Triamcinolone Acetonide

Oral paste, 0.1 %

Indications: adjunctive treatment and temporary relief of symptoms associated with oral inflammatory lesions and ulcerative lesions resulting from trauma.

Cautions: hypothyroidism, cirrhosis, nonspecific ulcerative colitis and patients at increased risk for peptic ulcer disease, hepatic impairment, diabetes, hypertension, osteoporosis, glaucoma, cataracts or tuberculosis.

Drug interactions: NSAIDs, barbiturates and phenytoin, rifampin, vaccine

Contraindications: fungal, viral, or bacterial infections of the mouth or throat

Side effects: hypertension, convulsions, fever, atrophy of oral mucosa, burning, and irritation

Dose and Administration: Oral topical: press a small dab (about ¼ inch) to the lesion until a thin film develops. A larger quantity may be required for coverage of some lesions. For optimal results use only enough to coat the lesion with a thin film; do not rub in.

Storage: store at room temperature

Xylometazoline Hydrochloride

Spray, 0.025%, 0.05%

Solution (Nasal drop), 0.05 %, 0.1 %

Indications: nasal congestion

Cautions: pregnancy, heart disease, hypertension, hyperthyroidism, Diabetes

Contraindications: monoamine oxidase inhibitors antidepressant (eg phenelzine, isocarboxazid, tranylcypromine or moclobemide)

Side effects: see under ephedrine sulfate

Dose and Administration: Adult: drops: instil 2 - 3 drops of 0.1 % solution into each nostril 2 - 3 times daily when required; maximum duration 7 days; not recommended for children under 12 years. Child: over 3 months instil 1 - 2 drops of 0.05 % solution into each nostril 1 - 2 times daily when required (not recommended for infants under 3 months of age, doctor's advice only under 2 years); maximum duration 7 days. Adults and children 12 years of age and over: spray; 2 or 3 sprays (0.05%) in each nostril not more often than every 8 to 10 hours.

17.2. Otic Agents

Otitis externa: Otitis externa or inflammation of the skin of the external auditory canal may be due to infections with bacteria, viruses, or fungi or secondary to skin disorders such as eczema, although more than one factor is often responsible for chronic otitis externa. The treatment includes thorough cleansing and the use of appropriate antibiotic eardrops, often containing a corticosteroid as well, even though some have doubted the value of topical antibiotics. Eardrops containing aminoglycosides, such as gentamicin, neomycin, or polymixins should not be used when the eardrum is perforated because of the risk of ototoxicity.

A solution of acetic acid 2 % acts as an antifungal and antibacterial in the external ear canal. It may be used to treat mild otitis externa but in severe cases an anti-inflammatory preparation with or without an anti-infective drug is required. Solutions containing an anti-infective and a corticosteroid are used for treating cases where infection is present with inflammation and eczema.

Otitis media or inflammation of the middle ear can be acute or chronic, serous (with effusion; secretary) or supportive local treatment of acute otitis media is ineffective and there is no place for drops containing a local anaesthetic. Many attacks are viral in origin and need only treatment with a simple analgesic such as paracetamol for pain. Severe bacterial infection should be treated with systemic antibiotics. The organisms recovered from patients with chronic otitis media are often opportunists living in the debris, keratin, and necrotic bone present in the middle ear and mastoid. *Thorough cleansing with an aural suction tube may completely resolve infection of many years duration. Acute exacerbations of chronic infection may require systemic antibiotics.*

Acetic Acid

Solution (ear drop), 2 % See notes above

Betamethasone

Solution (ear drop), 0.1 %

Indications: management of non-infected inflammatory conditions of the external ear.

Cautions: it should be avoided in the presence of infection, and excessive use also avoided.

Dose and Administration: Instill 2 or 3 drops into the ear every 2 - 3 hours until inflammation is controlled, after which the frequency may be reduced.

Chloramphenicol

Solution (ear drop), 1 %, 2 %, 5 %

Indications: used in the treatment of bacterial infection in otitis externa.

Cautions: over growth with non-susceptible organisms, Avoid prolonged use

Side effects: high incidence of sensitivity reactions to vehicle, optic and peripheral neuritis

Drug interactions: alfentanil, chlorpropamide, phenytoin, tolbutamide, rifampicin, warfarin, vitamin B₁₂, folic acid

Contraindications: hypersensitive to the drug or any ingredients in the formulations; perforated tympanic membrane. Mothers receiving otic chloramphenicol should not breast-feed their infants.

Dose and Administration: Apply 2 – 3 drops into the ear 2 – 3 times daily

Storage: Store below 30⁰C in a tight container protected from freezing

Ciprofloxacin

Ear drops, 0.3%, 5ml

Indications: treatment of Otitis externa, acute otitis media, chronic suppurative otitis media & prophylaxis during otic surgeries such as mastoid surgery

Cautions: If irritation persists or increases, discontinue. Do not touch the dropper, since this may contaminate solution.

Contraindications: Hypersensitivity to quinolone group of antibacterials or any of the Components of the formulation

Dosage and administration: 2-3 drops every 2-3 hours

Side effect: Discomfort, pain, or itching in the ear; headache

Storage: Store at room temperature

Clioquinol +Flumethasone Pivalate

Solution (ear drops), 1% +0.02%

Indications: treatment of external ear infections caused by bacterial and fungal organisms

Cautions: pregnancy

Contraindications: Viral infections of the skin (e.g., chickenpox, skin eruptions following vaccination, herpes simplex, herpes zoster), tuberculosis of the skin, syphilis, rosacea, acne vulgaris, perioral dermatitis, iodine, application to ulcerated areas; application to the eye; children under 2 years of age

Side effects: signs of irritation such as burning sensation, itching or skin rash at the site of application; hypersensitivity reactions.

Dose and Administration: children > 2 years and Adults: Instill 2 - 3 drops into the affected ear twice daily general limit duration to 10 days.

Storage: store between 15-30 °c

Clotrimazole

Solution (ear drop), 1 %

Indications: fungal infection in otitis externa

Side effects: occasional local irritation or sensitivity

Dose and Administration: *Ear*, apply 2 - 3 times daily continuing for at least 14 days after disappearance of infection

Cocain Hydrochloride

Topical Solution, 4% (40mg/ml), 10% (100mg/ml)

Indications: local (topical) anesthesia of accessible mucous membranes of the oral, laryngeal and nasal cavities.

Cautions: Pregnancy, breast feeding and severely traumatized mucosa and sepsis.

Contraindications: patients with a known history of hypersensitivity to the drug or to the components of the topical solution

Dosage and administration: the dosage varies and depends upon the area to be anesthetized, vascularity of the tissues, individual tolerance, and the technique of anesthesia. The lowest dose needed to provide effective anesthesia should be administered. Dose should be reduced for children and for elderly and debilitated patients. It can be administered by means of cotton applicators or packs, instilled into a cavity, or as a spray

Side effects: nausea, nervousness, unusual feelings of well-being, or restlessness

Storage: Store at room temperature

Dichlorobenzene + Chlorobutol + Turpentine oil

Solution (ear drop), 2 % + 5 % + 10 %

Dose and Administration: *Instill* 5 drops into the ear 10 to 30 minutes before syringing.

Gentamicin

Solution (ear drop), 0.3 %

Indications: bacterial infection in otitis externa

Cautions: avoid prolonged use.

Contraindications: perforated tympanic membrane

Side effects: local sensitivity

Dose and Administration: *Ear*, apply 3 - 4 drops 3 - 4 times daily; reduce frequency when relief obtained.

Hydrogen peroxide

Solution, 3 %

Hydrogen peroxide has antimicrobial properties, which are reduced in the presence of organic matter. Their frothing action

makes them useful to loosen and aid removal of debris in the ear canal.

Storage: at room temperature in airtight container. Solutions should not be stored for long periods. Those not containing a stabilizer should be stored at a temperature not exceeding 15 °C. Protect from light.

Neomycin Sulphate + Hydrocortisone + Polymixin B Sulphate

Ear drops, 3.5 mg + 10 mg + 10,000 units in each ml, 34,000units +1% +10,000units/ml

Indications: see section 15.5 (anti infective).

Cautions: pregnancy

Contraindications: hypersensitivity to any of its components; if the external auditory canal disorder is suspected or known to be due to cutaneous viral infection (for example, herpes simplex virus or varicella zoster virus).

Dose and Administration:Adult: instill 4 drops 3-4 times per day. **Child:** instill 3 drops into affected ear 3-4 times per day.

Ofloxacin

Ear drops, 0.3%

Indications: treatment of Otitis Externa, chronic suppurative otitis Media with perforated tympanic membranes and acute otitis media in the presence of tympanostomy tubes in children

Cautions: pregnancy; breast feeding; do not touch the dropper, since this may contaminate solution.

Contraindications: History of hypersensitivity to ofloxacin, to other quinolones, or to any of the components in this medication.

Dosage and administration:otitis externa: Adults: 10 drop twice daily. **Children (under 12):** 5 drops twice daily. *Chronic*

suppurative otitis media with perforated tympanic membranes:

Adults: 10 drops twice daily for 14 days. *Acute otitis media in the presence of tympanostomy tubes:***children:** Apply 5 drops twice daily for 14 days. *Note: Ofloxacin ear drops should be instilled into the ear canal of the infected ear, while the patient lies with the ear upwards. The position should be maintained for at least 5 minutes after administration.*

Side effects: Pruritus, ear ache, dizziness, headache, vertigo, nausea, seborrhea

Storage: Store at room temperature

Oxytetracycline

Ear drop, 0.5%

Indications: treatment of infections caused by a variety of Gram positive and Gram negative microorganisms including *Mycoplasma pneumoniae*, *Pasteurella pestis*, *Escherichia coli*, *Haemophilus influenzae* (respiratory infections), and *Diplococcus pneumoniae*.

Contraindications: pregnancy, breast feeding hypersensitivity to tetracycline or any component of the formulation

Oxytetracycline Hydrochloride + Hydrocortisone Acetate + Polymyxin B sulphate

Ear drop, 5 mg +15 mg + 10,000 units in each ml.

Indications: bacterial infection with eczematous inflammation in otitis external (see also notes above)

Caution: avoid prolonged use

Contraindications: perforated tympanic membrane

Side effects: local sensitivity reactions

18. DERMATOLOGICAL AGENTS

18.1. Anti-infective, Topical

Antifungals

Ringworm: infection can affect the scalp (tinea capitis), body (tinea corporis), groin (tinea cruris), hand (tinea manuum), foot (tinea pedis, athlete's foot) or nail (tinea unguium). Scalp and nail infection requires systemic treatment; additional topical application of antifungal may reduce the risk of transmission. Most other local ringworm infections can be treated adequately with topical antifungal preparations. **Benzoic acid** and **methylrosanilinium chloride (genetian violet)** solution are inexpensive and effective fungistatic compounds for the treatment of ringworm infections. Minor skin lesions due to ringworm can be cleared with repeated applications of compound benzoic acid ointment (Whitfield ointment), which combines the fungistatic action of benzoic acid with the keratolytic action of salicylic acid. However, the most effective topical treatment for dermatophyte infections is a cream containing an imidazole such as **clotrimazole**, **ketoconazole** and **miconazole**, which are effective for long established lesions but is more expensive than compound benzoic acid ointment.

Candidiasis: Candida can infect the oral cavity, the vagina or the skin. The most severe infections of candida are now seen in patients with HIV infection. Candidal skin infections may be treated with topical imidazole antifungals, **clotrimazole**, **ketoconazole**, **miconazole**. Topical application of **nystatin** is also effective for candidiasis but it is ineffective against dermatophytosis. Refractory candidiasis requires systemic treatment.

Pityriasis versicolor: Pityriasis (tinea) versicolor is caused by commensal yeast. It may be treated topically with a course of

selenium sulphide repeated after one month. Topical imidazole antifungals and topical terbinafine are alternatives but large quantities may be required. If topical therapy fails or if the infection is widespread, pityriasis versicolor is treated systemically with an azole antifungal. Relapse is common, especially in immunocompromised patients.

Choice of Antifungal formulation

Both vehicles and active ingredients are important in the treatment of skin conditions; the vehicle alone may have more than a placebo effect. The vehicle affects the degree of hydration of the skin, has mild anti-inflammatory effects, and aids the penetration of the active drug.

Lotions or sprays are suitable for application to large and hairy areas. Ointments are generally used on dry areas; they are best avoided on moist skin. Creams are cosmetically more acceptable than ointments and they are best suitable for moist areas.

Paints and solutions for application to the nail are occasionally effective for early dystrophy in onychomycosis. Dusting powders are of little therapeutic value in the treatment of fungal skin infections and may cause skin irritation; they may have some role in preventing re-infection.

Cautions: Contact with eyes and mucous membranes should be avoided.

Side effects: Occasional local irritation and hypersensitivity reactions include mild burning sensation, erythema, and itching. Treatment should be discontinued if these are severe.

Benzoic Acid + Salicylic Acid (Whitfield's Ointment)

Ointment, 6 % + 3 %, 12 % + 6 %

Indications: fungal infections of the skin (mild dermatophyte infections, particularly tinea pedis and tinea corporis).

Cautions: it should not be applied to broken or inflamed skin.

Side effects: skin irritation, dryness may occur and mild inflammatory reaction.

Dose and Administration: *Topical*, to the skin for several weeks until the infected stratum is shed usually at least 4 weeks. Prolonged use should be avoided and irritation of the skin occurs. Apply sparingly to the affected area every 8-12 hours daily.

Storage: at room temperature, in a tight container.

Castellani's paint (Magenta + Boric Acid + Phenol + Resorcinol + Alcohol 90 % + Acetone)

Solution each 100 ml contains: 400 mg + 800mg + 4g + 8g + 8.5 ml + 4 ml (water q.s. 100 ml).

Indications: castellani's paint is applied topically in the treatment of superficial fungal infections of the skin including tinea pedis and ringworm infections.

Cautions: the drug is poisonous when ingested. The drug should not be applied to eroded skin or over extensive areas.

Dose and Administration: Castellani's paint is applied topically by means of an applicator or swab. The skin should be cleansed with soap and water and thoroughly dried prior to application. It is usually applied once or twice daily; however, application of the drug 3 times daily may be necessary in chronic or stubborn infections. The solution should be applied no more often than once daily in infantile eczema. In dry, scaling dermatophytoses, application of the solution may be alternated with ointments containing other antifungal agents or keratolytics.

Storage: the solution should be stored in a tight, light resistant container at room temperature (30⁰); freezing should be avoided and protect from humidity.

Clotrimazole

Cream 1 %

Solution 1 %

Topical powder, 1%

Mouth paint, 1%

Indications. Treatment of susceptible fungal infection and topical clotrimazole is indicated in the treatment of cutaneous candidiasis (moniliasis) caused by *Candida albicans*. It is also indicated for treatment of *tinea corporis* (ring worm of the body), *tinea cruris* (ringworm of the groin, jock itch), and *tinea pedis* (ringworm of the foot; athlete's foot). It is also used in the treatment of *tinea versicolor* (*pityriasis versicolor*, 'sun fungus'), and in the treatment of paronychia, *tinea barbae*, and *tinea capitis*.

Cautions: sensitive to clotrimazole or any component of the formulation

Side effects: hypersensitivity (skin rash, hives, blistering, burning, itching peeling, redness, stinging, swelling and other sign of skin irritation not present before therapy).

Dose and Administration: **Adult** and **Child:** *topical*, to the skin and surrounding area, two times a day, morning and evening.

Storage: at room temperature in a tight container, protect from freezing.

Methylrosanilinium chloride (Genitian Violet)

Solution, 0.5 %, 1 %

Indications: for the treatment of skin infections caused by candida and bacteria, and genital candidiasis.

Contraindications: It should not be applied on ulcerative lesions of the face and if hypersensitivity to the gentian violet.

Side effects: skin or genital irritation may occur. It also stains skin and clothing.

Dose and Administration: *Topical*, to the skin. Do not cover the affected area with dressings after application.

Apply every 8 – 12 hours daily for about 3 days.

Storage: at room temperature, in tight containers.

Isoconazole

Cream, 1%, 2%

Indications: cutaneous mycotic infections.

Cautions, Side effects: see notes above

Dose and Administration: apply twice daily.

Itraconazole

Capsule, 100mg

Injection, 100mg/10ml

Indications, cautions, drug interactions, contraindications, and side effects, dose and administration and storage: see section 7.2.

Ketoconazole

Cream, 2 %

Ointment

Shampoo, 2 %

Indications*Cream:* Tinea infections: Rub gently into the affected area once daily. Duration of treatment: Tinea corporis, cruris: 2 weeks; tinea pedis: 6 weeks. Skin fungal infections if use cream and if we use *Shampoo* (ketoconazole 2%): Tinea versicolor: Apply to damp skin, lather, leave on 5 minutes, and rinse (one application should be sufficient)

Cautions: patients should be advised to avoid contact of ketoconazole shampoo with the eyes since irritation may occur. Ketoconazole 2 % cream or shampoo should be used with caution in nursing women, during pregnancy and pediatrics if and hypersensitivity reactions occurred.

Side effects: itching, stinging, or irritation not present before therapy for cream and shampoo; contact dermatitis for cream. *Note: Ketoconazole 2 % cream is intended for topical application to the skin only and should not be applied to the eye nor administered intravaginally.*

Dose and Administration: *Ketoconazole cream* **Adult:** Topical to the affected skin and surrounding area. *Tinea corporis or Tinea cruris, Tinea pedis or Pityriasis versicolor:* once a day. *Candidiasis, cutaneous:* once a day. More resistant cases may require twice a day treatment. *Seborrheic dermatitis:* two times a day.

Paronychia or Tinea barbae or Tinea capitis: two or three times a day. *Note: Safety and efficacy have not been established for pediatric use.*

Ketoconazole shampoo: **Adult:** *Dermatitis, seborrheic:* Topical, twice a week for 2 to 4 weeks. Leave in place for 3 to 5 minutes before rinsing. *Prophylaxis:* once a week every 1 or 2 weeks. *Pityriasis versicolor:* Topical, to the affected skin and surrounding area(s), as a single application. Leave in place for 5 minutes before rinsing. **Child:** safety and efficacy have not been established.

Storage: at room temperature. Protect from freezing.

Ketoconazole + Zinc Pyrithione

Shampoo, 2% + 1% w/w

Indications: seborrheic dermatitis and dandruff.

Cautions: allergic to ketoconazole and pyrithione zinc.

Dose and Administration: Wash hair and scalp daily or at least 2 times per week.

Miconazole Nitrate

Cream, 2 %

Lotion, 2 %

Tincture, 2 %

Indications: fungal skin infections

Cautions, Side effects: see notes above

Dose and Administration: Apply twice daily continuing for 10 days after lesions have healed; nail infections, apply 1 – 2 times daily.

Contraindications: Hypersensitivity to miconazole or any component of the formulation

Storage: at room temperature in a tight container

Nystatin

Cream, 100,000 IU/g

Ointment, 100,000 IU/g

Powder 100,000 IU/g

Indications: skin infections due to *Candida Spp.* (see also notes above)

Cautions: see notes above

Dose and Administration: Apply 2 – 4 times daily

Storage: Cream Store at room temperature; avoid excessive heat (40°C/104°F). Topical powder: Store at 20°C to 25°C (68°F to 77°F); avoid excessive heat (40°C/104°F).

Salicylic Acid

Ointment, 2 %, 5 %, 10 %

Indications: treatment of acne vulgaris, seborrheic dermatitis, psoriasis, and common wart (excluding on the face).

Cautions: avoid contact with eyes, mouth, and mucous membranes; avoid application to large areas. Significant peripheral neuropathy, patients with diabetes risk neuropathic ulcers.

Contraindications: broken or inflamed skin; children under 2 years.

Side effects: stinging, local irritation, and salicylism may occur when large areas are treated particularly in children.

Dose and Administration: *Topical to the skin:* Apply to affected area every 12-24 hours daily starting with the 2% progressively increasing the concentration up to 5% for *acne vulgaris* and up to 10% for *seborrheic dermatitis, psoriasis and common wart*. Apply until it gets better.

Storage: at room temperature, in tight containers.

Selenium Sulphide

Suspension, 2.5 %

Indications: seborrheic dermatitis; treatment of itching and flaking of the scalp associated with dandruff, to control scalp seborrheic dermatitis. Treatment of tinea versicolor.

Cautions: do not apply to damaged skin (risk of systemic toxicity); avoid contact with eyes; do not use within 48 hours of applying any type of hair coloring or permanent waving preparation.

Contraindications: children under 5 years. For external use only; avoid contact with eyes and genital areas. Due to the risk of systemic toxicity, do not use on damaged skin or mucous membranes.

Side effects: local irritation, hair discoloration or loss; absorption may result in systemic toxicity including tremors, weakness, lethargy, pain in lower abdomen, occasional vomiting (symptoms usually resolve within 10 days).

Dose and Administration: *Seborrheic dermatitis:* massage 5 – 10 mg of suspension into wet hair and leave for 2 – 3 minutes before rinsing thoroughly; repeat twice weekly for 2 weeks, then once weekly for 2 weeks, and then only when needed. *Note: To minimize absorption, rinse hair thoroughly after use and remove all traces from skin (including nails).* *Tinea versicolor:* apply the 2.5%

lotion to affected area and lather with small amount of water; leave on skin for 10 minutes, then rinse thoroughly; apply every day for 7 days.

Storage: at room temperature. Freezing should be avoided.

Nystatin

Cream, 1%

Indications: indicated for dermatophyte and yeast infections of the skin and appendages, including tinea versicolor.

Dose and Administration: clean and dry affected area before application. Apply 1-2 times daily until infection is clear (usually 1-2 weeks).

Tolnaftate

Solution, 1%

Indications: tolnaftate is an antifungal agent used topically in the treatment or prophylaxis of various forms of tinea and of pityriasis versicolor.

Note –Tolnaftate is not considered suitable for deep infections in nail beds or hair follicles but it may be used concomitantly with a systemic agent.

Contraindications: hypersensitivity to tolnaftate or any component of the formulation; nail and scalp infections

Cautions: if irritation or hypersensitivity occurs, or if the patient's skin disease does not improve within 10 days or becomes worse during self medication with tolnaftate, treatment should be discontinued and the patient should consult a physician or pediatrician. Tolnaftate preparations should not come in contact with the eyes.

Side effects: irritation, contact dermatitis.

Dose and Administration: Tolnaftate is applied twice daily for 2 to 6 weeks. Repeat treatment may be required.

Storage: It should be stored in tight container at room temperature. Freezing of the solution should be avoided.

Zinc undecenoate + Undecenoic Acid

Ointment, 20 % + 5 %

Powder, 20 % + 2 %

Powder (aerosol), 20 %+ 2 %

Indications: for the treatment of athlete's foot (tinea pedis), jock itch (tinea cruris), and other skin infections caused by dermatophytic fungi (ring worm)

Dose and Administration:*Athlete's foot ringworm: topically:* twice daily after cleansing the affected area, for 4 weeks.*Jock itch: topically,* twice daily after cleansing the affected area, for two weeks.

Note: The ointment or cream should be used at night and the powder may be used during the day.

Antibacterial preparations

Staphylococcal infections of the skin such as impetigo, folliculitis, and furunculi and streptococcal infections such as cellulitis and erysipelas are very common where the climate is hot and humid, where standards of hygiene are compromised, and in immunodeficient patients.

Skin infections such as erysipelas and cellulitis systemic antibacterial treatment is more appropriate because the infection is too deeply seated for adequate penetration of topical preparations.

An ointment containing 2% **mupirocin**, which is active against Gram-positive bacteria, is of value, particularly in impetigo.

Mupirocin is not related to any other antibacterial in use; it is effective for skin infections, particularly those due Gram-positive organisms but it is not indicated for pseudomonal

infection. Although *Staphylococcus aureus* strains with low-level resistance to mupirocin are emerging, it is generally useful in infections resistant to other antibacterials. To avoid the development of resistance mupirocin should not be used for longer than 10 days and its use in hospital should be avoided if possible.

Infected burns should be treated with **silver sulfadiazine** which is bactericidal against both Gram-positive and Gram-negative organisms. Topical preparations containing **neomycin and bacitracin** are also widely used but these carry a risk of sensitization particularly with continued or repeated use.

Topical use of preparations containing antimicrobials which are widely used systemically should be avoided. These include penicillins, sulfonamides, streptomycin and gentamicin which should be reserved for the systemic treatment of infections because of the possibility of including sensitivity and favouring the emergence of resistant organisms.

Clindamycin Phosphate

Solution 1%

Indications: treatment of severe acne.

Dose and Administration: apply a thin film twice daily.

Contraindications: Hypersensitivity to clindamycin, lincomycin, or any component of the formulation.

Side effects: Dryness, burning, itching, scaliness, erythema, or peeling of skin (lotion, solution); oiliness (gel, lotion)

Dose and Administration: Apply a thin film twice daily.

Clioquinol

Cream, 3%

Ointment, 3%

Indications: topically for treating primary skin infections such as impetigo, or skin conditions complicated by infection.

Side effects: allergic or irritant reactions of the skin occur occasionally; staining of fomites and hair can occur.

Dose and Administration: Apply 2- 3 times daily to affected areas.

Cautions **clioquinol** generally appears to be well tolerated following topical application to the skin. Local irritation, rash, and sensitivity reactions have been reported occasionally.

Storage: store at a temperature less than 30°C; freezing should be avoided.

Erythromycin

Cream, 2%

Ointment, 1%

Solution, 2%

Indications: treatment of acne vulgaris.

Dose and Administration: Apply over the affected area twice daily after the skin has been thoroughly washed and patted dry

Contraindications: hypersensitivity to erythromycin, any macrolides antibiotics, or any component of the formulation.

Storage: store solution at 15-30 °C, and ointment at a temperature less than 27°C.

Fusidic Acid

Cream, 2%

Indications: for staphylococcal infections and treatment of primary and secondary skin infections caused by susceptible organisms.

Cautions: should be used for acute skin infections (5 days) and not for prolonged periods. Prolonged use may result in superinfection (including fungal infections). *Discontinue use if superinfection occurs; evaluate and treat.*

Side effect: prolonged use may result in superinfection (including fungal infections). Discontinue use if superinfection occurs; evaluate and treat appropriately and local hypersensitivity reactions.

Dose and Administration: Apply 3 - 4 times daily.

Storage: Store at 15°C to 25°C.

Gentamicin

Cream, 0.1%

Ointment, 0.3%

Indications: treatment of superficial infections of the skin caused by susceptible bacteria.

Cautions: hypersensitivity to the drug.

Dose and Administration: Apply 3 - 4 times per day to affected area.

Storage: store at 2-30°C. But refrigeration is not recommended.

Metronidazole

Cream, 0.75%, 1%

Gel, 1%

Lotion, 1%

Indications: treatment of inflammatory lesions and erythema of rosacea.

Cautions and Contraindications: A history of hypersensitivity reactions to any of the components. Use with caution in those with blood dyscrasias. Avoid contact with the eyes.

Side effects: tearing of the eyes, transient erythema, dryness, burning and skin irritation.

Dose and Administration: *Acne rosacea: Topical:*

0.75%: Apply and rub thin film twice daily, morning and evening, to entire affected areas after washing. Significant therapeutic results should be noticed within 3 weeks. 1%: Apply thin film to affected area once daily.

Mupirocin

Ointment, 2%

Indications: bacterial skin infection (see also notes above)

Contraindications: mupirocin is contraindicated in patients with a history of hypersensitivity to the drug or any ingredient in the formulation.

Cautions: renal impairment; may sting

Dose and Administration: *Skin infection:* apply up to 3 times daily for up to 10 days. *Note: contains macrogol and manufacturer advises caution in renal impairment*

Storage: at room temperature

Neomycin + Bacitracin

Ointment, 4 mg + 500,000 IU

Powder, 0.25 % + 9.5 %

Indications: superficial bacterial infections of the skin due to staphylococci and streptococci

Cautions: avoid application to substantial areas of skin or to broken skin (risk of significant systemic absorption), over growth of resistant organisms on prolonged use.

Side effects: sensitization, especially to neomycin, causing reddening and scaling, anaphylaxis reported rarely; systemic absorption leading to irreversible ototoxicity, particularly in renal impairment.

Dose Administration: Apply thin layer 3 times daily.

Storage: at room temperature.

Nitrofurazone

Gauze Dressing

Indications: as an adjunctive therapy for second and third degree burns when resistance to other agents is a real or potential problem; in skin grafting when bacterial contamination

may cause graft rejection or donor site infection, especially in hospitals with a history of resistant bacteria.

Cautions: if over growth of nonsusceptible organisms occur, or if irritation, sensitization, or superinfection develops, treatment should be discontinued. Caution should be taken in patient with renal function impairment.

Side effects: contact dermatitis

Dose and Administration:Adult:*Burns or Skin infections:* Topical directly to lesion or place on gauze depending on the usual dressing technique

Child: safety and efficacy have not been established

Storage: at room temperature in a well-closed container. Protect from freezing.

Silver Sulphadiazine

Cream, 1 %

Indications: prophylaxis and treatment of infection in burns.

Cautions: renal or hepatic impairment; G6PD deficiency; breastfeeding.

Contraindications: hypersensitivity to sulfonamides; pregnancy; neonates.

Side effects: allergic reactions include rashes, burning and itching; argyria and sulfonamide – induced systemic toxicity, including blood disorders following application to large areas or prolonged use; transient leucopenia reported.

Dose and Administration: Apply using aseptic technique daily (more frequently if volume of exudate is large) whilst there is a possibility of infection, or until healing is complete. Therapy is usually continued until healing is progressing well or until the site is ready for grafting

Storage: At room temperature. Discard, if the cream changes its colour (dark) up on storage.

Sodium Fusidate

Ointment, 2 %

Indications: staphylococcal skin infections and treatment of primary and secondary skin infections caused by susceptible organisms

Cautions: avoid contact with eyes and treatment of primary and secondary skin infections caused by susceptible organisms.

Contraindications: hypersensitive to fusidates and hypersensitivity to fusidic acid or any component of the formulation.

Side effects: rarely hypersensitivity reactions

Dose and Administrations: Apply 3 – 4 times daily,

Storage: store in airtight containers at a temperature of 2°C to 8°C. Protect from light.

Tetracycline

Ointment, 3 %

Indications: bacterial skin infections

Cautions: sensitivity to tetracyclines; over growth with non-susceptible organisms; stains clothing

Side effects: rarely local hypersensitivity reaction

Dose and Administration: Adult: *Antibacterial (topical): Topical*, to the skin, one or two times a day.

Child: see adult dose.

Storage: store at room temperature in a well-closed container. Protect from freezing.

Scabies and Pediculicides

Permethrine are used for Scabies (*Sarcoptes scabiei*). Aqueous preparations are preferable to alcoholic lotion, which are not recommended owing to irritation of excoriated skin and the genitalia. *Older preparations include benzyl benzoate, which is an irritant and should be avoided in children; it is less effective than Permethrine.*

The itch of scabies persists for some weeks after the infestation has been eliminated and antipruritic treatment may be required. Application of **crotamiton** can be used to control itching after treatment with more effective acaricides, but caution is necessary if the skin is excoriated.

Head and body lice are readily treated with **permethrin**; **malathionis** effective against pubic lice. **Benzyl benzoate** may be used for all lice infections.

Benzyl Benzoate

Lotion, 25 %,

Indications: scabies; head, body and pubic lice.

Cautions: avoid contact with face, eyes, mucous membranes and urethral meatus. Do not apply to inflamed skin or weeping surfaces; not recommended for children; breastfeeding (withhold during treatment).

Side effects: slight local irritation, transient burning sensation, occasionally rashes. Frequent use causes contact dermatitis.

Dose and Administration: *Scabies: Adult:* apply from neck down at night for 2 nights; on each occasion wash off after at least 24 hours. A single treatment is usually effective but, if necessary, may be repeated after 1 week.

Dilute with an equal amount of water for children (12.5%), and 1 part with 3 parts of water for infants (6%). *Pediculosis: Adult:* apply to affected area and wash off 24 hours later; further applications possibly needed after 7 and 14 days.

Storage: At room temperature, in airtight, light resistant containers. Protect from heat.

Crotamiton

Cream, 10 %

Lotion, 10 %

Indications: topical treatment of scabies and pruritus.

Cautions: crotamiton should not be applied to acutely inflamed skin or raw, weeping surfaces and If primary irritation or hypersensitivity occurs, treatment. The drug is for topical use only and should *not* be administered orally or intravaginally. It should be discontinued and the drug should be removed with soap and water. Crotamiton should be used during pregnancy only when clearly needed. Contact with the face, eyes, mucous membranes and urethral meatus should be avoided.

Contraindications: a history of sensitivity or allergy to the drug and in those who exhibit a primary irritation response to topically applied medications. Acute exudative dermatoses

Side effects: slight local irritation, allergic skin sensitivity may occur with prolonged use

Dose and Administration: Crotamiton, in the form of a 10 % cream or lotion is applied topically. The drug should not be administered orally. A thin layer of the 10 % cream or lotion should be applied uniformly and massaged gently into all skin surfaces from the neck to the toes. A second coat of the cream should be applied after 24 hours. In adults, 30 g of the cream for one application; a proportionately smaller amount is used in children. Treatment may be repeated after 7 – 10 days if mites appear or new lesions develop. The patient should bath 48 hours after the last application to remove the drug. *Note: Before applying crotamiton, advise the patient to bath with soap and water, taking care to scrub and remove scaling or crusted detritus, then towel dry.*

Storage: It should be stored in tight, light resistant containers at a room temperature.

Gamabenzene Hexachloride (Lindane)

Cream, 1 %

Indications: for treatment of pediculosis (lice) infestation caused by *Pediculus humanus var. capitis* (head louse) and *phthirus pubis* (pubic or crab louse) and their ova. It is also indicated for the treatment of scabies infestation caused by *Sarcoptes scabies*.

Cautions: caution is required in children and infants. It is not recommended for use in premature neonates. Caution should be taken in patients with convulsive disorders, in those who are sensitive to lindane and in patients with skin rash or raw or broken skin.

Side effects: skin irritation not present before therapy (if it is applied in correctly and repeatedly), itching of skin, CNS toxicity (if absorbed systemically) - convulsions, dizziness, clumsiness, or unsteadiness, fast heartbeat, muscle cramp, nervousness, restlessness, or irritability, vomiting.

Dose and Administration: pediculicide, scabicide-*Topical*, to the skin, as a 1% cream for one application.

Storage: at room temperature in a tight container.

Malathion

Shampoo, 1%,

Indications: scabies, head lice and crab lice

Cautions: avoid contact with eyes; do not use on broken or secondarily infected skin; children under 6 months, medical supervision required

Contraindications: use in neonates and/or infants; hypersensitivity to Malathion.

Side effects: skin irritation and hypersensitivity reactions; chemical burns also reported

Dose and Administration: Head lice: rub 0.5% preparation into dry hair and scalp, allow to dry naturally, and remove by washing after 12 hours repeat application after 7 days. *Crab*

lice: apply 0.5% aqueous preparation over whole body, allow to dry naturally, wash off after 12 hours or overnight; repeat application after 7 days.

Storage: Read the manufacturer's life information

Permethrin

Cream, 5 %

Lotion, 1%, 5%

Indication: scabies, head and body lice

Cautions: do not use on inflamed or broken skin: avoid contact with eyes; breast feeding (with hold during treatment). That means the drug is for external use only and should *not* be administered orally.

Side effects: local irritation; rarely rashes and oedema

Dose and Administration: *Scabies and body lice*: apply cream over whole body and wash off after 8 – 12 hours.

Note: for external use only.

Storage: store between 15 to 25°C. Protect from freezing.

Sulphur

Ointment, 5 %, 10 %

Indications: for the treatment of seborrheic dermatitis, scabies especially infants under 2 months of age and in pregnant and nursing women. It is also indicated as an aid in the treatment of acne vulgaris.

Cautions: sensitivity to sulfur.

Drug interactions: medicated soaps, acne preparations or preparations containing a peeling agent, such as benzoyl peroxide, resorcinol, salicylic acid, tretinoin, after shave lotions, astringents, perfumed toiletries, shaving creams or lotions, cosmetics, isotretinoin, medicated cosmetics or “cover-ups”, topical mercury compounds.

Side effect: skin irritation not present before therapy, redness and peeling of skin.

Dose and Administration: **Adult and Child** (>2 years)

Antiacne agent: topical, to the skin, as a 0.5% ointment as needed. *Antiseborrheic or keratolytic: topical*, to the skin, as to 10% ointment once or two times a day.

Scabicides: Topical, to the entire body from the neck down, as 6% sulfur in petrolatum at bedtime for 3 nights, patients may bath before each application and should bath after 24 hours following the last application to remove the drug.

Storage: at room temperature, protect from freezing

Antiviral

Acyclovir

Ointment, 5%

Indications: treatment of mucocutaneous herpes simplex infections, herpes labialis, for serious skin and mucosal (including genital) herpetic infections.

Cautions: indiscriminate use of topical aciclovir may result in the emergence of resistance. It has no role in the treatment of herpes zoster.

Side effects: mild pain, burning or stinging often occurs when applied to ulcerated lesions. Erythema, itch, mild dryness and skin hypersensitivity rashes occur.

Dose and Administration: *topical: Adult:* 1.3cm ribbon of ointment for a 10cm square surface area every 3 hours (6 times/day) for 7 days.

Storage: store at room temperature.

Others

Fluorouracil

Cream, 2%, 4%

Indications: management of actinic or solar keratoses and superficial basal cell carcinomas.

Contraindications.hypersensitivity to fluorouracil or any component of the formulation; dihydropyrimidine dehydrogenase (DPD) enzyme deficiency; pregnancy.

Dose and Administration: apply 10 minutes after washing, rinsing, and drying the affected area. Apply using fingertip (wash hands immediately after application) or nonmetal application. Avoid eyes, nostrils, and mouth. Do not cover area with an occlusive dressing.

Storage: store at controlled room temperature.

18.2. Anti-Inflammatories, Topical

Topical corticosteroids often produces dramatic suppression of skin diseases, such as eczema, infantile eczema, atopic dermatitis, dermatitis herpetiformis, contact dermatitis, seborrhoeic dermatitis, neurodermatitis, some forms of psoriasis, and intertrigo, in which inflammation is a prominent feature. However, the disease may return or be exacerbated when corticosteroids are withdrawn.

Application of the corticosteroids to the skin has lead to loss of skin collagen, subcutaneous atrophy local hypopigmentation of deeply pigmented skins. Topical corticosteroids should not be applied with an occlusive dressing to large areas of the body because of the risk of systemic absorption. Also they should not be used for the treatment of rosacea and should not be used indiscriminately for pruritus. Corticosteroids should not be applied to ulcers of the leg and long term topical use is best avoided, especially in children. Patients should be advised that topical corticosteroids should be applied sparingly in thin layers, by smoothing gently into the skin preferably after a bath and that no benefit is gained from more frequent than twice daily application or by vigorous rubbing. Treatment should be discontinued as soon as a positive result is obtained.

Cautions: Avoid prolonged use of topical corticosteroids in the face (keep away from eyes). In children avoid prolonged use and use potent or very potent corticosteroids under special supervision; extremely caution is required in dermatoses of infancy including naapy rash-treatment should be limited to 5-7 days. The use of potent and very potent corticosteroids in psoriasis can result in rebound relapse, development of generalized postural psoriasis and local and systemic toxicity.

Contraindications: these drugs are contraindicated in untreated bacterial, fungal and viral skin lesions, in acne rosacea and perioral dermatitis; potent cortecosteroids are contraindicated in wide spread plaque psoriasis.

Dose Administration:*see above.* Topical corticosteroids are spread thinly on the skin; the length of cream or ointment expelled from a tube may be used to specify the quantity to be applied to a given area of skin. This length can be measured interms of a fingertip unit. One fingertip unit (approximately 500 mg) is sufficient to cover an area that is twice of the flat adult palm.

<i>Suitable quantities of corticosteroid preparations to be prescribed for specific areas of the bodies</i>	
	Creams and Ointments
Face and nack	15 to 30 g
Both hands	15 to 30 g
Scalp	15 to 30 g
Both arms	30 to 60 g
Both legs	100 g
Trunk	100 g
Groins and genitalis	15 to 30 g
<i>These amounts are usually suitable for an adult for a single daily application for two weeks</i>	

Topical corticosteroid preparation potencies are a result of the formulation as well as the corticosteroid.

Betamethasone

Betamethasone Dipropionate, Cream, 0.025%, 0.05%

Betamethasone Valerate, Cream, 0.1%; Ointment, 0.1%; Scalp application, 0.1%

Indications: inflammatory dermatoses such as seborrheic or atopic dermatitis, neurodermatitis, anogenital pruritus, psoriasis, inflammatory phase of xerosis.

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply thin film 2-4 times per day. Therapy should be discontinued when control is achieved; if no improvement is seen, reassessment of diagnosis may be necessary.

Clobetasol Propionate

Cream, 0.05% w/w

Ointment, 0.05% w/w

Scalp Application, 0.1%

Indications: short term relief of inflammation of moderate to severe corticosteroid-responsive dermatoses (very high-potency topical corticosteroid).

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: discontinue when control is achieved; if improvement not seen within 2 weeks, reassessment of diagnosis may be necessary.

Adult and Child \geq 12 years: Steroid responsive dermatoses: apply twice daily for up to 2 weeks (maximum dose: 50 g/week).

Desoximethasone

Cream, 0.05% 0.25%

Gel, 0.05%

Lotion, 0.25%

Ointment, 0.25%

Indications: relieves inflammation and pruritic symptoms of corticosteroid-responsive dermatoses (intermediate-to high-potency topical corticosteroid).

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply a thin film to affected area twice daily. *Ointment:* **Child** ≥ 10 years and **Adult:** apply a thin film to affected area twice daily.

Dexamethasone sodium Phosphate

Cream, 0.1%

Indications: systemically and locally for chronic swelling; allergic diseases.

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply 1-4 times /day.

Flucinolone Acetonide

Cream, 0.025%

Ointment, 0.025%

Indication: Inflammatory skin disorders such as eczema, psoriasis

Caution and contraindications: see notes above

Dose and administration: Apply thinly 2-4 times daily, reducing strength as condition responds.

Hydrocortisone Acetate

Cream 1%

Ointment 1%

Indications: contact dermatitis, atopic dermatitis (eczema), lichen planus; intractable pruritus and phototoxic reactions, including polymorphic light eruptions and actinic prurigo; short-term treatment of psoriasis of the face and flexures.

Cautions: children (avoid prolonged use); occlusive dressings increase penetration into keratinized lesions (use occlusive dressing only at night and for no longer than 2 days; avoid use on weeping lesions); secondary infection requires treatment with an appropriate antimicrobial.

Contraindications: untreated skin infections or broken skin; rosacea, acne, perioral dermatitis.

Side effect: exacerbation of local infection; atrophic changes less likely with mild corticosteroids, but infants and children particularly susceptible. Contact dermatitis (burning and itching of skin, apparent chronic therapeutic failure), folliculitis, furunculosis, pustules, pyoderma, or vesiculation (painful, red or itchy, pus containing blisters in hair follicles), hyperaesthesia (increased skin sensitivity). Burning, dryness, irritation, itching, or redness of skin, mild and transient increased redness or scaling of skin lesions, minor and transient skin rash.

Dose and Administration:Adult: *topical*, to the skin, as a 0.1 - 1% cream or 0.5 - 2.5% ointment one to four times a day.**Child** 2 years of age and older: *topical*, to the skin, as 0.5% cream one to four times a day or as a 1% ointment one or two times a day.

Note: Advise patient not to use it in or around the eye.

Storage: at room temperature in a well closed container, protect from freezing.

Mometasone furoate

Cream, Lotion, Ointment 0.1 %

Indications: see under hydrocortisone and notes above

Cautions; Side effects, Contrindications: see under hydrocortisone and notes above.

Dose and Administration: Adult: *Topical*, to the site, once a day. **Child:** dosage has not been established.

Storage: Store between 2 °C to 30°C in a well-closed container.

Note: For external use only. Do not use in or around the eye

Nimesulide

Gel (transdermal), 1%

Indication: Symptomatic relief of pain associated with sprains and acute traumatic tendinitis.

Cautions: Pregnancy, breast feeding mother and children under 12 years, should not be applied to skin wounds or open injuries. Simultaneous use with other topical creams.

Contraindications: Known hypersensitivity to nimesulide or to any other excipients in the gel; use in patients in whom aspirin, or other medicinal products inhibiting prostaglandin synthesis, induced allergic reactions such as rhinitis, urticaria or bronchospasm.

Dosage and administration: Adults: It should be applied in a thin layer to the affected area 3-4 times daily and massaged until it is completely absorbed. However it may vary depending on the size of the affected area and response. Therapy should be reviewed after 4 weeks.

Children under 12 years: It has not been studied in children. Therefore, safety and efficacy have not been established and the product should not be used in children.

Side-effects: mild or moderate local irritation, erythema, rash, desquamation, pruritus and related local reactions at the application site. Mild, but transient skin discoloration and staining of clothing have been noted.

Storage: Do not store above 30°C.

Pimecrolimus

Cream, 1%

Indications: short-term and intermittent long-term treatment of mild to moderate atopic dermatitis in patients not responsive to conventional therapy or when conventional therapy is not appropriate.

Cautions: do not apply to areas of active cutaneous viral infection. Minimize or avoid natural/artificial sunlight exposure. *Not recommended in children < 2 years of age.*

Drug interactions: CYP3A inhibitors.

Contraindications: hypersensitivity reactions.

Side effects: headache, pyrexia, burning at application site, nasopharyngitis, cough, bronchitis.

Dose and Administration: **Adult and Child \geq 2 years:** *Topical:* Apply thin layer to affected area twice daily; rub in gently and completely.

Note: Continue as long as signs and symptoms persist; discontinue if resolution occurs; re-evaluate if symptoms persist > 6 weeks.

Storage: store at room temperature. Do not freeze.

Triamcinolone

Ointment, 0.1%

Indications: inflammatory dermatoses responsive to steroids.

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply thin film to affected areas 2-4 times/day.

18.3. Anti-infective/Anti-inflammatory Combinations

Combination of an imidazole and a mild corticosteroid (such as hydrocortisone 1%) may be of value in the treatment of eczematous intertrigo and in the first few days only of a severely inflamed patch of ringworm.

Such combinations should only be used under supervision because of the risk that signs of resistant infection may be suppressed.

Clioquinol+ Hydrocortisone

Cream, 3 % + 0.5 or 1 %

Ointment, 3% + 0.5% or 1%

Indications: see notes above, and under hydrocortisone

Cautions: see notes above and under section. 16.2

Dose and Administration: *Topical*, Apply thinly 1 – 2 times daily

Clotrimazole + Hydrocortisone

Cream, Ointment, 1% + 1%

Indications: athlete's foot and fungal infection of skin folds with associated inflammation; see notes above and under hydrocortisone

Cautions, Side effects, Contraindications; see notes above and section 16.2 and clotrimazole (sec. 16.1)

Dose and Administration: *Topical*, apply thinly 1 – 2 times daily

Storage: protect from light.

Dexamethasone Acetate + Clotrimazole

Cream, 0.4mg +100mg

Indication: Inflammation and infection of skin involving fungi.

Dosage and administration: Apply twice daily

Fluocinolone Acetonide + Neomycin

Cream, 0.025% w/w+0.5% w/w

Indications: Indicated for the treatment of corticosteroid-responsive dermatoses with secondary infection. (Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.)

Cautions: Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of the more potent steroids, Avoid contact with the eyes, The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician, Because of the concern of nephrotoxicity and ototoxicity associated with neomycin, this combination product should not be used over a wide area or for extended periods of time.

Contraindications: Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation. This product should not be used in the external auditory canal if the eardrum is perforated.

Side effects: Burning; Itching; Irritation; Dryness; Folliculitis; Hypertrichosis; Acneiform eruptions; Hypopigmentation; Perioral dermatitis; Allergic contact dermatitis; Maceration of the skin; Secondary infection; Skin atrophy; Striae; Miliaria; Ototoxicity; Nephrotoxicity.

Dose and administration: Generally applied to the affected area as a thin film from two to four times daily depending on the severity of the condition.

Storage: Store at room temperature; avoid freezing and excessive heat, above 40°C

Fusidic Acid/ Sodium Fusidate + Bethamethasone

Cream, 2% +0.064%,

Ointment, 2% +0.064%, 2% +1%

Indications: Inflammatory dermatoses where bacterial infection is present or likely to occur eg, atopic eczema, discoid eczema, stasis eczema, seborrhoeic dermatitis, contact

dermatitis, lichen simplex chronicus, psoriasis, discoid lupus erythematosus.

Caution: Children, Atrophic striae likely to occur on prolonged application (>4 weeks). Systemic absorption resulting in adrenal suppression may occur especially under occlusion with weekly doses of >30 g. Avoid prolonged use on flexures and intertriginous areas.

Contraindication: Hypersensitive to the medicine, or any component of the formulation. Viral disease of the skin, perioral dermatitis, acne rosacea, fungal skin infections and ulcerative conditions.

Side effect: Skin irritation, eg itching, burning, stinging; Rash; Worsening of eczema; Skin thinning; thread veins or stretch marks (prolonged use only); Groupings of fine blood vessels becoming prominent under the skin (telangiectasia); Inflammation of hair follicles (folliculitis); Decreased skin pigmentation at application area, Puffiness of skin on the face.

Dose and administration: Uncovered lesions: Apply 2 - 3 times a day. Covered lesions: Less frequent applications may be adequate.

Note: Atrophic striae likely to occur on prolonged application (>4 weeks). Systemic absorption resulting in adrenal suppression may occur especially under occlusion with weekly doses of >30 g. Avoid prolonged use on flexures and intertriginous areas.

Mupirocin+BetamethasoneDipropionate

Ointment, 2% +0.05% w/w

Indication: For the treatment of primary and secondary skin infections, such as: Impetigo, Hypoderma, Cellulitis, Balanitis, Folliculitis, Furunculosis, Styme, Abrasions, Infected burnings, infected psoriasis, infected ulcers

18.4. Keratolytics/Caustics and Antiacne Agents

Benzoyl peroxide is a keratolytic drug with bacteriostatic activity against *propionibacterium acnes* and *staphylococcus epidermidis*. It is used mainly in the treatment of acne usually in topical preparations containing 2.5 to 10 %. Adverse effects include initial stinging effect & contact sensitization. Caution is required when applying it near the eyes, the mouth and other mucous membranes, and to sensitive areas of the neck.

Salicylic acid may be used in all hyperkeratotic and scaling conditions to enhance the rate of loss of surface scale. Coal tar is more active than salicylic acid and has anti-inflammatory and antiscaling properties. Some preparations contain both preparations of **Glutaraldehyde**, and combination of **salicylic acid, lactic acid** and **polidocanol** are available. They are suitable for the removal of warts on hands and feet. The topical retinoids, which include tretinoin and isotretinoin, are effective in treating acne vulgaris in which comedones, papules and pustules predominate, but are usually inadequate in eradicating severe pustular or deep nodular cystic lesions. They act by normalizing keratinisation, but their exact mechanism of action remains to be fully elucidated. Comedone formation is inhibited and they thus provide prophylactic treatment for acne. The antimicrobial effect on *Propionibacterium acnes* and its influence on follicular hyperkeratosis make azelaic acid a suitable topical agent for moderate acne vulgaris.

Podophyllum resin is a mixture of resins, strongly irritant to normal skin and mucous membranes. It has an antimitotic action and is used as paint in the topical treatment of soft venereal warts, or as an ointment (with salicylic acid) for plantar and non mucosal warts. The main active component of podophyllin is podophyllotoxin. Purified podophyllotoxin is being used in

newer preparations at low concentration with good effect. It is also useful for the treatment of molluscum contagiosum.

Adapalene

Gel, 0.1%

Indication: It helps the skin renew itself. Adapalene topical is used to treat severe acne in people who are at least 12 years old.

Contraindication: Allergic to adapalene, products that contain alpha hydroxy or glycolic acid

Caution: Sunburned, windburned, dry, chapped, irritated, or broken skin.

Dose and Administration: Applied once daily in the evening. Apply the medication in a thin layer to the entire face or other affected skin areas.

Storage: At room temperature away from moisture and heat.

Azelaic Acid

Cream, 20%

Indications: topical treatment of mild to moderate inflammatory acne vulgaris and rosacea.

Cautions: about 2% of applied azelaic acid is systemically absorbed and excreted unchanged in urine; a daily application of 10 g cream (2 g azelaic acid) should not be exceeded; avoid contact with the eyes; safety and efficacy have not been proven for use for more than 6 months.

Contraindications: hypersensitivity to propylene glycol or azelaic acid.

Side effects: local skin irritation (redness, itching, scaling, burning) may occur initially, but usually regresses. If persistent, reduce frequency of application.

Hypersensitivity and photosensitivity reactions have been reported.

Dose and Administration: apply to clean skin twice daily; maximum 10 g/day (2 g azelaic acid). *Sensitive skin:* start with daily applications and gradually increase to twice daily. Improvement occurs after 4 weeks.

Storage: store at room temperature.

Benzoyl peroxide

Gel, 2.5 %, 5 %, 10 %

Solutions, 2.5 %, 5 %, 10 %

Indications: mild to moderate acne and as an adjunct to oral therapy in more severe cases.

Cautions: avoid contact with eyes, mouth, and mucous membranes; avoid use of occlusive dressings; avoid excessive exposure to sunlight.

Side effects: initial irritation common but subsides with continued use; rarely, contact sensitivity occurs, occasionally even 1 application can cause severe irritation; may bleach fabrics, hair and skin.

Dose and Administration: Apply 1 – 2 times daily preferably after washing with soap and water, start treatment with lower – strength preparations

Storage: at 2 to 8°C in a container that has been treated to reduce static charges and that has a device for the release of excess pressure. *Note: caution, Benzoyl peroxide on heat.*

Coal Tar + Salicylic Acid

Ointment, 2 % + 5 % or 2 % + 10 %

Indications: hyperkeratotic skin disorders associated with psoriasis and occasionally chronic atopic eczema.

Cautions: avoid eyes, mucous, genital or rectal areas and broken or inflamed skin. Use suitable chemical protection gloves for extemporaneous preparation. Salicylate toxicity. If

large areas of skin are treated; salicylate toxicity may be a hazard.

Side effects: skin irritation and acne-like eruptions, photosensitivity; stains skin, hair and fabric, excessive drying.

Dose and Administration: Apply 1 – 2 times daily.

Glutaraldehyde

Solution, 10 %

Indications: warts, particularly planar warts (see also notes above)

Cautions: protect surrounding skin, not for application to face, mucosa, or anogenital areas.

Side effects: rashes, skin irritation (discontinue if severe), stains skin brown.

Dose and Administrations: Apply twice daily.

Storage: store at a temperature not exceeding 15°C.

Podophyllin Paint

Solution, 25%

Indications: topical treatment of benign growths including external genital and perianal warts, papillomas, fibroids.

Cautions: avoid application to healthy tissues; do not use for treating facial or oral mucosal warts; use of large amounts of drug should be avoided; should not be applied to or near mucous membranes.

Contraindications: pregnancy, diabetic patient.

Side effects: pruritus, nausea, vomiting, abdominal pain, and diarrhea.

Dose and Administration: 10% to 25% solution in compound benzoin tincture; apply drug to dry surface, use 1 drop at a time allowing drying between drops until area is covered; total volume should be limited to < 0.5 ml per treatment session.

Storage: store at room temperature.

Retinoic Acid (Tretinoin)

Cream, 0.025%

Gel, 0.01%, 0.025%

Lotion, 0.025%, 0.05%

Ointment, 0.05%

Indications: treatment of acne vulgaris, photodamaged skin; palliation of fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin as part of a comprehensive skin care and sun avoidance program.

Caution: eczema.

Drug interactions: topical application of sulphur, benzoyl peroxide, salicylic acid, resorcinol, photosensitizing medications (thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides).

Contraindications: hypersensitivity to retinoic acid.

Side effects: most likely to occur with incorrect use. Transient burning, excessive redness, dryness, oedema or blistering, heightened susceptibility to sunlight and temporary hyper and hypopigmentation, apparent exacerbation of inflammatory lesions.

Dose and Administration: apply to dry skin, after thorough cleansing, before bedtime. Frequency of application should be individualized.

Storage: store at 25 °C; gel is flammable, keep away from heat and flame.

Salicylic Acid

Ointment, 2%, 5%, 10%

Indications: treatment of acne vulgaris, seborrheic dermatitis, psoriasis, and common wart (excluding on the face).

Cautions: avoid contact with eyes, mouth, and mucous membranes; avoid application to large areas.

Contraindications: broken or inflamed skin; children under 2 years.

Side effects: stinging, local irritation, and salicylism may occur when large areas are treated particularly in children.

Dose and Administration: *Topical to the skin:* Apply to affected area every 12-24 hours daily starting with the 2% progressively increasing the concentration up to 5% for *acne vulgaris* and up to 10% for *seborrheic dermatitis, psoriasis and common wart*. Apply until it gets better.

Storage: at room temperature, in tight containers.

Salicylic Acid +Betamethasone Dipropionate

Ointment/Lotion, 2% +0.06%

Indications: Subacute and chronic hyperkeratotic and dry dermatoses. Betamethasone Dipropionate is a synthetic fluorinated corticosteroid. In combination with salicylic acid it is indicated for the treatment of chronic lichenified eczema, lichen planus, lichen simplex and non bullous ichthyosiform erythroderma. It is also effective in the less responsive conditions such as psoriasis of the scalp and chronic plaque psoriasis of the hands and feet but excluding widespread plaque psoriasis. Topical salicylic acid softens keratin, loosens cornified epithelium and desquamates the epidermis.

Cautions: Pregnancy and breast feeding mother. Not to be used in or near the eyes. Avoid contact with mucous membranes. Prolonged topical corticosteroid treatment may result in systemic corticosteroid effects; may also lead to formation of striae or atrophy of the skin or subcutaneous tissue. Absorption of corticosteroid through the skin is increased when used with occlusive dressings. Caution when used in patients with stasis dermatitis or other skin diseases with impaired blood circulation.

Contraindications: Rosacea, acne, perioral dermatitis, perianal and genital pruritus. Hypersensitivity to any of the ingredients of the preparations contra-indicates their use as does tuberculosis and most viral lesions of the skin, particularly herpes simplex, vaccinia, varicella. It should not be used in napkin eruptions, fungal or bacterial skin infections without suitable concomitant anti-infective therapy.

Side effects: Pruritus, irritation, folliculitis, maceration of skin, skin atrophy, hypertrichosis, acneiform eruptions, secondary infection, hypopigmentation, perioral dermatitis, allergic contact dermatitis, striae and miliaria.

Dose and administration: Adults: In most cases a few drops should be applied to the affected areas once or twice daily and massaged gently and thoroughly into the skin. For some patients adequate maintenance therapy may be achieved with less frequent application.

It is recommended that preparations are prescribed for two weeks. The maximum weekly dose should not exceed 60g. **Children:** Dosage in children should be limited to 5 days.

Storage: Do not store above 25°C.

Silver Nitrate + Potassium Nitrate

Toughened, 95% + 5%

Indications: cauterization of wounds and sluggish ulcers, removal of granulation tissue and warts; aseptic prophylaxis of burns.

Cautions: do not use application sticks on the eyes; prolonged use may result in skin discoloration.

Contraindications: not for use on broken skin, cuts, or wounds

Side effects: burning and skin irritation, staining of the skin, hyponatremia, methemoglobinemia.

Dose and Administration: *Sticks:* Apply to mucous membranes and other moist skin surfaces only on area to be treated 2 - 3 times/ week for 2- 3 weeks.

Storage: store in a tight, light- resistant container and in dry place.

18.5. Medicines for Psoriasis and Eczema

Zinc oxide is mildly astringent and is used topically as a soothing and protective application in eczema and slight excoriations and for hemorrhoids. It is usually mixed with purified talc, which is used in massage to allay irritation and prevent chafing. Zinc oxide reflects UV radiation and is used as sunscreens.

Ichthammol is usually used in chronic lichenified forms of eczema or to control pruritus.

Dithranol is an effective, but difficult-to-administer, topical treatment for psoriasis. When used optimally, responsive plaques should clear with approximately 3 weeks of treatment. Dithranol needs to be incorporated into a suitable base to minimize side-effects. The presence of salicylic acid is necessary to prevent its inactivation. It is most commonly used in a stiff paste.

Vitamine D has both keratinocyte differentiation and inflammatory modifying effects. The synthetic analogue of 1, 25-dihydroxyvitamin D₃, calcipotriol, is less calcaemic than the parent compound. It has been shown to be effective in plaque psoriasis.

Calcipotriol

Cream, Ointment, Scalp application, 0.005%

Indication: treatment of moderate plaque psoriasis.

Cautions: hypercalcaemia.

Contraindication: hypersensitivity to calcipotriol.

Side effects: skin irritation and allergic rashes, facial dermatitis with applications to the face; indiscriminate use of calcipotriol can cause hypercalcaemia.

Dose and Administration: Apply twice daily to affected areas to a maximum of 100 g/week. Wash off immediately if face becomes contaminated.

Dithranol

Paste, 1%

Scalp application, 0.25%, 0.5%

Indications: treatment of psoriasis

Cautions and Contraindications: dithranol is an irritant; avoid contact with the eyes and tender parts of the body. Its use on the face should be limited to carefully supervised inpatient management only. It should not be used on acute eruptions or excessively inflamed areas.

Side effects: irritation of normal and psoriatic skin. Fever, rigors, flu-like symptoms and lymphadenopathy. It stains skin, hair, nails, fabrics and fomites a reddish brown color.

Dose and Administration:*Skin application:* Apply sparingly only to psoriatic lesions and rub gently and carefully into the skin until absorbed. Avoid applying an excessive quantity, which may cause unnecessary soiling and staining of the clothing or bed linen.*Scalp application:* comb hair to remove scalar debris, wet hair and after suitably parting, rub cream well into the lesions, taking care to prevent the cream from spreading on to the forehead.*Remove by washing or showering; optimal period of contact will vary according to the strength used and the patient's response to treatment. Continue treatment until the skin is entirely clear (i.e. when there is nothing to feel with the fingers and the texture is normal).*

Storage: store at a temperature of 8-15 °C in airtight containers.

Ichthammol

Ointment, 10 %

Indications: for treatment of chronic lichenified eczema.

Side effect: skin irritation.

Dose and Administration: topically, apply to the skin 1-3 times daily.

Zinc Oxide

Ointment 15 %

Lotion 15 %

Indication: protective coating for mild skin irritations and abrasions, smoothing and protective to promote healing of chapped skin, diaper rash.

Contra indications: Hypersensitivity to zinc oxide or any component of the formulation

Side effects: Skin sensitivity, irritation

Dose and administration: Adult, Child, Protectant: Topical: Apply as required to affected areas several times daily

Zinc oxide + Talc

Paste, 15 % + 25 %

Indications: treats and prevents diaper rash, protects minor skin irritation.

Cautions: avoid contact with eyes and face, do not use on broken skin.

Storage: store at a temperature of 15-25°C.

18.6. Antipruritics

Pruritus (itching) is a common symptom of many skin disorders as well as of several systemic diseases and may be extremely distressing. However, contact with certain substances, conditions that dry the skin, stress, and extremes of temperature may also be a cause. Thus, an important part of treatment is to eliminate or minimize the reason for the irritation. Preparations

containing crotamiton are used as an antipruritic agent. One application may be effective for 6 to 10 hour.

Preparations containing calamine are often ineffective.

Calamine

Lotion (oily), 5 %

Indications: mild pruritus

Dose and Administrations: *Topically:* Apply liberally 3 to 4 time daily

Calamine + Zinc Oxide

Cream, 4 % + 3 %

Lotion, 15 % + 5 %

Indications: mild pruritus

Dose and Administrations: *Topically:* Apply liberally 3 to 4 times daily

Crotamiton

Cream, 10%

Lotion, 10 %

Indications: treatment of scabies and symptomatic treatment of pruritus.

Cautions: crotamiton should not be applied to acutely inflamed skin or raw, weeping surfaces. If primary irritation or hypersensitivity occurs, treatment should be discontinued and the drug should be removed with soap and water. Crotamiton should be used during pregnancy only when clearly needed. Contact with the face, eyes, mucous membranes and urethral meatus should be avoided, use on physician's advice for children under 3 years.

Contraindications: a history of sensitivity or allergy to the drug and in those who exhibit a primary irritation response to topically applied medications. Acute exudative dermatoses

Side effects: slight local irritation, allergic skin sensitivity may occur with prolonged use

Dose and Administration: Adult and Child: Scabicide: Wash thoroughly and scrub away loose scales, then towel dry; apply a thin layer and massage drug onto skin of the entire body from the neck to the toes (with special attention to skin folds, creases, and interdigital spaces). Repeat application in 24 hours. Take a cleansing bath 48 hours after the final application. Treatment may be repeated after 7-10 days if live mites are still present.

Pruritus: Massage into affected areas until medication is completely absorbed; repeat as necessary.

18.7. Depigmenting Agents

Hydroquinone

Solution, 2%, 4%

Skin cream: 4%

Indications: gradual bleaching of hyperpigmented skin conditions.

Cautions: pregnancy, limit application to area no larger than face and neck or hands and arms.

Contraindications: hypersensitivity to hydroquinone, sunburn, depilatory usage.

Side effects: dermatitis, dryness, erythema, stinging, inflammatory reaction, sensitization, irritation.

Dose and Administration: Adult and Child \geq 12 years:
topical: apply thin layer and rub in twice daily.

18.8. Pigmenting Agents

Psoralens (furocoumarins) occur in nature and are found primarily in plants. They are photosensitisers. Photochemotherapy using 8-methoxypsoralen, 5-

methoxypsoralen or 4,5,8-trimethoxypsoralen with ultraviolet light (usually UVA) is an effective method of treating several dermatological conditions including psoriasis, vitiligo, mycosis fungoides and atopic eczema. Because specialized facilities and expertise are required, it is recommended that this therapy be limited to hospitals and specialist practices. Psoralens applied topically (lotion, cream) are useful for localized disease or when oral administration is contraindicated or not tolerated.

Methoxsalen(8-Methoxypsoralen)

Solution, 1 %

Capsule, 10 mg, 20 mg

Tablet, 10 mg, 20 mg

Indications: symptomatic control of severe, recalcitrant disabling psoriasis; repigmentation of idiopathic vitiligo; palliative treatment of cutaneous T-cell lymphoma (CTCL).

Cautions: albinism, erythropoietic protoporphyria, lupus erythematosus, porphyria cutanea tarda, xeroderma pigmentosum, aphakia, cataracts.

Drug interactions: anthracin, certain organic dyes (methylene blue, methylene orange), coal tar or coal tar derivatives, diuretics, griseofulvin, bacteriostatic soaps, naldixic acid, phnothiazines, sulfonamides, tetracyclines.

Contraindications: cataract, melanoma, and pregnancy.

Side effects: Immediate nausea, vomiting, headache, pruritus, oedema and CNS disturbances (dizziness, nervousness, insomnia, depression and excitation). Delayed- actinic damage (accelerated ageing, carcinomas, cataracts, pigmented naevi); immunosuppression; precipitation of lupus erythematosus and herpes simplex.

Dose and Administration: Adult: Psoriasis: Oral: 10-70mg 1.5-2 hours before exposure to UVA light; dose may be repeated 2-

3 times per week, based on UVA exposure; doses must be given at least 48 hours apart; dosage is based upon patient's body weight and skin type: <30kg: 10mg; 30-50kg: 20mg; 51-65kg: 30mg; 66-80kg: 40mg; 81-90 kg: 50mg; 91-115kg: 60mg; >115kg: 70mg. *Vitiligo: Oral*: 20mg 2-4 hours before exposure to UVA light; dose may be repeated based on erythema and tenderness of skin; do not give on 2 consecutive days.

Adult and Child>12 years: *Vitiligo: Topical* Apply up to 1% solution 2 hours before exposure to UVA light, treatment is repeated usually once weekly.

Psoriasis: apply approximately 0.15% solution 15 minutes before UVA exposure.

Storage: store at room temperature and protect from light.

18.9. Dermatological, systemic

Acitretin

Capsule, 10 mg, 25 mg, 50 mg

Indications: severe psoriasis not responsive to make conventional therapy; pustular psoriasis; severe extensive disorders of keratinisation resistant to conventional treatments, such as congenital ichthyosis, Darrier's disease and pityriasis rubra pilaris.

Cautions: hepatic and renal impairment; hypervitaminosis A; hyperlipidaemias; known hypersensitivity.

Drug interactions: agents causing intracranial pressure (e.g. tetracyclines), hepatotoxic agents (e.g. methotrexate), protein bound drugs (e.g. phenytoin), vitamin A.

Contraindications: pregnancy or breast-feeding, patients under 18 years of age.

Side effects: hypervitaminosis A, e.g. dryness of mucosae (dry mouth, nose and eyes, cheilitis, keratitis, stomatitis, epistaxis);

reversible hair loss; nail dystrophies and paronychia; thin fragile skin, exfoliation especially of palms and soles.

Skin rashes; reversible impairment of dark adaptation; raised intracranial pressure; musculoskeletal pains with hyperostosis and extra skeletal soft-tissue calcification, osteoporosis; premature epiphyseal closure; gastrointestinal irritation; hepatitis and transient reversible elevations of liver enzymes; elevation of serum lipids; disturbance in glucose metabolism, malaise; sweating; drowsiness.

Dose and Administration: Adult: Individually adjusted to limit side effects and to maximize therapeutic response. *Oral:* Initially, 25 - 30 mg once daily with a meal for 2 - 4 weeks, increasing to 50 mg/day for a further 6-8 weeks; maximum 75 mg/day.

Maintenance: 50 mg/day or less, based on therapeutic results and tolerability.

Storage: store at room temperature.

Cyproterone acetate and Ethinyl estradiol

Tablet, 2mg + 35mcg

Indications: indicated for resistant and severe acne, severe signs of androgenisation in women (e.g. hirsutism), male sexual deviation, and inoperable prostatic carcinoma.

Cautions: cyproterone should be administered only after full endocrine assessment.

Contraindications: pregnancy, cardiac disease, diabetes mellitus, liver disease.

Side effects: abnormal vision, allergic reaction, anemia, cerebrovascular accident, liver failure, depression, in women weight gain, decreased libido and dry vagina.

Dose and Administration: Cyproterone acetate 2mg and ethinylestradiol 0.035 mg daily from day 1 of cycle.

Storage: store at room temperature.

Etretinate

Capsule, 10mg, 25mg

Indications: treatment of severe, extensive psoriasis that has not responded to other treatment, especially generalized and palmoplantar pustular psoriasis.

Cautions, Contraindications, Drug interactions and Side effects see isotretinoin.

Dose and Administration: *Oral:* 0.75 to 1mg/kg daily in divided doses. A maximum dose of 1.5 mg/kg daily.

Erythrodermic psoriasis: 250 mcg/kg daily, increased at weekly intervals by 250 mcg/kg daily until optimal response occurs. Following the initial response, generally after 8-16 weeks of therapy, maintenance doses of 500 to 750 mcg/kg daily have been given.

Finasteride

Tablet, 1mg

Indications: androgenetic alopecia in men

Cautions: obstructive uropathy

Side effects: testicular pain, hypersensitivity reactions (including lip and face swelling, pruritus and rash)

Dose and Administration: Oral: 1 mg daily

Hydroxychloroquine

Tablet, 200mg

Indications: Active rheumatoid arthritis (including juvenile idiopathic arthritis), systemic and discoid lupus erythematosus; dermatological conditions caused or aggravated by sunlight.

Cautions: Hepatic impairment, renal impairment, pregnancy and Breast-feeding. Manufacturers recommend regular

ophthalmological examination but the evidence of practical value is unsatisfactory. It should be used with caution in neurological disorders (especially in those with a history of epilepsy), in severe gastro-intestinal disorders, in G6PD deficiency, in acute porphyria, and in the elderly. It may exacerbate psoriasis and aggravate myasthenia gravis. Concurrent use of hepatotoxic drugs should be avoided.

Drug interactions: Agalsidase (Alfa and Beta), Amiodarone, antacids, antiepileptics, ciclosporin, cimetidine, digoxin, droperidol, kaolin, laronidase, mefloquine, moxifloxacin, neostigmine, pyridostigmine, artemether with lumefantrine and histamine.

Side effects: gastro-intestinal disturbances, headache and skin reactions (rashes, pruritus); those occurring less frequently include ECG changes, convulsions, visual changes, retinal damage, keratopathy, ototoxicity, hair depigmentation, hair loss, and discoloration of skin, nails, and mucous membranes. Side-effects that occur rarely include blood disorders (including thrombocytopenia, agranulocytosis, and aplastic anaemia), mental changes (including emotional disturbances and psychosis), myopathy (including cardiomyopathy and neuromyopathy), acute generalised exanthematous pustulosis, exfoliative dermatitis, Stevens-Johnson syndrome, photosensitivity, and hepatic damage; angioedema has also been reported. Important: very toxic in overdose—immediate advice from poisons centres essential

Dose and administration: Administered on expert advice, 200–400 mg daily (but not exceeding 6.5 mg/kg daily based on ideal body-weight, see also recommendations above). Child 1 month–18 years: based on ideal body-weight, 5–6.5 mg/kg (max. 400 mg) once daily.

Isotretinoin

Capsules, 10 mg, 20 mg

Indications: mainly for the management of intractable acne, but may also be effective in controlling keratinisation disorders such as the ichthyoses and keratosis follicularis.

Cautions: history of depression.

Drug interactions:tetracyclines, acitretin, tretinoion, vitamin A.

Contraindications: pregnancy, hypervitaminosis A; hepatic and renal insufficiency; hyperlipidaemia's; known hypersensitivity.

Side effects: dryness of mucosa; reversible hair loss, nail dystrophies and paronychia, thin fragile skin, exfoliation especially of palms and soles.Skin rashes; reversible impairment of dark adaptation; raised intracranial pressure; musculoskeletal pains with hyperostosis and extraskeletal soft-tissue calcification, osteoporosis; premature epiphyseal closure; gastrointestinal irritation; hepatitis and transient reversible elevations of liver enzymes; elevation of serum lipids; disturbance in glucose metabolism; malaise; sweating; drowsiness, haematological abnormalities. Depression, psychosis, behavioral disorders, and seizures have been reported.

Dose and Administration:Adult: *Oral:*Initially: 0.5 mg/kg/day in a single or 2 divided doses with food. Adjust after 2 - 4 weeks, if necessary, according to response and adverse effects. If the response is slight, increase up to a maximum of 1 mg/kg/day, if well tolerated.Maintenance: 0.5 - 1 mg/kg/day for a further 12 weeks. In the event of intolerance of the initial dose, reduce to 0.1 - 0.2 mg/kg/day with longer duration of therapy. Total dose 120 mg/kg.Usual treatment period, 16 - 24 weeks.Repeat treatment: allow an interval of 3 - 4 months (at least 8 weeks) as improvement may continue despite stopping therapy.

Storage: store at room temperature.

Methylprednisolone

Tablet, 4mg

Indications: suppression of inflammatory and allergic disorders; severe inflammatory bowel disease

Cautions, Contraindications, Side effects: see notes

Dose and Administration: *Oral:* usual range 2–40 mg daily

Prednisolone

Tablets, 1mg, 2mg, 5mg

Indications: short-term suppression of inflammation in allergic disorders.

Cautions: tuberculosis, amebiasis, strongyloidiasis, risk of severe chicken pox in non-immune patient, avoid exposure to measles, diabetes mellitus; peptic ulcer; hypertension.

Contraindications: untreated systemic infection; administration of live virus vaccines.

Side effects: nausea, dyspepsia, malaise, hiccups, hypersensitivity reactions including anaphylaxis.

Dose and Administration: Adult and Child: *Oral:* initially up to 10 - 20 mg daily as a single dose in the morning (in severe allergy up to 60 mg daily as a short course of 5 - 10 days).

Storage: store at room temperature.

18.10. Skin Disinfecting Agents

The choice of disinfectant is an important factor in treating skin conditions. For example, scaling disorders are best treated with emulsifying ointment or other disinfectants that do not irritate the skin. Some of the useful disinfectants for skin cleansing available at district hospital level include Chlorhexidine; Potassium permanganate and Povidone - iodine. Povidone-iodine is preferred to chlorinated solutions (such as dilute

sodium hypochlorite solution; not described here) which are too irritant and are no longer recommended. Astringent preparations, such as potassium permanganate solution are useful for oozing eczematous reactions.

Chlorhexidine Gluconate + Cetrimide

Solution 1.5 % + 15 %, 0.3% + 3%w/v

Indications: for skin disinfection and wound cleansing, and also for the cleansing and disinfection of equipments.

Side effects: skin sensitivity may occur rarely. Strong solutions may cause irritation of the conjunctiva and other sensitive tissues.

Dose and Administration: *Topically* For skin disinfection and wound cleansing: Apply to the affected area the diluted solution (1 in 100 (1%) with water).

For disinfection of equipment (e.g bowls, tables), spraying wards: Use 1 in 2000 dilution with water.

Storage: at room temperature protected from light.

Ethyl Alcohol

Solution, 70 %

Indications: for disinfection of the skin in preparation for injections.

Cautions: it should not be applied to fresh wounds.

Dose and Administration: Topical, to the skin.

Storage: in airtight containers, in a cool place.

Hydrogen peroxide

3 %, 6 %

Indications: skin disinfectant, particularly cleansing and deodorizing wounds and ulcers.

Cautions: in large and deep wounds, avoid use in normal skin.

Dose and Administration: topically, apply to the wound to cleanse.

Iodine

Solution, 2 %

Indications: for the disinfection of minor superficial skin wounds.

Cautions: do not apply to sensitive area such as the axillary, perianal, or genitalia.

Side effects: skin sensitivity, irritation, sloughing of soft tissues and staining of the skin may occur.

Dose and Administration: Topical to the affected areas as necessary. Do not cover with a tight bandage.

Storage: at room temperature. In yellowish brown coloured glass bottles, preferably glass stoppered.

Potassium permanganate

Tablet (for solution), 50 mg, 120 mg, 200 mg, 250 mg, 300 mg

Indications: as skin disinfectant for cleansing and deodorizing suppurating eczematous reactions and wounds.

Cautions: irritant to mucous membrane and it stains skin and clothing

Side effect: irritation to tissues, corrosive burns,

Dose and Administration: 1 tablet dissolved in suitable amount of water to provide a 0.01% solution. It is applied as wet dressings or baths, approximately of 0.01% solution.

Povidone - Iodine

Solution (aqueous), 4 %, 7.5 %, 10 %

Indications: as skin disinfectant and antiseptic mainly for the treatment of contaminated wounds and pre-operative preparation of the skin and mucous membranes.

Cautions: during pregnancy and breast-feeding, in patients with broken skin and renal impairment. The application of povidone - iodine to large wounds or severe burns may produce systemic adverse effects such as metabolic acidosis, hyponatremia and impairment of renal function.

Contraindications: avoid regular use in patients with thyroid disorders or those receiving lithium therapies, very low birth weight infants.

Side effects: rarely sensitivity may interfere with thyroid function tests; see also caution.

Dose and Administration:*Alcoholic solution, povidone iodine 10%: Adult:* to be applied undiluted in pre- and post-operative skin disinfection. **Child:** not recommended for regular use in neonates (and contraindicated in very low birth weight infants)

Antiseptic solution, povidone - iodine, 10% in aqueous solution: Adult: to be applied undiluted in pre- and postoperative skin disinfection. **Child:** not recommended for regular use in neonates (and contraindicated in very low birth weight infants).

Scalp and skin cleanser solution, povidone - iodine, 7.5%, in a surfactant basis:

Adult: use of seborrhoeic condition of scalp and acne vulgaris of face and neck 1-2 times daily child dose. **Child** under 2 years not recommended.*Skin cleanser solution, povidone - iodine, 4% in a surfactant basis:*

Adult: for infective condition of the skin. Retain on skin for 3-5 minutes before rinsing, repeat twice daily. **Child** under 2 years not recommended

18.11. Dermatologicals, Others

Aluminum Chloride

Solution (alcoholic), 20%, 25%

Indications: used for control of hyperhidrosis.

Dose and Administration: Applied to dry skin at night (and washed off in the morning); especially if occluded and the patient sedated.

Betamethasone Dipropionate + Salicylic Acid

Ointment and Lotions, 0.064%+2%

Indications: Subacute and chronic hyperkeratotic and dry dermatoses. Betamethasone Dipropionate is a synthetic fluorinated corticosteroid. In combination with salicylic acid it is indicated for the treatment of chronic lichenified eczema, lichen planus, lichen simplex and non bullous ichthyosiform erythroderma. It is also effective in the less responsive conditions such as psoriasis of the scalp and chronic plaque psoriasis of the hands and feet but excluding widespread plaque psoriasis. Topical salicylic acid softens keratin, loosens cornified epithelium and desquamates the epidermis.

Cautions: Pregnancy and breast feeding mother. Not to be used in or near the eyes. Avoid contact with mucous membranes. *Prolonged topical corticosteroid treatment may result in systemic corticosteroid effects; may also lead to formation of striae or atrophy of the skin or subcutaneous tissue. Absorption of corticosteroid through the skin is increased when used with occlusive dressings. Caution when used in patients with stasis dermatitis or other skin diseases with impaired blood circulation.*

Contraindications: Rosacea, acne, perioral dermatitis, perianal and genital pruritus. Hypersensitivity to any of the ingredients of the preparations contra-indicates their use as does tuberculosis and most viral lesions of the skin, particularly herpes simplex, vaccinia, varicella. It should not be used in napkin eruptions, fungal or bacterial skin infections without suitable concomitant anti-infective therapy.

Side effects: Pruritus, irritation, folliculitis, maceration of skin, skin atrophy, hypertrichosis, acneiform eruptions, secondary infection, hypopigmentation, perioral dermatitis, allergic contact dermatitis, striae and miliaria.

Dose and administration: Adults: In most cases a few drops should be applied to the affected areas once or twice daily and massaged gently and thoroughly into the skin. For some patients adequate maintenance therapy may be achieved with less frequent application. It is recommended that preparations are prescribed for two weeks. The maximum weekly dose should not exceed 60g. *Children: Dosage in children should be limited to 5 days.*

Storage: Do not store above 25°C.

Imiquimod

Cream, 5%

Indication: Imiquimod cream is used to treat certain types of actinic keratoses (flat, scaly growths on the skin caused by too much sun exposure) on the face or scalp. Imiquimod cream is also used to treat superficial basal cell carcinoma (a type of skin cancer) on the trunk, neck, arms, hands, legs, or feet and warts on the skin of the genital and anal areas. It treats genital and anal warts by increasing the activity of the body's immune system.

Contraindication: allergic to imiquimod or any ingredients in imiquimod cream.

Dose and administration: Actinic keratoses: apply it once a day for 2 days a week, 3 to 4 days apart

Superficial basal cell carcinoma: apply once a day for 5 days a week. Genital and anal warts: apply once a day for 3 days a week.

Side effects: redness, itching, burning, or bleeding of the treated area; flaking, scaling, dryness, or thickening of the skin; swelling, stinging, or pain in the treated area; blisters, scabs, or bumps on the skin; headache; diarrhea; back pain; tiredness

Storage: Store it at room temperature

Methylsalicylate[❧]

Methyl salicylate is irritant to the skin and is used topically in rubefacient preparations in musculoskeletal, joint and soft-tissue disorders and for minor peripheral vascular disorders such as chilblains. It is absorbed through intact skin and can produce effects typical of systemic salicylates.

Minoxidil

Solution, 20mg/ml (2%), 5%

Indications: The treatment of alopecia androgenetica (male pattern baldness).

Contraindications: Hypersensitivity to minoxidil, propylene glycol or ethanol; Pregnancy and Lactation.

Side effects: Local irritation is the most common, including scaling, erythema/flushing, dermatitis, dry skin, hypertrichosis, burning sensation and rash.

Dose and Administration: A total dose of 1 mL minoxidil topical solution should be applied twice per day to the scalp, beginning at the centre of the affected area.

Paraffin Gauze Dressing

Paraffin Gauze Dressing - is Fabric of Leno weave, weft and warp threads of cotton and/or viscose yarn, impregnated with white or yellow soft paraffin.

[❧] Any other rubefacient proven to be therapeutically effective can be used

Indications: treatment of abrasions, burns, and other injuries of skin, and ulcerative conditions; post-operatively as a penile and vaginal dressing and for sinus packing; heavier loading for skin graft transfer.

Pimecrolimus

Cream, 1%

Indications: short-term treatment of mild to moderate atopic eczema (including flares) when topical corticosteroids cannot be used.

Cautions: UV light (avoid excessive exposure to sunlight and sunlamps), avoid other topical treatments except emollients at treatment site; alcohol consumption (risk of facial flushing and skin irritation)

Contraindications: contact with eyes and mucous membranes, application under occlusion, infection at treatment site; congenital epidermal barrier defects; generalised erythroderma; immunodeficiency; concomitant use with drugs that cause immunosuppression (may be prescribed in exceptional circumstances by specialists); application to malignant or potentially malignant skin lesions

Side effects: burning sensation, pruritus, erythema, skin infections (including folliculitis and less commonly impetigo, herpes simplex and zoster, molluscum contagiosum); rarely papilloma, skin discoloration, skin local reactions including pain, paraesthesia, peeling, dryness, oedema, and worsening of eczema; skin malignancy reported

Dose and Administration: Apply twice daily until symptoms resolve (stop treatment if eczema worsens or no response after 6 weeks); child under 2 years not recommended

Talc Dusting powder

Indications: used in folds where a friction may occur between opposing skin surfaces.

Cautions: they should not be applied in areas that are very moist as they tend to take and abrade the skin.

Urea

Cream, 10%, 15%, 20%, 40%

Indications:hydrating agent and keratolytic for dry, scaling and itching skin conditions, including mild psoriasis.

Cautions:avoid application to face or broken skin; avoid contact with eyes.

Side effects:transient stinging and local irritation.

Dose and Administration: Adult and Child: Dry, scaling skin disorders, *apply* directly to the affected area twice daily, preferably to damp skin.

19. ANTIDOTES and SUBSTANCES USED in POISONING

In the treatment of acute poisoning most patients require only supportive and symptomatic therapy. The active removal of poisons from the stomach by gastric lavage or emesis induction may be considered, as should the administration of substances like activated charcoal by mouth to reduce their absorption. However, the use of emetics and gastric lavage has been questioned and these measures, including the administration of charcoal are for instance inappropriate in corrosive poisoning, and aspiration should only be carried out with great care. Some poisons, in particular pesticides, may be absorbed through the skin and clothing should be removed and the skin thoroughly washed to avoid continued absorption. Techniques such as forced diuresis, haemodialysis, or haemoperfusion are only of value for a limited number of poisons in a few severely poisoned patients.

The drugs included in this section act in a variety of ways. These are the antagonists, such as the opioid antagonist naloxone hydrochloride, that compete with the poison for the receptor sites. There are compounds that inhibit the poison by reacting with it to form less active or inactive complexes or by interfering with its metabolism; a typical examples of the first group.

Atropine sulphate is given in the case of organo-phosphorus poisoning which is characterized by intense muscarinic effects by inhibiting cholinesterase activity thereby prolonging and intensifying the effects of acetylcholine. Atropine will reverse the muscarinic effects of acetylcholine and is given in a dose of 2 mg as atropine sulphate (intramuscularly or intravenously according to the severity of poisoning) every 20 to 30 minutes

until the skin becomes flushed and dry, the pupils dilate, and tachycardia develops.

Pralidoxime mesylate, a cholinesterase reactivator, is indicated, as an adjunct to atropine, in moderate or severe poisoning but is only effective if given within 24 hours.

Other specific antagonists include **acetylcysteine** used in paracetamol poisoning. Sodium nitrite is used in the treatment of cyanide poisoning in conjunction with sodium thiosulphate. And Flumazenil, a benzodiazepine antagonist, is used in anesthesia and intensive care to reverse benzodiazepine – induced sedation; it is also used to treat benzodiazepine over dosage.

Acetylcysteine

Injection, 200 mg/ml in 10 ml ampoule

Indications: antidote to acetaminophen overdose, to protect against hepatotoxicity.

Cautions: patients with history of asthma, conditions predisposing to gastrointestinal hemorrhage such as esophageal varices, peptic ulceration, and in patients sensitive to acetylcysteine.

Side effects: drowsiness, fever, nausea, or vomiting, bronchospastic allergic reaction (troubled breathing, tightness in chest, wheezing), skin rash or hives.

Dose and Administration:Adult and Child: Antidote: IV: 300mg per kg of body weight administered over twenty hrs and fifteen minutes, divided as follows:

Initial loading dose - 150mg per kg of body weight in up to 200ml of 5% dextrose injection, administered over fifteen minutes. Second infusion- 50mg per kg of body weight in 500ml of 5% dextrose injection, administered over four hours. Third

infusion - 100mg per kg of body weight in 1000ml of 5% dextrose injection, administered over the next sixteen hours.

Activated Charcoal

Tablet, 125mg, 250mg

Powder for reconstitution, 15gm/120ml, 25gm

Gel, 300ml

Indications: treatment of acute poisoning.

Cautions: intestinal obstructions, drowsy or unconscious patients (risk of aspiration; intubate before administration via nasogastric or gastric tube); not effective for poisoning with alcohols, clofenotane (dicophane, DDT), cyanides, malathion, and metal salts including those of iron and lithium.

Drug interactions: charcoal decreases the effect of Ipecac syrup.

Contraindications: poisoning by hydrocarbons with high potential for harm if aspirated; poisoning by corrosive substances (may prevent visualization of lesions caused by the poison).

Side effect: black stools; vomiting, constipation or diarrhoea; bowel obstruction pneumonitis (due to aspiration).

Dose and Administration: Poisoning (reduction of absorption), Oral: as soon as possible after ingestion of poison, **Adult**, 50–100 g as a single dose; **Infant**, 1 g/kg as a, single dose; **Child** 1–12 years, 25 g as a single dose (50 g in severe Poisoning). Poisoning (active elimination), Oral: **Adult**, 50 g every 4 hours (in case of intolerance 25 g every 2 hours); **Infant**, 1 g/kg every 4–6 hours; **Child** Over 1 year, 25–50 g every 4–6 hours.

Apomorphine Hydrochloride

Injection, 3 mg/ml in 1 ml ampoule

Indications: emetic in the treatment of acute poisoning; diagnosis and management of parkinsonism.

Cautions: if vomiting does not result from the first dose of apomorphine, then a second dose should not be given. Caution should be taken in children debilitated or elderly patients or those with cardiac decomposition.

Drug interactions: the effectiveness of apomorphine as an emetic is diminished by drugs that depress the vomiting center and they in turn may enhance its central depressant effects.

Contraindications: respiratory or central nervous system depression, in shock or seizure, or in patients suffering from the effects of corrosive poisons.

Side effects: protracted vomiting, shock, CNS stimulation, depression and respiratory depression.

Dose and Administrations: **Adult:** *subcutaneous* 5 or 6 mg as a single dose; **Child:** *subcutaneous* 70 to 100 mcg per Kg body weight as a single dose:

Note: A glass of water being given before injection.

Storage: store in tight container. Protect from light.

Atropine Sulphate

Injection, 1 mg/ml in 1 ml ampoule

Indications: for the treatment of poisoning from cholinesterase inhibitors such as neostigmine, pilocarpine, physostigmine, and methacholine, and in the treatment of the rapid type of mushroom (muscarine) poisoning. It is also indicated in the treatment of poisoning caused by pesticides that are organophosphate cholinesterase inhibitors, chemical warfare, and 'nerve' gases.

Cautions: pregnancy and breastfeeding in children and in elderly, urinary retention, prostatic enlargement, tachycardia,

cardiac insufficiency, paralytic ileus, ulcerative colitis, and pyloric stenosis.

Drug interactions: antacids, antidiarrhoeals, other anticholinergics, cyclopropane, ketoconazole, haloperidol.

Contraindications: closed angle glaucoma.

Side effect: dryness of mouth, skin, blurred vision, loss of accommodation constipation, bradycardia followed by tachycardia, difficulty with micturation, flushing.

Dose and Administration:Adult: *Antidote to cholinesterase inhibitors: IV:* 2-4mg initially, then 2mg repeated every five to ten minutes until muscarinic symptoms disappear or signs of atropine toxicity appears. *Antidote to muscarine in mushroom poisoning: IM, or IV:* 1 to 2mg every hour until respiratory effects subside. *Antidote to organophosphate pesticides: IM or IV:* 1 to 2mg repeated in twenty or thirty minutes as soon as cyanosis has cleared. Continue dosage until definite improvement occurs and is maintained, sometimes for two days or more. **Child:** *Antidote to cholinesterase inhibitors: IV or IM:* 1mg initially, then 0.5 - 1mg every five to ten minutes until muscarinic symptoms disappear or signs of atropine toxicity appear.

Storage: at room temperature, protect from freezing

Calcium folinate and Folinic acid (See section 12.4)

Calcium Gluconate (Levulinate, or Chloride)

Injection, 10 % in 10 ml ampoule

Indications: fluoride toxicity; hypocalcaemia and of calcium deficiency states (see sec.11.2)

Side effects, Drug interactions, Cautions, Contraindications: see sec. 11.2

Dose and Administrations: 10 ml of Calcium gluconate 10 % IV repeated after one hour; 30 ml should be given if tetany is present. The short term affected skin and tissue should be injected with a 10 % solution of calcium gluconate at a dose of 0.5 ml per cm².

Note: Inorganic fluoride is corrosive to skin and mucous membranes and acute intoxication disrupts many physiological systems and severe burns and profound hypocalcaemia may ensue. Absorption of the fluoride can be prevented by conversion to an insoluble form such as calcium fluoride and thus irrigation with limewater, milk, or a 1 % solution of calcium chloride or gluconate at the portable of entry (mouth, skin, stomach) is recommended.

Desferrioxamine Mesylate

Powder for injections, 0.5 g in vial

Indications: it is a chelating agent used in the treatment of acute iron poisoning, and chronic iron or aluminium over load.

Cautions: impaired renal function, if infection is suspected treatment with desferrioxamine should be stopped and appropriate antimicrobial treatment given.

Drug interactions: prochlorperazine

Contraindications: severe renal disease or anuria, pregnant women or women who may become pregnant.

Side effects: anaphylactic reactions, and hypotension when given too rapidly by intravenous injection

Dose and Administration: *Continuous IV infusion:* up to 15 mg/kg /hour; maximum 80mg /kg in 24 hours.

IM: 1 - 2 g in 10 - 20 ml of water for injections every 3 - 12 hours; maximum 6g in 24 hours.

Storage: reconstituted solutions of desferrioxamine mesylate are stable for 1 week at room temperature when protected from light.

Note: Inform the patient that the drug may colour the urine reddish brown

Digoxin Immune Fab (Ovine)/Digoxin-specific, Antibody fragments

Powder for injection, 40mg

Indications: treatment of life-threatening or potentially life threatening digoxin intoxication, associated with hyperkalaemia, life- threatening cardiac dysrhythmias or digoxin levels > 6ng/ml.

Cautions: renal or cardiac failure.

Drug interaction: digoxin.

Contraindications: hypersensitivity to sheep products or any component of the formulation.

Side effects: hypersensitivity reactions and hypokalemia.

Dose and Administration: Each vial of 40mg will contain \approx 0.5 mg of digoxin or digitoxin. Estimation of the dose is based on the body burden of digitalis. This may be calculated if the amount ingested is known or the post distribution serum drug level is known (round dose to the nearest whole vial). See the next table. Digoxin Immune Fab

Tablet Ingested (0.25 mg)	Fab Dose(Vials)
5	2
10	4
25	10
50	20
75	30
100	40
150	60
200	80

If neither amount ingested nor drug level are known, dose empirically as follows: For acute toxicity: 20 vials, administered in 2 divided doses to decrease the possibility of a febrile reaction, and to avoid fluid overload in small children.

For chronic toxicity: 6 vials, for infants and small children (\leq 20kg), a single vial may be sufficient.

Storage: store in refrigerator (2 to 8°C).

Dimercaprol

Injection, 5% in 2ml ampoule.

Indications: antidote to gold, arsenic, mercury poisoning; adjunct to edetate calcium disodium in lead poisoning; possibly effective for antimony, bismuth, chromium, copper, nickel, tungsten, or zinc.

Cautions: oliguria; glucose 6-phosphate dehydrogenase deficiency.

Drug interactions: toxic complexes with iron, cadmium, selenium, or uranium.

Contraindications: hepatic insufficiency (unless due to arsenic poisoning); iron, cadmium, or selenium poisoning.

Side effects: hypertension, headache, nausea, vomiting.

Dose and Administration: Adult and Children: *Deep I.M.: Arsenic, mercury, and gold poisoning:* 3mg /kg every 4 - 6 hours for 2 days, then every 12 hours for 7 - 10 days or until recovery (initial dose may be up to 5mg if severe poisoning). *Lead poisoning (in conjunction with calcium EDTA):* For symptomatic acute encephalopathy or blood level $>$ 100 mcg/dl: 4 - 5mg/kg every 4 hours for 3 - 5 days.

Storage: store at 2-8 °C; protect from light.

Flumazenil

Injection, 0.1 mg/ml in 5 ml ampoule

Indications: flumazenil is indicated for the management of benzodiazepine over dose.

Cautions: hypersensitivity to benzodiazepines; patients receiving benzodiazepines for prolonged periods; pediatrics, elderly; pregnant and breast-feeding women.

Drug interactions: cyclic (tricyclic or tetracyclic) antidepressants

Contraindications: cyclic (tricyclic or tetracyclic) antidepressant; status epilepticus severe head injury

Side effects: nausea, vomiting, flushing and very occasionally convulsions

Dose and Administration: Adult: IV:0.2mg over 15 seconds; if a response is not achieved within 60 seconds; 0.1mg may be repeated at 60-second intervals as required to a total dose of 1mg (2mg in intensive care). Usual range 0.3-0.6 mg. If there is no response, aetiology should be questioned.

Storage: at room temperature.

Ipecac

Syrup, 7% powdered Ipecac

Indications: an emetic for emergency use in the treatment of drug overdose and in some cases of poisoning

Cautions: children under 1 year of age; heart disease active or impending seizures and in conditions of strychnine poisoning or ingestion of petroleum distillates, such as kerosene, gasoline, coal oil, fuel oil, paint thinner, or cleansing fluid.

Drug interactions: activated charcoal, milk or milk products, carbonated beverages, antiemetics.

Contraindications: impending coma, severe inebriation, corrosive poisoning with alkali and strong acids, depressed gag reflex, impending shock states.

Side effect: diarrhoea, fast or irregular heartbeat, nausea or vomiting, stomach cramps or pain, troubled breathing, unusual

tiredness or weakness, aching, and stiffness of muscles, especially those of the neck, arms, and legs.

Dose and Administration: *Oral:Adult: emetic:* 15 to 30ml followed immediately by one glass (240ml) of water. Dose may be repeated in twenty minutes if emesis does not occur. The dosage should be reversed by gastric lavage if emesis does not occur after the second dose.

Child:*Emetic:*Children up to 1 year of age: 5 to 10ml
Children 1-12 years of age: 15 ml, preceded or followed by ½-1 full glass (120-240ml) of water.

Storage: at a temperature below 25⁰c.

Methionine

Tablet, 250mg

Indications: management of paracetamol (acetaminophen) overdose. The efficacy and safety of late (> 15 hours post ingestion) or prolonged administration (> 16 hours) have not been sufficiently explored.

Dose and Administration: *Oral:* 2.5g 4 hourly for a total of 4 doses, started within 10 - 12 hours after paracetamol ingestion.

Storage: protect from light.

Methylene Blue

Injection, 1% in 10ml ampoule.

Indications: antidote for cyanide poisoning and drug-induced methemoglobinemia.

Cautions: G6PD deficiency, pregnancy and breastfeeding.

Contraindication: renal insufficiency.

Side effects: hypertension, precordial pain, dizziness, mental confusion, headache, fever, staining of skin, fecal discoloration, nausea, vomiting, abdominal pain, discoloration of urine, bladder irritation, anemia, diaphoresis.

Dose and Administration: Adult and Child:IV:

Methemoglobinemia: 1 - 2 mg/kg over several minutes; may be repeated in 1 hour if necessary.

Naloxone Hydrochloride

Injection, 0.02 mg/ml in 2 ml ampoule. 0.4 mg/ml in 1 ml and 10 ml ampoule, 1mg/ml

Indications: over dosage with opioids; postoperative respiratory depression

Cautions: physical dependence on opioids, cardiac problems or those patients receiving cardiotoxic drugs.

Dose and Administrations:By IV, 0.8 to 2 mg repeated at intervals of 2 - 3 minutes to maximum of 10 mg if respiratory function does not improve (then question diagnosis); **Child** 10 microgram/kg; subsequent dose of 100 micrograms/kg if no response.

SC or IM: as intravenous injection but only if intravenous route not feasible (onset of action slower).

Continuous IV infusion: 2 mg diluted in 500 ml intravenous infusion solution at a rate adjusted according to the response

Storage: in airtight containers. Protect from light

Penicillamine

Capsule, 250mg

Indications: treatment of copper, mercury, arsenic, lead and zinc poisoning; Wilson's disease and cystinuria; adjunctive treatment of rheumatoid arthritis.

Caution: penicillin allergy.

Drug interactions: antacids, iron salts, digoxin.

Contraindications: renal insufficiency and pregnancy (in patients with rheumatoid arthritis); patients with previous penicillamine-related aplastic anemia or agranulocytosis; breast-feeding.

Side effects: vasculitis, anxiety, agitation, fever, psychiatric disturbances, alopecia, rash, urticaria, wrinkling, anorexia, diarrhea, hematuria, nephrotic syndrome and renal failure.

Dose and Administration: *Oral: Rheumatoid arthritis:*

Adult: 125 - 250mg/day, may increase dose at 1- 3 month intervals up to 1 - 1.5g/day; *Wilson's disease:* **Adult:** 250 mg/4 times /day. **Child**< 12 years: 20mg/kg/day in 2-3 divided doses, round off to the nearest 250 mg dose; maximum 1g/day. *Cystinuria:* **Adult:** 1-4g/day in divided doses every 6 hours; usual dose: 2g/day. **Child:** 30mg/kg/day in 4 divided doses.

Chelation therapy: **Adult:** 0.5 - 1.5 g daily in 4 divided doses.

Child: 20 - 40 mg/kg daily in 4 divided doses.

Storage: store in tight, well - closed containers.

Physostigmine salicylate

Injection, 1mg/ml in 1ml and 2ml ampoule

Indications: reverse toxic CNS effects caused by anticholinergic drugs.

Cautions: epilepsy, asthma, diabetes, gangrene, cardiovascular disease, bradycardia.

Drug interactions: bethanechol, methacholine, succinylcholine.

Contraindications: GI or GU obstruction.

Side effects: bradycardia, palpitations, restlessness, nervousness, hallucinations, seizure, nausea, salivation, diarrhea, stomach pain, frequent urge to urinate, muscle twitching, lacrimations, miosis, dyspnea, bronchospasm, respiratory paralysis, pulmonary edema, diaphoresis.

Dose and Administration: **Adult:** *IM, IV, SC:* 0.5 - 2mg to start, repeat every 20 minutes until response occurs or adverse effect occurs. Repeat 1- 4mg every 30 to 60 min as life - threatening signs. **Child:** *IV:* 0.01 - 0.03 mg/kg /dose (maximum: 0.5 mg/min); may repeat after 5 - 10 minutes to a maximum total dose of 2mg.

Storage: store at controlled room temperature.

Phytomenadione (Vitamin k₁)

Injection, 10mg/ml in 1ml ampoule

Indications: overdose of warfarin and related agents used in rodent poisons.

Cautions: G6PD deficiency.

Drug interactions: warfarine.

Contraindications: impaired hepatic function.

Side effects: shock- like reactions with bronchospasm, cyanosis, tachycardia and vascular collapse.

Dose and Administration:Adult: *IM:* 10mg. **Child:** *IM:* 1-5mg. With severe toxicity, vitamin k₁ may be given *I.V.*

Storage: store in airtight containers.

Protamine Sulphate

Injection, 10mg/ml in 5ml ampoule, 250mg (10mg/ml), 25ml

Indications: treatment of heparin overdosage.

Cautions: allergic to fish, vasectomised or infertile males, and prior exposure to protamine or protamine containing insulin; porphyria.

Side effects: anaphylaxis, transient neutropenia, bradycardia, flushing, systemic hypotension and pulmonary hypertension.

Dose and Administration:

Heparin route	Time elapsed since heparin given	Protamine Sulfate Per 100u heparin
IV	<15 minutes	1mg
IV	30 -60 minutes	0.5 - 0.75mg
IV	> 2 hours	0.25 - 0.375mg
SC	—	1mg

Protamine sulphate usually is administered by very slow IV injection over 10 minutes. No more than 50mg of the drug should be administered in any 10 minute period.

Storage: store at 2-8 °C.

Pralidoxime Chloride

Tablet, 500 mg

Powder for injection, 1 g in vial

Indications: It is used as an adjunct to but not as a substitute for atropine in the treatment of poisoning by certain cholinesterase inhibitors. Its main indication is in poisoning due to organophosphorus pesticides or related compounds.

Cautions: It should be used cautiously in patients with impaired renal function (a reduction in dosage may be necessary); myasthenia gravis. It should not be used to treat poisoning by carbamate pesticides.

Drug interactions: succinylcholine, theophylline, aminophylline and respiratory depressants.

Side effects: drowsiness, dizziness, disturbances of vision, nausea, tachycardia, headache, hyperventilation, and muscle weakness; laryngospasm, muscle rigidity (due to rapid IV injection of pralidoxime)

Dose and Administration: The usual initial parenteral dose of pralidoxime chloride is 1 – 2 g for **adult**, or 20-40 mg/kg for **children**; repeat the dose in about 1 hour if muscle weakness has not been relieved (*IV infusion* of 500mg of the drug per hrs). *For prophylactic use in workers exposed to organophosphate insecticides:* 1-3g of pralidoxime chloride has been given orally just before exposure to the organophosphate and a second dose has been given after conclusion of exposure or 5 hours after the first dose whichever came first.

Sodium Calcium Edetate

Injection, 200 mg/ml in 5 ml ampoule.

Indications: treatment of symptomatic acute and chronic lead poisoning.

Cautions: severe renal disease, anuria.

Drug interactions: zinc insulin preparation: do not mix in the same syringe with dimercaprol.

Side effects: arrhythmias, hypotension, chills, skin lesions, hypercalcemia, anorexia, anemia, renal tubular necrosis, sneezing, nasal congestion.

Dose and Administration: **Adult:** *IV infusion or IM:* usually 1g twice daily or 50-75mg/kg/day for 5 days, followed by a 2-day interruption if a repeat dose is considered. **Child:** *IV infusion* (over 8 - 12 hours) or *IM:* usually 1000 - 1500 mg/m² /day for 3- 5 days, followed by a 2-day interruption if a repeat course of therapy is necessary.

Storage: store at controlled room temperature.

Sodium Nitrite

Injection, 3 % (30 mg/ml)

Indications: sodium nitrite is used in the treatment of cyanide poisoning in conjunction with sodium thiosulphate.

Side effects: nausea and vomiting, abdominal pain, dizziness, headache, cyanosis, tachypnoea, and dyspnea; flushing and headache due to vasodilatation.

Dose and Administration: 10 ml *by intravenous injection* over 3 minutes, followed by 25 ml of sodium thiosulphate injection 50 % *by intravenous injection* over 10 minutes. The usual dosage regimen in children is 0.15 to 0.33 ml (approximately 4.5 to 10.0 mg per kg) followed by 1.65 ml per kg of a 25 % solution of sodium thiosulphate.

Storage: store in airtight container.

Sodium Polystyrene Sulphonate

Powder, 15g

Indications: treatment of hyperkalemia.

Cautions: severe CHF, hypertension, edema, or renal failure.

Drug interactions: antacids, laxatives (magnesium hydroxide, aluminum carbonate), digitalis.

Contraindications: hypernatremia, hypokalemia, obstructive bowel disease.

Side effects: hypernatremia, hypokalemia, hypocalcemia, hypomagnesemia, anorexia, constipation, fecal impaction, intestinal obstruction, nausea, vomiting.

Dose and Administration: Adult: *Oral:* 15g (60ml) 1 - 4 times per day. *Rectal:* 30 - 50g every 6 hours. **Child:** *Oral:* 1g/kg/dose every 6 hours. *Rectal:* 1g/kg /dose every 2 - 6 hours.

Storage: store prepared suspensions at 15-30 °C, store repackaged product in refrigerator and use within 14 days.

Sodium Thiosulphate

Injection, 10 % in 50 ml ampoule

Indications: poisoning with cyanides (used in conjunction with sodium nitrite)

Dose and Administration: See under sodium Nitrite

Universal Antidote(charcoal+tannic acid+magnesium oxide)

Powder, 2 parts + 1 part + 1 part

Indications: treatment of selected cases of acute poisoning to adsorb the toxic substance and thereby reduces its systemic absorption.

Note: The "Universal antidote" is inferior to activated charcoal alone. In addition, the tannic acid component is potentially hepatotoxic. Thus, there is no justification for the use of the "Universal antidote".

20. IMMUNOLOGICAL PREPARATIONS

Immunoglobulins

Immunoglobulins are preparations containing antibodies against infectious micro-organisms and are prepared usually from human plasma or serum. They are used for passive immunization, thus conferring immediate protection against some infectious diseases. They are preferred to antisera of animal origin as the incidence of adverse reactions is less.

Side effects: Local reactions with pain and tenderness at the site of intramuscular injection; hypersensitivity reactions, including rarely anaphylactic reactions, have also been reported; systemic reactions with fever, chills, facial flushing, headache, and nausea may occur following intravenous administration, particularly at high rates of infusion.

Cautions: If immunoglobulins are given after administration of a live vaccine at interval of at least 3 weeks should be allowed to elapse. An interval of 3 months should be allowed between the use of live vaccines and the prior administration of immunoglobulins.

Antisera: Antisera (immunosera) are sterile preparations containing immunoglobulins obtained from the serum of immunised animals by purification. Antisera have the specific power of neutralising venoms or bacterial toxins, or combining with the bacterium, virus, or other antigen used for their preparation.

Side effects and cautions: Anaphylactic reaction may occur, with hypotension; dyspnoea, urticaria, and shock; serum sickness frequently 7 to 10 days after the injection of serum of animal origin.

Before injecting serum, information should be obtained whenever possible as to whether previous injections of serum

have been received and whether the patient is subject to hypersensitivity disorders. Sensitivity testing should be performed before the administration of antisera.

Vaccines: Vaccines are preparations of antigenic materials which are administered with the object of inducing in the recipient active immunity to specific bacteria or viruses. They may contain living or killed microorganisms, bacterial toxoids, or antigenic material from particular parts of the bacterium, rickettsia or virus.

The term vaccination and immunization are often used synonymously and interchangeably. Vaccination is strictly only the administration of a vaccine whereas immunization results in the demonstrable presence of protective levels of antibodies confirmed usually by serological testing.

Cautions: Vaccination should be postponed in patients suffering from any acute illness although minor infections without fever or systemic upset are not regarded as contra-indications. Before injection of a vaccine any alcohol or disinfectant used for cleansing the skin should be allowed to evaporate otherwise inactivation of live vaccines may occur.

Contraindications: Vaccines are contra-indicated in those who have a confirmed anaphylactic reaction to a preceding dose of a vaccine containing the same antigens or vaccine component (such as antibacterial in viral vaccines).

Hypersensitivity to egg with evidence of previous anaphylactic reaction, contra-indicates influenza vaccine (prepared in hens' eggs), tick-borne encephalitis vaccine, and yellow fever vaccine. Live vaccines may be contra-indicated temporarily in individuals who are immunosuppressed (see Impaired immune response, below); Pregnant (see Pregnancy and breast-feeding, below).

Impaired immune response: Immune response to vaccines may be reduced in immunosuppressed patients and there is also a risk of generalized infection with live vaccines. Severely immunosuppressed patients should not be given live vaccines (including those with severe primary immunodeficiency). Specialist advice should be sought for those being treated with high doses of corticosteroids (dose equivalents of prednisolone: adults, at least 40 mg daily for more than 1 week; children, 2 mg/kg daily for at least 1 week or 1 mg/kg daily for 1 month), or other immunosuppressive drugs and those being treated for malignant conditions with chemotherapy or generalised radiotherapy

Pregnancy: Live vaccines should not be administered routinely to *pregnant women* because of the theoretical risk of fetal infection but where there is a significant risk of exposure to disease (e.g. to yellow fever), the need for vaccination usually outweighs any possible risk to the fetus. Termination of pregnancy following inadvertent immunisation is not recommended. There is no evidence of risk from vaccinating pregnant women with inactivated viral or bacterial vaccines or toxoids. For use of specific vaccines during pregnancy, see under individual vaccines.

Breast-feeding: Although there is a theoretical risk of live vaccine being present in breast milk, vaccination is not contra-indicated for women who are breast-feeding when there is significant risk of exposure to disease. There is no evidence of risk from vaccinating women who are breast-feeding, with inactivated viral or bacterial vaccines or toxoids. For use of specific vaccines during breast-feeding, see under individual vaccines.

Side effects: Injection of a vaccine may be followed by local reactions such as pain, inflammation, redness, and lymphangitis.

An induration or sterile abscess may develop at the injection site. Gastro-intestinal disturbances, fever, headache, irritability, loss of appetite, fatigue, myalgia, and malaise are among the most commonly reported side-effects. Other side-effects include influenza-like symptoms, dizziness, paraesthesia, asthenia, drowsiness, arthralgia, rash, and lymphadenopathy. Hypersensitivity reactions, such as bronchospasm, angioedema, urticaria, and anaphylaxis, are very rare but can be fatal.

Oral vaccines such as cholera, live poliomyelitis, rotavirus, and live typhoid can also cause gastro-intestinal disturbances such as nausea, vomiting, abdominal pain and cramps, and diarrhoea.

Route of administration: Vaccines should not be given intravenously. Most vaccines are given by the intramuscular route; some vaccines are given by others routes—the intradermal route for BCG vaccine, and the oral route for cholera, live poliomyelitis, rotavirus, and live typhoid vaccines. The intramuscular route should not be used in patients with bleeding disorders such as haemophilia or thrombocytopenia. Vaccines usually given by the intramuscular route.

Storage and use: Care must be taken to store all vaccines and other immunological products under the conditions recommended in the product literature; otherwise the preparation may become ineffective. Refrigerated storage is usually necessary; many vaccines and immunoglobulins need to be stored at 2–8°C and not allowed to freeze. Vaccines and immunoglobulins should be protected from light. Reconstituted vaccines and opened multi-dose vials must be used within the period recommended in the product literature. Particular attention must be paid to instructions on the use of diluents. Vaccines which are liquid suspensions or are reconstituted before use should be adequately mixed to ensure uniformity of the material to be injected.

Indications: to prevent a rhesus (Rh) negative mother actively forming antibodies to fetal rhesus positive (Rh+) red blood cells that may pass into the maternal circulation during child birth, abortion, or certain other sensitizing events causing disease of the new born (erythroblastosis fetalis). Anti-D immune globulune should be administered following any sensitizing episode (e.g. abortion, miscarriage and birth), it should be injected within 72 hours of the episode but even if a longer period has elapsed it may still give protection and should be administered. The dose of Anti-D immunoglobuline is determined according to the level of exposure to rhesus-positive blood. Routine antenatal anti -D prophylaxis should be offered to all non-sensitised pregnant women who are rhesus negative.

Anti-Rho (D) Immune Globulin

Injection, 2ml in vial, 120mcg, 300mcg

Indications: see notes above

Cautions: as for immunoglobuline in general; Rho (D) immune globulin should be used with caution in individuals with a history of prior allergic reactions to preparation containing human immune globulins. Caution also in those with thrombocytopenia or bleeding disorders.

Contraindications: Rho (D)-positive individuals, Rho (D)-negative individuals who have been previously sensitized to Rho (D) antigens, anaphylactic reaction to preparation containing human immune globulins.

Side effects: as for immunoglobulin in general; pain tenderness, and discomfort at site of injection, slight temperature elevations, fever, myalgia, lethargy.

Dose and Administration: *After full-time delivery: IM:* 500 units (100ug). A higher dose may be required depending on the amount of transplacental bleeding.

Termination of pregnancy: Rh-negative women having spontaneous or induced up to 13 weeks of gestation or more:IM: 250 units (50mcg) of anti-DImmunoglobulin.

Occurrence of risk of sensitization during pregnancy from threatened abortion, amniocentesis or external version: IM: 250-500 units (50-100mcg) of anti Rho (D) immunoglobulin.

Storage: at a temperature between 2^oc and 8^oc.

BCG Vaccine

Injection, 500,000 organisms /ml in 0.05ml and 0.1ml

Indications: active immunization against tuberculosis.

Cautions: pregnancy, eczema, scabies-vaccine site must be lesion-free; see also notes above.

Drug interactions: asparaginase, azathioprine, bleomycin, ciclosporin, daunorubicin, dactinomycin, fluorouracil, vinblastin, vincristine.

Contraindications: generalized edema, children with symptomatic HIV, antimycobacterial treatment see also notes under general description above.

Side effects: lymphadenitis and keloid formation; osteitis and localized necrotic ulceration, rarely, disseminated BCG infection in immunodeficient patients.

Dose and Administration: Intradermal injection:Adult and Child > 3 month: 0.1 ml; Infants up to 3 months: 0.05ml.

Storage: store in refrigerator.

Botulism Antitoxin, polyvalent types A, B and E

Indications: treatment of botulism, caused by the injection of infected food.

Note: Treatment should be given as early as possible in the course of the disease. Botulism antitoxins are generally not effective for infant botulism.

Cautions, Contraindications, Side effects: see notes above, as for antisera in general.

Dose and Administrations:*Prophylaxis: IM:* 20 ml as soon as possible after exposure.*Treatment:* 20 ml (diluted to 100 ml with sodium chloride 0.9%), *slow IV infusion* followed by 10 ml 2 - 4 hours later if necessary, and further doses at intervals of 12 - 24 hours.

Storage: store at 2° to 8° c in single use containers.

Cyclosporin A

Capsules, 10mg, 25mg, 50mg, 100mg

Oral solution, 100mg/ml

IV infusion (oily), 50mg/ml

Indications: prevention and treatment of graft rejection following organ and tissue transplantation; severe chronic plaque - type psoriasis, and severe atopic dermatitis.

Cautions: renal or hepatic disease; porphyria.

Contraindications: hypersensitivity to ciclosporin, malignancy, uncontrolled hypertension, or uncontrolled infections.

Drug interactions: amphotericin B, cimetidine, omeprazole, ketoconazole, itraconazole, fluconazole, erythromycin, doxycycline, diltiazem, verapamil, metoclopramide, colchicine, methyl prednisolone, oral contraceptives, danazol, norethisterone, androgens, alopurinol, amiodarone, and grapefruit juice, rifampicin, carbamazepine, phenytoin, phenobarbital, isoniazid, prubucol, ACE inhibitors, potassium-sparing diuretics, aminoglycosides, amphotericin B, ciprofloxacin, vancomycin, co-trimoxazole, NSAIDs, digoxin, colchicine, simvastatin, pravastatin, other immuno suppressants, fat rich meal.

Side effects: nephrotoxicity, hyperkalaemia, hyperuricaemia, hypomagnesaemia and hyperlipidaemia, microangiopathic

haemolytic anaemia, hypertension, nausea, vomiting, headaches, hepatotoxicity, neurotoxicity includes tremor, seizures, dysarthria, confusion, drowsiness, hallucinations, visual disturbances and mental changes.

Dose and Administration: Adult: *Organ transplantation (single therapy): Oral:* 10 - 15 mg/kg/day in 2 divided doses, reduced gradually according to blood levels; maintenance 2 - 6 mg/kg/day in 2 divided doses. *IV infusion:* 2 - 6 mg/kg/day (diluted in 0.9% sodium chloride solution or 5% glucose and given as a continuous infusion over 24 hours) continued until patient can take oral therapy. *Severe psoriasis: Oral:* 2.5 mg/kg/day in 2 divided doses; may be increased gradually up to maximum of 5mg /kg/day if no improvement after 1 month. Discontinue if response still not adequate within 6 weeks on 5mg/kg /day.

Severe atopic dermatitis: Oral: initially 2.5mg/kg/day in 2 divided doses; may be increased rapidly if response inadequate in 2 weeks, up to a maximum of 5mg/kg day. If very severe, initiate with 5 mg/kg/day and reduce gradually once response is satisfactory. Duration of treatment should not exceed 8 weeks. *Child: organ transplantation:* As for adults. Higher or more frequent doses may be required.

Storage: store at room temperature.

Diphtheria Antitoxin

Injection, 2000 units/ml in 5ml

Indications: for passive immunization in suspected cases of diphtheria and should be given without waiting for bacteriological confirmation of the infection.

Note: An antibacterial agent such as erythromycin or benzyl penicillin is usually given concomitantly. Diphtheria antitoxin is generally not used for the prophylaxis of diphtheria because of the risk of provoking a hypersensitivity reaction. Contacts of a diphtheria case should be

promptly investigated, given a prophylactic course of erythromycin and active immunization with a suitable diphtheria containing vaccine as appropriate and kept under observation.

Cautions, Contraindications, Side effects; as for antisera in general, see notes above.

Dose and Administration: Note: A test dose of diphtheria antitoxin should always be given to eliminate hypersensitivity. 10,000 - 30,000 units increased to 40,000 - 100,000 units in severe cases: doses of up to 30,000 units should be given *intramuscularly* but for those over 40,000 units a portion is given *intramuscularly* followed by the bulk of the dose *intravenously* after an interval of ½ to 2 hours.

Note: children require the same dose as adults, depending on the severity of the awe.

Storage: store at 2^o to 8^oc, do not freeze.

Diphtherial and Tetanus Toxoid

Injection, 0.5 ml

Indications: Infants and Children through 6 years of age: Active immunity against diphtheria and tetanus when pertussis vaccine is contraindicated. Children ≥ 7 years of age and Adults: Active immunity against diphtheria and tetanus; tetanus prophylaxis in wound management.

Cautions: bleeding disorders or anticoagulant therapy.

Drug interactions: antimetabolites, alkylating agents, cytotoxic drugs, corticosteroids, irradiation.

Contraindications: hypersensitivity to diphtheria, tetanus toxoid.

Side effects: dizziness, seizure, rash, nausea, vomiting, local reactions, myalgia, arthralgia.

Dose and Administration: *I.M.:* Infants and Child ≤ 6 years (DT): *Primary immunization:* 6 weeks to 1 year: three 0.5 ml

doses at least 4 weeks apart; administer reinforcing doses 6 - 12 months after the third injection.

1 - 6 years: two 0.5 ml doses at least 4 weeks apart, reinforcing dose 6 - 12 months after second injection;

Booster immunization: 4 - 6 years: 0.5 ml; not necessary if the fourth dose was given after fourth birthday; routinely administer booster doses at 10 -year intervals with the adult preparation.

Child ≥ 7 years and Adult:

Primary immunization: Patients previously not immunized should receive 2 primary doses of 0.5ml each, given at an interval of 4 - 6 weeks; third (reinforcing) doses of 0.5ml 6 - 12 months later.

Booster immunization: 0.5ml every 10 years; to be given to children 11 - 12 years of age if at least 5 years have elapsed since last dose of toxoid containing vaccine.

Storage: store at 2 - 8 °C. Do not freeze.

Diphtheria, Tetanus Toxoid and Pertussis Vaccine

Injection, 0.5ml

Indications: active immunization against diphtheria, tetanus, and pertussis from age 6 weeks through seventh birthday.

Cautions: children with coagulation disorders; seizure disorder.

Drug interactions: anticoagulants, corticosteroids and immunosuppressant agents.

Contraindications: children ≥ 7 years of age.

Side effects: drowsiness, irritability, decreased appetite, redness, swelling, fever, vomiting, pain, redness, and tenderness.

Dose and Administration: Child 6 weeks to < 7 years: *I.M:* 0.5ml. *Primary series:* Three doses, usually given at 2, 4, and 6 months of age; may be given as early as 6 weeks of age and repeated every 4 - 8 weeks, use same product for all 3

doses. *Booster series: Fourth dose:* given at \approx 15-20 months of age, but at least 6 months after third dose. *Fifth dose:* Given at 5 - 6 years of age, prior to starting school or kindergarten; If the fourth dose is given at \geq 4 years of age, the fifth dose may be omitted.

Storage: store in refrigerator at 2 to 8 °C; do not freeze.

Gas Gangrene Antitoxin, Mixed

Injection, 25,000 units in 20 ml

Indications: treatment of gas gangrene and for prophylaxis in patients at risk following injury.

Note: They are now seldom used and have been superseded by antibacterials such as benzyl penicillin or metronidazole.

Cautions, Contraindications and Side effects; as for antisera in general,

Storage: Store at 2⁰ to 8⁰C, and not be allowed to freeze.

Haemophilus Influenza type B (Hib) vaccine

Injection, 0.5 ml

Indications: for active immunization against Haemophilus influenzae type b infections, one of the major causes of meningitis and other severe systemic illnesses in young children.

Cautions, Contraindications and Side effects: As for vaccines in general, see notes above; and Erythema multiforme has been reported rarely in children.

Note: Different proprietary vaccines may be conjugated to differing proteins and therefore the same vaccine should be used for an immunization course; if a different vaccine needs to be employed the entire primary course should be repeated.

Dose and Administrations: By deep SC or IM injection in doses of 0.5 ml; doses are given at 2, 3 and 4 months of age. *Note: The vaccine may be administered at the same time as combined diphtheria, tetanus, and pertussis vaccines of the primary*

immunization schedule children aged under 13 months who have already commenced or completed their primary immunization schedule should receive three doses of Hib at intervals of one month. Children aged 13 to 48 months should be given a single dose as they are at lower risk and the vaccine is effective after a single dose in this age group.

Hepatitis B Vaccine, inactivated

Injection, 16.5 % in 2 ml and 10 ml.

Indications: for active immunization against hepatitis B infections in persons at high risk of contracting the disease.

Cautions; Side effects; see notes above.

Note: The high risk group include: health care personnel, laboratory workers, or any other personnel who have direct contact with patients or their body fluids; patients requiring haemodialysis; haemophiliacs and those receiving regular blood transfusions or blood products; contacts or sexual partners of cases or carriers of hepatitis B; individuals who frequently change sexual partners; parenteral drug abusers; and some travelers to areas where hepatitis B is endemic.

Dose and Administrations:*Note: refere Ethiopian Immunization schedules. Immunization of Children against hepatitis B: IM: infant 0.5 ml either at birth Or at 6 and 14 weeks of age, or at 6, 10 and 14 weeks of age.*

Immunization of unimmunized high risk persons against hepatitis B: IM: Adult and child over 15 years of age 3 doses of 1 ml, with an interval of 1 month between the first and second dose and 5 months between the second and third doses; child under 15 years, 0.5 ml.

Note: Different products may contain different concentrations of antigen per ml. Consult manufacturer's literature. The vaccine should be given in the deltoid region in adults; anterolateral thigh is the preferred site in infants and children; it should not be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with hemophilia.

Storage: store at 2° to 8° c, not be allowed to freeze.

Hepatitis B vaccine, Recombinant yeast DNA

Injection, 0.5ml

See under Hepatitis B Vaccine, Inactivated.

Dose and Administration: The basic immunization schedule consists of 3 doses of a hepatitis B vaccine, with the second and third doses 1 and 6 months, respectively, after the first. Typical doses for adults are 10 or 20mcg and for children 2.5 to 10mcg.

Storage: store at 2° to 8° c, not be allowed to freeze, and be protected from light. Under these conditions it may be expected to retain its potency for months.

Human Antirabies Immunoglobulin

Injection, 150 IU/ml, in 2 ml

Indications: Passive immunization either post-exposure or in suspected exposure to rabies in high-risk countries in unimagined individuals (in conjunction with rabies vaccine).

Cautions, Side effects: see notes above, as for immunoglobulin in general.

Contraindications: see notes above; avoid repeat doses after vaccine treatment initiated; intravenous administration. *Note: If schedule requires rabies vaccine and rabies immunoglobulin to be administered at the same time, they should be administered using separate syringes and separate sites.*

Dose and Administration: *Immunization against rabies: Post-exposure (or suspected infiltration):* Adult and Child: 20 units/kg (half by intramuscular injection and half by wound infiltration)

Storage: store at 2° to 8°C.

Human Papiloma Virus Vaccine:

Injection, HPV6L1 20mcg +HPV11L140mcg + HPV16L1 20mcg +HPV18L120mcg /0.5mldose.

Human papilloma virus vaccine is available as a bivalent vaccine or a quadrivalent vaccine. Bivalent vaccine is licensed for use in females for the prevention of cervical cancer and other pre-cancerous lesions caused by human papilloma virus types 16 and 18. Quadrivalent vaccine is licensed for use in females for the prevention of cervical cancer, genital warts and pre-cancerous lesions caused by human papilloma virus types 6, 11, 16, and 18. The two vaccines are not interchangeable and one vaccine product should be used for an entire course.

Indications: prevention of cervical cancer, genital warts and other pre-cancerous lesions caused by human papilloma virus types 6, 11, 16 and 18.

Cautions: See notes above

Contraindications: See notes above

Pregnancy: not known to be harmful, but vaccination should be postponed until completion of pregnancy

Side effects: See notes above

Dose and administration: Human papilloma virus vaccine will be most effective if given before sexual activity starts. The first dose is given to females aged 12 to 13 years, the second and third doses are given 1–2 and 6 months after the first dose; all 3 doses should be given within a 12-month period. If the course is interrupted, it should be resumed but not repeated, allowing the appropriate interval between the remaining doses. Where there are significant challenges in scheduling vaccinations, or a high likelihood that the third dose will not be given, the third dose of bivalent vaccine can be given 3 months after the second dose. The duration of protection has not been established, but current studies suggest that protection is maintained for at least 6 years after completion of the primary course. As the vaccines do not protect against all strains of human papilloma virus, routine cervical screening should continue.

Immune Serum Globulin, Human (Gamma Globulin, Human)

Injection, 16.5% in 2ml, 5ml and 10ml

Indications: for replacement therapy in patients with immune deficiency states, e.g. agammaglobulinaemia or hypogammaglobulinaemia, and for the immediate protection of susceptible contacts against hepatitis A or measles.

Cautions: thrombocytopenia or coagulation disorders.

Drug interactions: Live virus, vaccines (measles, mumps, rubella).

Contraindications: IgA deficiency.

Side effects: flushing, angioedema, chills, lethargy, fever, urticaria, erythema, nausea, vomiting, local (myalgia, pain, tenderness, muscle stiffness at I.M site), hypersensitivity.

Dose and Administration: *IM: Hepatitis A prophylaxis: Contacts:* 0.02 - 0.04 ml/kg within 1 week of exposure.

Pre-exposure prophylaxis for travellers: Period of stay < 3 months, 0.02 ml/kg. Period of stay > 3 months (continued exposure), 0.06 ml/kg 4-6 monthly.

Measles prophylaxis: within 1 week of contact: 0.2 - 0.25 ml/kg (maximum 15 ml).

Immunocompromised patients: 0.5 ml/kg (maximum 15 ml).

Follow after 3 months with active immunisation in patients \geq 15 months of age, unless contraindicated.

Replacement therapy: congenital immunoglobulin deficiencies: 0.2 - 0.5 ml/kg, repeated 4 - 8 weekly.

Transient hypogammaglobulinaemia: 0.2 - 0.5 ml/kg, repeated when necessary.

Storage: store in refrigerator, do not freeze.

Influenza Virus Vaccine, Polyvalent

Injection, 0.5 ml

Indications: provide active immunity to influenza virus strains contained in the vaccine.

Cautions: thrombocytopenia or any coagulation disorder.

Drug interactions: DTP

Contraindications: hypersensitivity reaction.

Side effects: fever, malaise, angioedema, urticaria, local (tenderness, redness, or induration at the site of injection), myalgia, allergic or anaphylactoid reactions.

Dose and Administration: Adult: *I.M. or deep SC*, 0.5 ml.

Storage: store between 2-8°C.

Interferon Alpha

Injection, 3, 5, 10 million units.

Indications: treatment of malignant neoplasms such as non-Hodgkin's lymphoma, hairy-cell and chronic myeloid leukaemias, and renal cell carcinoma. Has some efficacy in chronic viral hepatitis B and C.

Cautions: depression, autoimmune disease, preexisting cardiac disease, renal and hepatic impairment, myelosuppression, diabetes, thyroid disease.

Drug interactions: theophylline, ACE inhibitors, melphalan, prednisolone, clozapine, warfarin and zidovudine.

Contraindications: hypersensitivity reaction, autoimmune hepatitis.

Side effects: fever, chills, myalgia, depression, unusual tiredness, hypo and hypertension, arrhythmias, transient confusion, somnolence, delirium, extrapyramidal symptoms, mania and neurasthenia with catatonic episodes. Clinical hypothyroidism preceded by appearance in the blood of thyroid autoantibodies reported with long-term interferon. Myelosuppression (granulocytopenia and thrombocytopenia); GI effects and elevation of liver enzymes reported.

Dose and Administration: Doses for individual products may differ; package insert should be consulted.

Hairy-cell leukaemia: SC, 2 million IU/M² administered (on alternate days) 3 times a week;

Chronic viral hepatitis: Chronic Hepatitis B is usually treated with 5 - 10 million IU thrice weekly for 16 weeks. Chronic hepatitis C is usually treated with 3 - 5 million IU thrice weekly for 24 weeks.

Storage: store in refrigerator at 2-8 °C; do not freeze.

Interferon Gamma

Injection, 3, 5, million units / 0.5ml

Indications: reduce frequency and severity of serious infections associated with chronic granulomatous disease; delay time to disease progression in patients with severe malignant osteopetrosis.

Cautions: cardiac disease, seizure disorders, CNS disturbances, or myelosuppression.

Contraindications: hypersensitivity reaction.

Side effects: fever, headache, chills, fatigue, rash, diarrhea, vomiting, injection site erythema or tenderness (local), depression, nausea, abdominal pain, myalgia, arthralgia, back pain.

Dose and Administration: *Chronic granulomatous disease:* Child > 1 year and Adult: SC: BSA ≤ 0.5 m²: 1.5 mcg /kg/dose 3 times /week. BSA > 0.5 m²: 50 mcg/m² (1 million int. units/m²) 3 times/week. *Severe, malignant osteopetrosis:* Child > 1 year: SC: BSA ≤ 0.5m²: 1.5mcg/kg/dose 3 times /week. BSA > 0.5m²: 50mcg/m² (1 million int. units/m²) 3 times/week.

Storage: store in refrigerator. Do not freeze.

Measles Virus Vaccine, Live Attenuated

Injection, 0.5 ml

Indications: active immunization against measles.

Side effects: as for vaccines in general, see notes above, and fever and skin rashes may occur following the administration of measles vaccines. The fever generally starts 5 to 10 days after the injection, lasts for about 1 or 2 days, and has sometimes been accompanied by convulsions. Conjunctivitis, coryza, pharyngitis, and cough may also occur. More serious effects reported rarely after the use of the vaccine include encephalitis and thrombocytopenic purpura.

Cautions: see notes above; pregnancy

Contraindications: see notes above; hypersensitivity to any antibiotic present in vaccine - consult manufacturer's literature; hypersensitivity to egg.

Dose and Administration:*Immunization of children against measles:IM or deep SC injection: infant at 9 months of age, 0.5 ml. Prophylaxis in susceptible children after exposure to measles:IM or deep SC injection within 72 hours of contact, child over 9 months of age 0.5 ml*

Storage: store at 2° to 8° c and be protected from light.

Meningococcal polysaccharide vaccine

Injection, 0.5ml

Indications:for active immunization against *Neisseria meningitidis* infections which include meningitis and septicaemia. *Note: Meningococcal vaccines are indicated in persons at risk, in epidemic or endemic areas, of meningococcal disease caused by the specific serotypes contained in the vaccine. It is given as an adjunct to chemoprophylaxis in close contacts of persons traveling to countries where the disease is endemic. Asplenic persons or those who have terminal complement component deficiencies are at higher than normal risk of acquiring meningococcal infection.*

Cautions: as for vaccines in general; Immunity to some meningococcal vaccines may be insufficient to confer adequate protection against infection in infants under 2 years of age.

Contraindications: contraindicated for children under 2 years of age. Other contraindications and Side effects; as for vaccines in general.

Dose and Administration: *SC or IM:* A single injection of 0.5ml.

Storage: store both the freeze-dried and the reconstituted vaccine between 2 and 8°C. Protect from freezing.

Mycophenolic Acid (as Mycophenolate sodium/Mofetil)

Tablet (e/c), 180mg, 360mg (as Mycophenolate Sodium), 250mg, 500mg, 1gm (as Mycophenolate Mofetil equivalent to 720mg Mycophenolic Acid)

Capsule, 250mg

Indications: prophylaxis of acute renal, cardiac, or hepatic transplant rejection (in combination with ciclosporin and corticosteroids) under specialist supervision

Cautions: full blood counts every week for 4 weeks then twice a month for 2 months then every month in the first year (consider interrupting treatment if neutropenia develops); elderly (Increased risk of infection, gastro-intestinal haemorrhage and pulmonary oedema); children (higher incidence of side-effects may call for temporary reduction of dose or interruption); active serious gastro-intestinal disease (risk of haemorrhage, ulceration and perforation); delayed graft function; increased susceptibility to skin cancer (avoid exposure to strong sunlight); bone marrow suppression Patients should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. infection or inexplicable bruising or bleeding

Contraindications:pregnancy (exclude before starting and avoid for 6 weeks after discontinuation), breast-feeding.

Drug interactions:antacids, metronidazole, norfloxacin, rifampicin, phenytoin, clozapine, aciclovir, ganciclovir, digoxin,iron, colestyramine sevelamer.

Side effects:gastro-intestinal disturbances (including diarrhoea, vomiting, and abdominal pain), gastrointestinal ulceration and bleeding, abnormal liver function tests, hepatitis, jaundice, pancreatitis; oedema, tachycardia, hypertension, hypotension,vasodilatation; cough, dyspnoea; insomnia, agitation, tremor, dizziness, headache; influenza-like syndrome, infections (viral, bacterial, and fungal); hyperglycaemia; renal impairment; increased risk of malignancies, particularly of the skin; blood disorders (including leucopenia, anaemia, thrombocytopenia,pancytopenia), disturbances of electrolytes and blood lipids; arthralgia; alopecia, acne, and rash; progressive multifocal leucoencephalopathy reported

Dose and administration:*Renal transplantation*, by *mouth*, 1 g twice daily starting within 72 hours of transplantation or by *intravenous infusion*, 1 g twice daily starting within 24 hours of transplantation for max. 14 days (then transfer to oral therapy);

Child and adolescent: 2–18 years, by *mouth*600 mg/m²/dose twice daily (max. 2 g daily), *Note* :Tablets and capsules not appropriate for dose titration in children with body surface area less than 1.25m² .*Cardiac transplantation*, by *mouth*, 1.5 g twice daily starting within 5 days of transplantation. *Hepatic transplantation*,by intravenous infusion, 1g twice daily starting within 24 hours of transplantation for 4 days (up to max. 14 days), then by mouth, 1.5 g twice daily as soon as is tolerated.

Storage: see notes above

Pentavalent (Diphtheria, Pertusis, Tetanus, Hepatitis B, Haemophilus InfluenzaeB) Vaccine

Injection, 0.5 ml

Indications: Active immunization against diphtheria, tetanus, pertussis, hepatitis B and Haemophilus Influenzae B at completion of 2, 4 and 6 months of age.

Cautions: Administration of any subsequent dose of Pentavalent should be carefully considered if, in connection with the administration of vaccine, one or more of the following effects have been observed: 40°C temperature within 48 hours following vaccination (not due to other identifiable causes); collapse or shock (hypotonic hyporesponsive episodes) within 48 hours following vaccination; persistent crying lasting more than 3 hours during the 48 hours following vaccination; convulsions, with or without fever, within 3 days following vaccination; subjects with thrombocytopenia or a bleeding disorder.

Contraindications: avoided only for children with:

A history of a severe allergic reaction (e.g. generalized urticaria, difficulty in breathing, swelling of mouth and throat, shock) to a previous dose of Pentavalent vaccine or with known hypersensitivity to any vaccine component. A history of an encephalopathy of unknown aetiology after a previous immunization with a vaccine containing pertussis. In these circumstances, the vaccination course should be continued with Diphtheria and Tetanus Toxoid (DT) and Hepatitis B.

A severe acute illness with temperature above 38.5°C. As with other vaccines, vaccination should be postponed in children suffering from acute febrile illness

A progressive neurological disease.

The following are NOT contraindications; Minor illnesses such as respiratory tract infection or diarrhea with temperature below

38.5°C. Allergy or asthma, family history of convulsions, Treatment with antibiotics, Treatment with topical corticosteroids or systemic use of corticosteroids at low dosage (<0.5 mg/kg of prednisone or equivalent) in case of skin diseases like dermatitis, eczema, or other localized skin disorders, Infection with HIV. Breast feeding, History of seizures (Convulsions, fits). Chronic illnesses such as those of heart, lung, kidney or liver, Stable neurological conditions e.g. cerebral palsy, Down syndrome, Prematurity or low birth weight, History of jaundice at birth.

Dose and administration:The standard dose for infants and children is 0.5 ml. 4 Pentavalent vaccine should be given as an *Intramuscular (IM)* injection to the anterolateral aspect of the thigh in infants. Pentavalent vaccine **SHOULD NOT** be given in the buttock or administered intradermally because this route of administration does not produce an adequate antibody response. In addition there may be a risk of injury to the sciatic nerve, if it is given in the buttock. Unlike the present practice of administering two injectable vaccines (DPT and Hep.B) in the same clinic session, where it is advised that the two injections are administered in different sites/thighs, in Pentavalent there is no special concern of which side/site to be used. However, it is advisable to use the left thigh/deltoid muscle to maintain a uniform practice.

Storage:Pentavalent vaccine should be stored and transported between 2°C to 8°C. It should not be frozen. Hence this vaccine should never be stored in the freezer and should preferably be kept in the middle shelf of the main compartment of the refrigerator in all places. While transporting the vaccine vials should not be kept in contact with ice in vaccine carriers and

during clinic sessions Pentavalent vials should not be kept in contact with ice.

Pneumococcal Polysaccharide Vaccine

Injection, 0.5ml

Indications: people at risk of developing serious pneumococcal infection, such as patients with chronic cardiac or pulmonary disease, and with illnesses or conditions known to predispose to pneumococcal infection (such as sickle cell disease, nephritic syndrome, previous splenectomy, multiple myeloma and Hodgkin's disease); also in immunocompromised patients, including those with HIV infection.

Contraindications: pregnancy, active infection and children under 2 years old.

Side effects: transient, local pain and erythematic at the injection site, fever may occur occasionally.

Dose and Administration: *SC or IM, 0.5 ml.*

Storage: store in refrigerator at 2- 8°C.

Poliomyelitis Vaccines

Poliomyelitis is an acute viral infection spread by the faecal-oral route, which can cause paralysis of varying degree. There are two types of vaccine against poliomyelitis: oral and injectable. Oral poliomyelitis vaccine (OPV) is composed of three types of live attenuated poliomyelitis viruses.

Poliomyelitis vaccine, Trivalent

Types I, II, III

Oral suspension, 0.5 ml, 10ml and 20 ml.

Indications: active immunization against Poliomyelitis.

Cautions: pregnancy

Drug interactions: asparaginase, azathioprine, ciclosporin, immunoglobulin.

Contraindications: patients with diarrhea or vomiting; food which contains a preservative.

Side effects: rarely, vaccine-associated poliomyelitis in recipients of vaccine and contacts of recipients.

Dose and Administration: *Oral: Adult: Primary immunization of unimmunized adults:* 3 doses each of drops with an interval of at least 4 weeks between each dose. *Reinforcing immunization:* 3 drop 10 years after completion of primary course. *Child: Primary immunization:* 3 drops at birth and at 6, 10 and at 14 weeks of age. *Reinforcing immunization:* 3 drops at least 3 years after completion of primary course and a further 3 drops at 15 - 19 year of age.

Storage: store between 2-8 °C or in the frozen state.

Rabies Antiserum, Equine

Injection, 200 units in 5ml

Indications: rabies antiserum, equine is used to provide passive immunization to Rabies in patients who have received bites from rabid animals or animals suspected of being rabid.

Cautions: as for antisera in general; caution should be taken in allergic patients. The patient must be kept under observation after the administration of full doses of antisera and adrenaline injection kept in readiness for emergency use.

Side effects: as for antisera in general; nephritis, myocarditis, polyarthritis, neuritis and ureitis.

Dose and Administration: usual dose 40 units per kg of body weight given at the same time, but at different sites, as the first dose of a Rabies vaccine. It has been recommended that 50% of the dose should be administered by *local infiltration* at the site of the wound and the remainder given by *IM injection* unless the wound involves mucous membranes when the entire dose should be given *intramuscularly*.

Storage: between 2° and 8°C.

Rabies Vaccine

Injection, 100 ml in vial

Indications: for active immunization against rabies. They are given, with rabies immunoglobulin or antisera, for post exposure treatment to patient who have been bitten by rabid animals or animals suspected of being rabid. They are also used for pre-exposure prophylaxis against rabies in persons at high risk of exposure to rabies vaccine.

Cautions: as for vaccines in general; see notes above.

Note: when this vaccine is injected into the gluteal region, there is a poor response. Concomitant administration of chloroquine may also affect the antibody response. Because of the potential consequences of inadequately treated rabies exposure and because there is no indication that fetal abnormalities have been associated with rabies vaccination, pregnancy is not considered a contraindication to post exposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy.

Side effects: as for vaccines in general, see notes above; and patients may experience pain, eurhythmic, and in duration at the injection site after the use of any type of rabies vaccine; nausea, headache, fever, malaise, or myalgia may also occur. Neuroparalytic and hypersensitivity reactions have been associated with the vaccines derived from animal nerve tissues or duck embryos.

Dose and Administration: *Prophylactic: deep SC or IM injection* in the deltoid region, 1 ml on days 0, 7, and 28; also booster doses every 2 – 3 years to those continued risk.

Storage: store at 2° to 8°C, not be allowed to freeze, and be protected from light. *Under these conditions it may be expected to retain its potency for at least 2 years.*

Rabies Vaccine, Duck Embryo

Injection; 100 ml in vial

See under Rabies vaccine

Dose Administration: *Prophylactic, IM injection* in the deltoid muscle or anterolateral thigh in small children, 1 ml on days 0, 7 and 21 or 28; also booster doses every 2 - 5 years for those at continued risk. *Post exposure, IM injection* in the deltoid muscle or anterolateral thigh in small children, 1ml.

Storage: store at 2° to 8°C.

Rabies (Human diploid cell) vaccine

Injection, 2.5IU/ml

Indications: rabies human diploid cell vaccine is used for active immunization against rabies. They are used as a part of post exposure treatment, for the prevention of rabies in patients who have been bitten by rabid animals or animals suspected of being rabid.

Cautions: as for vaccine in general; the vaccine should be administered with caution in patients with a history of allergic disorders or who have exhibited previous systemic allergic reaction to human diploid cell vaccine.

Drug interactions: rabies immunoglobulin, antimalarial agents, corticosteroids immuno suppressive agents.

Side effects: as for vaccine in general; pain, erythema and induration at injection site, pruritis, nausea, headache, fever.

Dose and Administration: *For post exposure therapy:* deep SC or IM: 6 doses of human diploid cell vaccine, each of 1ml on days 0, 3, 7, 14, 30 and 90.

For pre-exposure prophylaxis against rabis: IM or ID: 2 doses of human diploid cell vaccine given 4 weeks apart with a third dose after 12 months, either 1ml may be given by deep SC or IM injection or 0.1ml ID. Booster doses should be given every 1 to 3 years depending upon the risk of exposure.

Storage: between 2° and 8⁰C.

Rota Virus Vaccine Monovalent (P1 [8], G1), Bivalent, Pentavalent (G1, 2, 3, 4, 5 and P1 [8])

Oral solution, 2ml

Indications: immunization against gastro-enteritis caused by rotavirus

Cautions: see notes above, also diarrhoea or vomiting (postpone vaccination); immunosuppressed.

Contraindications: see notes above, also predisposition to, or history of intussusceptions.

Scorpion Venom Antisera (Scorpion Antivenom)

Injection, 0.5ml

Indications: to neutralize the venom of one or more species of scorpion

Cautions: allergic to the antivenin, sensitivity testing should be preformed.

Side effect: as for antisera in general; urticaria, nephritis, myocarditis, polyarthritis, neuritis, ureitis.

Dose and Administration: The use of a scorpion antiserum suitable for the species of scorpion can prevent symptoms provided it is done with the least possible delay, other general supportive measures may also be needed. The volume stated on the label as the dose, should preferably be made directly into the site of the sting but if this cannot be done, as much as possible should be injected into the site and the remainder *intramuscularly* into a convenient proximal position.

Snake Venom Antiserum Polyvalent

Injection, 10ml

Indications: antivenin (crotalidae) polyvalent neutralizes absorbed venom of crotalid snakes (pit vipers), including the rattlesnake, copperhead, water moccasin and tropical and asiatic

crotalids, and is used to prevent or minimize the effects of poisoning by these snakes.

Cautions: in people who have been snake-bitten if they have a history of asthma hay fever, urticaria, or other allergic manifestation. Intradermally sensitivity testing should be performed before administration.

Side effect: as for antisera in general; itching, edema of the face, tongue and throat, cough, vomiting, cardiovascular collapse.

Dose and Administration: For *IV infusion*, a 1:1 to 1:10 dilution of reconstituted antivenin in 0.9% sodium chloride or 5% dextrose injection is prepared. Usual dose *IV infusion*, 5-10ml of diluted antivenin, infused over 3-5 minutes with careful observation of the patient.

Tacrolimus

Capsule, 500mcg, 1mg, 2mg, 5mg Infusion, 5mg/ml

Indications: prophylaxis of organ rejection in liver, kidney, and heart allograft recipients and allograft rejection resistant to conventional immunosuppressive regimens, moderate to severe atopic eczema

Cautions: pregnancy; see under Cyclosporin A (section 19); also monitor ECG (important: also echocardiography, visual status, blood glucose, haematological and neurological parameters and whole-blood 'trough' concentrations (especially during episodes of diarrhoea); prolonged QT interval; hepatic impairment; if contraception needed non-hormonal methods should be used.

Drug interactions: NSAIDs; Angiotensin-II Receptor Antagonists: Antibacterials: (clarithromycin; rifampicin; aminoglycosides; chloramphenicol and vancomycin); Antidepressants; Antiepileptics; Antifungals (fluconazole, itraconazole, ketoconazole and voriconazole; amphotericin;

imidazoles and triazoles); Antipsychotics: droperidol; Antivirals: aciclovir or ganciclovir; atazanavir, nelfinavir and ritonavir; efavirenz; saquinavir; Barbiturates: phenobarbital; Calcium-channel Blockers: felodipine, nifedipine and verapamil ; diltiazem and nifedipine; Cyclosporin; potassium-sparing diuretics and aldosterone antagonists; Hormone Antagonists: ethinylestradiol; Potassium Salts; Progestogens; omeprazole

Contraindications: hypersensitivity to macrolides; breast-feeding; avoid concurrent administration with cyclosporin A (care if patient has previously received cyclosporine A)

Side effects: *For Kidney Transplant Patients:* infection, headache, tremors, diarrhea, constipation, nausea, high blood pressure, changes in the amount of urine, and trouble sleeping. *For Liver Transplant Patients:* headache, tremors, diarrhea, high blood pressure, nausea and changes in the amount of urine.

Dose and Administration: *Liver transplantation:* Adult: starting 12 hours after transplantation, *by mouth*, 100–200 micrograms /kg daily in 2 divided doses or by *intravenous infusion* over 24 hours, 10–50 micrograms /kg daily for up to max. 7 days (then transfer to oral therapy); CHILD: *by mouth*, 300 micrograms/kg daily in 2 divided doses or by *intravenous infusion* over 24 hours, 50 microgram s/kg daily for up to max. 7 days (then transfer to oral therapy).

Renal transplantation: Adult: starting within 24 hours of transplantation, *by mouth*, 200–300 micrograms /kg daily in 2 divided doses or by *intravenous infusion* over 24 hour s, 50–100 microgram s/kg daily for up to max. 7 days (then transfer to oral therapy); CHILD: *by mouth*, 300 micrograms/kg daily in 2 divided doses or by *intravenous infusion* over 24 hour s, 75–100 micrograms/kg daily for up to max. 7 days (then transfer to oral therapy).

Heart transplantation (with or without antibody induction): starting within 5 days of transplantation, *by mouth*, 75 micrograms/kg daily in 2 divided doses or by *intravenous infusion* over 24 hours, 10–20 micrograms/kg daily for up to max. 7 days (then transfer to oral therapy); child, without antibody induction, initially by *intravenous infusion* over 24 hours, 30–50 micrograms/kg daily, then *by mouth*, 300 micrograms/kg daily in 2 divided doses as soon as clinically possible (give 8–12 hours after discontinuing intravenous infusion); following antibody induction, *by mouth*, 100–300 micrograms/kg daily in 2 divided doses.

Storage: store at 20°-25°C.

Tetanus Antitoxin, Equine

Injection, 1500 units, 3000 units, 20,000 units

Indications: tetanus antitoxin, equine is indicated for temporary passive immunization against tetanus and also to prevent tetanus infection that arise from the toxins produced by *Clostridium tetani*.

Cautions: allergic to the antitoxin. For this sensitivity testing should be performed.

Side effects: Anaphylaxis (with hypotension, dyspnoea, urticaria, shock), serum sickness (fever, vomiting, diarrhoea, bronchospasm, urticaria).

Dose and Administration: Adult: *prophylaxis after injury of non-immune or partially immune persons: SC, or IM: 3000 - 5000 units of tetanus antitoxin.*

Treatment of established tetanus: 50,000 - 100,000 units part of which is administered by IV injection with the remainder being given intramuscularly.

Tetanus Immune-Human Globulin

Injection, 3000 units

Indications: for passive immunization against tetanus.

Note: The use of tetanus immunoglobulins is recommended as part of the management of tetanus-prone wounds in persons unimmunized or incompletely immunized against tetanus, in persons whose immunization history is unknown, and in persons who received the last dose of tetanus vaccine more than 10 years previously.

Cautions: as for immunoglobulin in general; tetanus immunoglobulins should not be injected in to the same site or in the same syringe.

Contraindications and Side effects; see notes under general description above.

Dose and Administration: The usual dose of tetanus immunoglobulin is 250 units by *intramuscular injection* but if more than 24 hours have elapsed since the wound was sustained, if there is a risk of heavy contamination, or following burns 500 units should be given irrespective of the immunization history. Tetanus immunoglobulin is also used in the treatment of tetanus, a recommended dose being 150 units per kg body-weight given *intramuscularly* in to different sites. *Note: The pediatric dose is the same as for adults. Alternatively, in children younger than 7 years of age, tetanus immunoglobulin can be given in doses of 4 units per kilogram of body weight.*

Storage: store between 2 and 8°C. Do not freeze.

Tetanus Toxoid

Injection, 0.5 ml, 1ml

Indications: active immunization against tetanus and neonatal tetanus; wound management (tetanus - prone wounds and clean wounds).

Cautions: patients on anticoagulants.

Drug interactions: anticoagulants, corticosteroids.

Contraindications: hypersensitivity to tetanus toxoid.

Side effects: hypotension, fever, rash, urticaria, nausea, local (edema, redness, warmth), arthralgia.

Dose and Administration: *Unimmunized patients: IM*, 2 doses of 0.5ml, 6 – 8 weeks apart. A third dose is recommended 6 -12 months after the second dose, and is essential when tetanus immunoglobulin was given at the time of the first injection. In these cases the interval between the first and second doses should be reduced to 4 weeks. A booster should be given every 10 years, or following an injury.

Storage: store in refrigerator at 2-8 °C.

Yellow fever Vaccine

Injection, 500LD, 50 Doses

Indications: active immunization against yellow fever.

Cautions: pregnancy.

Contraindications: infants under 6 months of age; hypersensitivity to any antibiotic present in vaccine and egg.

Side effects: rarely encephalitis, generally in infants under 9 months.

Dose and Administration: Child \geq 9 months and Adult: SC: one dose (0.5ml). Infant 6-9 months of age: 0.5ml, only if risk of yellow fever is unavoidable.

Booster: Every 10 years.

Storage: store at a temperature between 0- 5 °C. Do not freeze.

21. MISCELLANEOUS

Aluminum Sulphate + Calcium Hypochlorite + Sodium Carbonate

Water treatment powder in the ratio of 23:1:1 by weight

Indications: used as a disinfectant in water.

Anticoagulant Citrate Dextrose solution (ACD Solution) Sodium Citrate + Citric Acid + Dextrose

Solution, 1.32g +0.44g +1.47g

Barium Sulfate

Powder in Sachet

Indications: use as a contrast medium in x-ray photography of the digestive tract.

Contraindications: in patients with known or suspected obstruction of the colon, known or suspected gastrointestinal tract perforation, suspected tracheoesophageal fistula, obstructing lesions of the small intestine, pyloric stenosis or known hypersensitivity to barium sulfate formulations.

Side effects: Constipation, cramping, diarrhea

Storage: Store at room temperature and Keep out of reach of children.

Calcium Hypochlorite+IronSulphate+ Bentonite+Potassium Permanganet Polyacrylamide + Sodium Carbonate

Water treatment Powder

Indications: used as a disinfectant in water.

Dicophane (DDT)

Dusting Powder, 10%

It is an effective pediculocide. Its prolonged residual effect makes it lethal to the larva which hatches out later.

Formaldehyde Solution

Solution, 3%, 8% (w/w, v/v)

Indications: It is a disinfectant active against bacteria, fungi, and many viruses, with a slow action against bacterial spores. It is used for the disinfection of the blankets, bedding, and membranes in dialysis equipment.

Cautions and Side effects: Ingestion of formaldehyde solution causes intense pain, with inflammation, ulceration, and necrosis of mucous membranes. There may be vomiting, haematemesis, blood-stained diarrhoea, haematuria, and anuria; metabolic acidosis, vertigo, convulsions, loss of consciousness, and circulatory failure may occur. Death has occurred after the ingestion of the equivalent of about 30ml of formaldehyde solution. If the patient survives 48 hours, recovery is probable. Formaldehyde vapour is irritant to the eyes, nose, and upper respiratory tract, and may cause coughing, dysphagia, spasm and oedema of larynx, bronchitis, pneumonia, and rarely, pulmonary oedema. Asthma has been reported after repeated exposure.

Storage: at temperature between 15 and 25°C in airtight containers. Avoid contact with plastics.

Gadodamide

Injection 0.5mmol/ml

Indication: It is a gadolinium-based MRI contrast agent, used to diagnose problems in the brain, spine, chest, stomach, hip area, and other parts of the body.

Cautions: In patients with history of asthma, infection, kidney or liver impairment, seizures, diabetes, high blood pressure, any allergy, during pregnancy and breastfeeding. *Note: It may cause dizziness or lightheadedness, do not drive a car or operate machinery while taking this medication. Patient may develop with increased risk of nephrogenic systemic fibrosis (NSF), if it is so consult with your healthcare provider.*

Contra-indications: Hypersensitivity to the medicine and in patient with severe kidney disease.

Side-effects: Nausea, headache and dizziness.

Dose and Administration: CNS Adults: The recommended dose is 0.2 ml/kg (0.1mmol/kg) administered as a bolus intravenous injection. The recommended dose is 0.1 ml/kg (0.05mmol/kg).

Storage: Store at room temperature (20°-25°C).

Glutaraldehyde

Solution, 2%

Indications: It is a bactericidal disinfectant which is rapidly effective against Gram-positive and Gram-negative bacteria. It is also effective against *mycobacterium tuberculosis*, some fungi, and viruses, including hepatitis B virus and HIV, and is slowly effective against bacterial spores.

Side effects: as for Formaldehyde solution.

Glycine

Bladder irrigation solution, 1.5%

Indications: used as urogenital irrigation solutions during certain surgical procedures, particularly transurethral resection of the prostate.

Cautions: hepatic and renal impairment, cardiopulmonary.

Contraindications: anuric patients.

Side effects: systemic absorption of glycine irrigation solutions can lead to disturbances of fluid and electrolyte balance and cardiovascular and pulmonary disorders.

Halazone

Tablet, 4mg

Indications: Halazone is a disinfectant with the general properties of chlorine in aqueous solution and is used for the

disinfection of drinking water. One tablet containing 4mg of Halazone, stabilized with sodium carbonate and sodium chloride, is sufficient to treat about a litre of water in about 30 minutes to 1hour, more being required for heavily contaminated water. The taste of residual chlorine may be moved by adding sodium thiosulphate.

Storage: in airtight containers. Protect from light.

KY Jelly (Hydroxyethyl cellulose)

Indications: It is present in lubricant preparations, some of which are used as artificial tears in ocular disorder or dry eye.

Iodized Salt

Indications: prevention and treatment of iodine deficiency.

Cautions: those over 45 years old or with nodular goiter (especially susceptible to hyperthyroidism when given iodine supplements); pregnancy

Side effects: hypersensitivity reactions; goiter and hypothyroidism; hyperthyroidism

Oxidized Cellulose

Indications: Oxidized cellulose is absorbable haemostatics, when applied to bleeding surface; it swells to form a gelatinous mass that is gradually absorbed by the tissues, usually within 2 to 7 days. Complete absorption of large amounts of such material may take 6 weeks or more.

Cautions: Oxidized cellulose should not be used as a surface dressing, except for immediate control of bleeding, as it inhibits epitheliasation. It should not be used for packing or implantation in bone surgery

Drug interactions: silver nitrate or other escharotic chemicals should not be applied prior to use as cauterization might inhibit

absorption of oxidized cellulose. It should not be impregnated with other haemostatic or antibiotics.

Contraindication: use should be avoided in infected wounds.

Side effects: foreign body reaction, headache, burning, stinging, sneezing.

Dose and Administration: the gauze, lint or knitted material should be laid on the bleeding surface or held firmly against the tissue until haemostasis is achieved. Removal of excess oxidized cellulose should then be considered.

Oxygen (white-colored cylinder)

Indications: oxygen is given by inhalation to correct hypoxia in conditions causing under ventilation of the lungs, such as exacerbations of chronic bronchitis, pneumonia, or pulmonary oedema, where bronchospasm causes hypoxia, as in asthma, in extensive fibrosing alveolitis after general anaesthesia and in conditions where the oxygen content of the air breathed is inadequate as at high altitudes.

Cautions: any fire or spark is highly dangerous in the presence of increased oxygen concentrations especially when oxygen is used under pressure.

Metal cylinders containing oxygen should be fitted with a reducing valve by which the rate of flow can be controlled.

Side effects: CNS, toxicity (nausea, mood change, vertigo, twitching, convulsions, loss of consciousness), pulmonary toxicity (decrease in vital capacity, cough, substernal distress, and later atelectasis), retinopathy of prematurity.

Dose and Administration: *by inhalation.* It is administered by means of nasal catheter, facemask, endotracheal tube, or oxygen tent. Concentration of oxygen in inspired anesthetic gases should never be less than 21 % sideline (carbondioxide absorbent).

Saccharin

Tablet

Indications: Saccharin and its salts (sodium, calcium, and potassium) are intense sweeteners being several hundred times sweeter than sucrose and are used as food additives and artificial sweetener for diabetes. The salts are more often used as they are considered to be the most palatable.

Side effects: allergic and photosensitivity reaction.

Dose and Administration: 5mg per kg of saccharine salt taken daily.

Sodium Chloride Free Salt

Indications: treatment of extracellular volume depletion and sodium depletion

Cautions: Sodium chloride should be used with extreme caution, if at all, in patients with hypertension, congestive heart failure, or other edematous or sodium-retaining conditions, in patients with liver cirrhosis and in patients receiving corticosteroids or corticotropin. Particular caution is necessary in geriatric and post-operative patients.

Contraindications: sodium chloride is contraindicated in patients with conditions in which administration of sodium and chloride is detrimental.

Side effects: nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduce salivation and lachrymation, sweating, fever, tachycardia, hypertension, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache.

Dose and Administration:*Oral:* 1-2 gm 3 times daily depending on individual needs either with food or as a solution; doses of up to 12g daily may be necessary in severe cases.

Sodium Dichloroisocyanurate

Tablet, 67mg, 75mg

Indications: used as a disinfectant in water. It dissociates in water to form a number of chemical species, notably free chlorine and cyanuric acid.

Cautions: Harmful if swallowed, contact with the skin or eyes, or if inhaled. Do not expose the product to flames, do not mix with detergents

Storage: Store in a dry, well-ventilated area.

Sorbitol

Indications: Sorbitol is used in limited quantities either as a sweetening agent or as a source of carbohydrate in diabetic food products. It is also used as a sweetening agent instead of sucrose in many sugar-free oral liquid preparations and in sugar free-preparation of dental caries.

Cautions: impaired kidney function or severe liver damage.

Side effects: flatulence, abdominal pain, diarrhoea, and lactic acidosis hyperuricemia.

Storage: store in airtight container.

Supportive hepatic preparations that contain Essential Phospholipids and Vitamins

Water for injections

In 2ml, 5ml, 10ml

Water for injection is distilled water free from pyrogens used to produce solutions for injections.

GLOSSARY

Abstinence syndrome: symptoms that occur if a drug causing physical or psychological dependence is suddenly discontinued

Active immunity: occurs when the person is exposed to a disease and develops the disease, and the body makes antibodies to provide future protection against the disease

Addiction: a compulsive desire or craving to use a drug or chemical with a resultant physical dependence

Adrenergic drug: a drug that acts like or mimics the actions of the sympathetic nervous system

Aerobic: organisms that require oxygen to live

Agonist: drug that binds with a receptor to produce a therapeutic response

Agonist-antagonist: drug with both agonist and antagonist properties

Agranulocytosis: a decrease or lack of granulocytes (type of white bloodcell)

Aldosterone: hormone secreted by the adrenal cortex and contributing to a rise in blood pressure

Alopecia: abnormal loss of hair; baldness

Amenorrhea: absence or suppression of menstruation

Anaerobic: organisms that do not require oxygen to live

Analgesic: a drug that relieves pain

Anaphylactic reaction: a sudden, severe hypersensitivity reaction with symptoms that progress rapidly and may result in death if not treated

Anemia: a decrease in the number of red blood cells and hemoglobin value below normal

Androgens: testosterone and its derivatives

Angina pectoris (angina): acute pain in the chest resulting from decreased blood supply to the heart muscle

Angioedema: localized wheals or swellings in subcutaneous tissues or mucous membranes, which may be due to an allergic response; also called angioneurotic edema

Anorexia: loss of appetite

Anorexiant: a drug used to suppress the appetite

Antagonist: drugs that join with a receptor to prevent the action of an agonist

Anthelmintic: a drug used to treat helminthiasis (worms)

Antibacterial: active against bacteria

Antibody: molecule with the ability to bind with a specific antigen responsible for the immune response

Antiemetic: drug that is used to treat or prevent nausea

Antiflatulent: drug that works against flatus (gas)

Antigen: substance that is capable of inducing a specific immune response

Anti-infective: a drug used to treat infection

Antipsoriatics: drugs used to treat psoriasis

Antipyretic: a drug that lowers an elevated body temperature

Antiseptic: an agent that stops or slows, or prevents the growth of microorganisms

Anxiolytics: term used to describe the anti-anxiety drugs

Aplastic anemia: a blood disorder caused by damage to the bone marrow resulting in a marked reduction in the number of red blood cells and some white blood cells

Arrhythmia: abnormal heart rate or rhythm; also called dysrhythmia

Asthenia: weakness; loss of strength

Ataxia: unsteady gait; muscular incoordination

Atherosclerosis: a disease characterized by deposits of fatty plaques on the inner walls of arteries

Atrial fibrillation: quivering of the atria of the heart

Attenuate: weaken

Aura: sense preceding a sudden attack, as in the aura that occurs before a convulsion

Auscultation: the process of listening for sounds within the body

Autonomic nervous system: a division of the peripheral nervous system concerned with functions essential to the life of the organism and not consciously controlled (ie, blood pressure, heart rate, gastrointestinal activity)

Azotemia: retention of excessive amounts of nitrogenous compounds in the blood caused by failure of the kidney to remove urea from the blood

Bactericidal: a drug or agent that destroys or kills bacteria

Bacteriostatic: a drug or agent that slows or retards the multiplication of bacteria

Biliary colic: pain caused by the pressure of passing gallstones

Blood–brain barrier: ability of the nervous system to prohibit large and potentially harmful molecules from crossing into the brain

Bone marrow suppression: a decreased production of all blood cells

Booster: an immunogen injected following a specified interval; often after the primary immunization to stimulate and sustain the immune response

Bradycardia: slow heart rate, usually at a rate below 60 beats per minute

Bronchospasm: spasm or constriction of the bronchi resulting in difficulty breathing

Bulla: blister or skin vesicle filled with fluid

Bursa: pad-like sac found in connecting tissue usually located in the joint area

Candidiasis: infection of the skin or mucous membrane with the species *Candida*

Cardiac output: amount of blood discharged from the left or right ventricle per minute

Central nervous system: one of two main divisions of the nervous system consisting of the brain and spinal cord

Cervical mucorrhea: increased cervical discharge

Cheilosis: cracking of the edges of the lips

Chemoreceptor trigger zone: a group of nerve fibers located on the surface of the fourth ventricle of the brain that, when stimulated, results in vomiting

Chemotherapy: drug therapy with a chemical, often used when referring to treatment with an antineoplastic drug

Cholesterol: a fat-like substance produced mostly in the liver of animals

Cinchonism: quinidine toxicity or poisoning

Conjunctivitis: inflammation of the conjunctiva (mucous membrane lining the inner surfaces of the eye)

Convulsions: paroxysm (occurring suddenly) of involuntary muscular contractions and relaxations

Crohn's disease: inflammation of the terminal portion of the ileum

Cross-allergenicity: allergy to drugs in the same or related groups

Cross-sensitivity: see cross allergenicity

Crystalluria: formation of crystals in the urine

Cumulative drug effect: occurs when the body is unable to metabolize and excrete one dose of a drug before the next dose is given

Cushing's syndrome: a disease caused by the overproduction of endogenous glucocorticoids

Cyanosis: bluish, grayish, or dark purple discoloration of the skin due to abnormal amounts of reduced hemoglobin in the blood

Cycloplegia: paralysis of the ciliary muscle resulting in an inability to focus the eye

Cytomegalovirus (CMV): any of a group of herpes viruses infecting man, monkeys, or rodents; the human CMV is found in the salivary glands and causes cytomegalic inclusion disease

Debridement: removal of all foreign material and dead or damaged tissue from a wound or infected lesion

Delirium tremens: signs and symptoms of withdrawal from a drug or chemical including tremors, weakness, anxiety, restlessness, excessive perspiration, nausea, and vomiting

Diabetes insipidus: a disease resulting in the failure of the pituitary to secrete vasopressin or from the surgical removal of the pituitary gland

Diaphoresis: increased sweating or perspiration

Digitalization: administration of digitalis at intervals to produce and maintain a therapeutic blood level

Diluent: a fluid that dilutes

Diuretic drug: drug that produces urine secretion

Dyskinesia: impairment of voluntary movement

Dyspnea: labored or difficult breathing

Dystonia: prolonged muscle contractions that may cause twisting and repetitive movements of abnormal posture

Dysuria: painful or difficult urination

Edema: accumulation of excess water in the body

Emetic: drug that induces vomiting

Endogenous: normally occurring within the organism

Epilepsy: a permanent, recurring seizure disorder

Epiphysis: a center of ossification (conversion of tissue to bone) at each extremity of long bone

Epistaxis: nosebleed

Erythrocytes: red blood cells; one of several formed elements in the blood

Escherichia coli: a nonpathogenic colon bacillus; when found outside of the colon may cause infection

Estrogens: female hormones

Exacerbation: increase in severity

Exfoliative dermatitis: reddish rash in which scaling occurs following the erythema

Exogenous: normally occurring outside of the organism or community

Expectorant: drug that aids in raising thick, tenacious mucus from the respiratory tract

Extrapulmonary: occurring outside of the respiratory systems (ie, lungs)

Extrapyramidal effects: a group of adverse reactions occurring on the extrapyramidal portion of the nervous system causing abnormal muscle movements, akathisia and dystonia

Extravasation: escape of fluid from a blood vessel into surrounding tissue

Fibrolytic: term used to describe a drug that dissolves clots already formed within the vessel walls

Germicide: an agent that kills bacteria

Gingival hyperplasia: overgrowth of gum tissue

Gingivitis: inflammation of the gums

Glaucoma: a group of diseases of the eye characterized by increased intraocular pressure; results in changes within the eye, visual field defects, and eventually blindness (if left untreated)

Globulin: proteins that are insoluble in water and present in the plasma

Glossitis: inflammation of the tongue

Goiter: enlargement of the thyroid gland causing a swelling in the front part of the neck, usually caused by a lack of iodine in the diet

Gonadotropin: hormone that stimulates the sex glands(gonads)

Gonad: glands responsible for sexual activity and characteristics

Granulocytopenia: a reduction or decrease in the number of granulocytes (a type of white blood cell)

Gynecomastia: breast enlargement in the male

Habituation: a desire to continually use a drug or chemical for the desired effect with no physical dependence but some psychological dependence

Hallucinogen: drug capable of producing a state of delirium characterized by visual or sensory disturbances

Helminthiasis: invasion by helminths (worms)

Hemolytic anemia: disorder characterized by chronic premature destruction of red blood cells

Herb: plant used in medicine or as seasoning

High-density lipoproteins (HDL): macromolecules that carry cholesterol from the body cells to the liver to be excreted

Hirsutism: excessive growth of hair or hair growth in unusual places, usually in women

Histamine: a substance found in various parts of the body (ie, liver, lungs, intestines, skin) and produced in excess in response to a substance to which the body is sensitive

Humoral immunity: antibody-mediated immune response of the body

Hyperglycemia: high blood glucose (sugar) level

Hyperinsulinism: elevated levels of insulin in the body

Hyperkalemia: increase in potassium levels in the blood

Hyperlipidemia: an increase in the lipids in the blood

Hypersensitivity: allergic reaction to a drug or other substance

Hypertension: high blood pressure

Hypnotic: drug that induces sleep

Hypoglycemia: low blood glucose (sugar) level

Hypoinsulinism: low levels of insulin in the body

Hypokalemia: low blood potassium level

Hyponatremia: low blood sodium level

Hypotension: abnormally low blood pressure

Hypotension, orthostatic: a decrease in blood pressure occurring after standing in one place for an extended period

Hypotension, postural: a decrease in blood pressure after a sudden change in body position

Hypoxia: inadequate oxygen at the cellular level

Idiosyncrasy: unusual or abnormal drug response

Immunocompromised: having an immune system incapable of fighting an infection

Infiltration: the collection of fluid into tissue

Intraocular pressure: the pressure within the eye

Iritis: inflammation of the iris of the eye

Jaundice: yellow discoloration of the skin

Keratolyte: an agent that removes excessive growth of the epidermis (top layer of skin)

Ketoacidosis: a type of metabolic acidosis caused by an accumulation of ketone bodies in the blood

Ketonuria: presence of ketones in the blood

Laryngospasm: spasm of the larynx resulting in dyspnea and noisy respirations

Lethargic: sluggish, difficult to rouse

Leukopenia: a decrease in the number of leukocytes (white blood cells)

Lipids: a group of fats or fat-like substances

Lipodystrophy: atrophy of subcutaneous fat

Low-density lipoproteins (LDL): macromolecules that carry cholesterol from the liver to the body cells

Lumen: inside diameter, the space/opening within an artery

Lupus erythematosus: A chronic inflammatory connective tissue disease affecting skin, joints, kidneys, nervous system, and mucous membranes. A butterfly rash or erythema may be seen on the face, particularly across nose

Malaise: discomfort, uneasiness

Megacolon: dilatation and hypertrophy of the colon

Megaloblastic anemia: anemia characterized by the presence of large, abnormal, immature erythrocytes circulating in the blood

Melasma: discoloration of the skin

Melena: blood in the stools

Merozoites: cells formed as the result of asexual reproduction

Methemoglobinemia: clinical condition in which more than 1% of hemoglobin in the blood has been oxidized to the ferric form

Micturition: voiding of urine

Miosis: constriction of the pupils

Mucolytic: drug that loosens and thins respiratory secretions (lessens the viscosity of the secretions)

Myasthenia gravis: condition characterized by weakness and fatigability of the muscles

Mycotic: pertaining to a fungus or fungal infection

Mydriasis: dilation of the pupil

Myocardial infarction: heart attack

Myopia: nearsightedness

Myxedema: condition caused by hypothyroidism or deficiency of thyroxine and characterized by swelling of the face, periorbital tissues, hands, and feet.

Narcolepsy: a chronic disorder that results in recurrent attacks of drowsiness and sleep during daytime

necrosis: death of tissue (as adjective, necrotic)

Nephrotoxic: harmful to the kidney

Nephrotoxicity: damage to the kidneys by a toxic substance

Neurohypophysis: posterior lobe of the pituitary gland

Neuroleptic: drug that causes altered state of consciousness(ie, antipsychotic)

Neuromuscular blockade: acute muscle paralysis and apnea

Neurotoxicity: damage to the nervous system of a toxic substance

Neurotransmitter: chemical substances released at the nerve ending that facilitate the transmission of nerve impulses

Neutropenia: abnormally small number of neutrophil cells (type of white blood cell)

Objective data: information obtained by means of a physical assessment or physical examination

Oliguria: a decrease in urinary output

Ophthalmic: pertaining to the eye

Opportunistic infection: infection resulting from MOs commonly found in the environment, which normally do not cause an infection unless there is an impaired immune system

Orthostatic hypotension: see hypotension, orthostatic

Osteomalacia: a softening of the bones

Osteoporosis: a loss of calcium from the bones, resulting in a decrease in bone density

Otic: pertaining to the ear

Ototoxic: harmful to the ear

Ototoxicity: damage to the organs of hearing by a toxic substance

Overt: not hidden, clearly evident

Oxytocic: agent that stimulates contractions of the uterus resulting in labor

Palliative: therapy designed to treat symptoms, not to produce a cure

Pancytopenia: a reduction in all cellular elements of the blood

Paralytic ileus: paralysis of the bowel resulting in lack of movement of the bowel contents

Parasite: an organism living in or on another organism (host) without contributing to the survival or well-being of the host

Parenteral: administration of a substance, such as a drug, by any route other than the oral route

Paresthesia: an abnormal sensation such as numbness, tingling, prickling, or heightened sensitivity

Parkinsonism: referring to the symptoms of Parkinson's disease (ie, fine tremors, slowing of the voluntary movements, and muscular weakness)

Passive immunity: a type of immunity occurring from the administration of ready-made antibodies from another individual or animal

Pathogenic: disease producing

Peripheral: pertaining to the outward surface; away from the center

Petechiae: tiny purple or red spots that appear on the skin as a result of pinpoint hemorrhages within outer layers of the skin

Phenochromocytoma: tumor of adrenal medulla characterized by hypersecretion of epinephrine and norepinephrine

Phlebitis: inflammation of a vein

Phenylketonuria (PKU): a congenital disease due to a defect in the metabolism of phenylalanine (an amino acid); results from the lack of an enzyme necessary for the conversion of phenylalanine into tyrosine; untreated, the condition leads to mental retardation

Photophobia: an aversion to or intolerance of light

Photosensitivity: exaggerated sunburn reaction when the skin is exposed to sunlight or ultraviolet light

Physical dependence: compulsive need to use a substance repeatedly to avoid withdrawal symptoms

Plasma expanders: IV solutions used to expand plasma volume with shock due to burns, hemorrhage, or other trauma

Polydipsia: excessive thirst

Polyphagia: eating large amounts of food

Polypharmacy: taking a large number of drugs (may be prescribed or over-the-counter drugs)

Prepubertal: before puberty

Progesterone: a female hormone produced by the corpus luteum that works in the uterus (along with estrogen) to prepare the uterus for possible conception

Progestins: natural and synthetic progesterones

Prophylaxis: prevention

Prostaglandins: a fatty acid derivative found in almost every tissue of the body and body fluid that affects the uterus and other smooth muscles; also thought to increase the sensation of peripheral pain receptors to painful stimuli

Prostatic hypertrophy: abnormal enlargement of the prostate gland

Protein substrates: amino acids essential to life

Pruritus: itching

Pseudomembranous colitis: a severe, life-threatening form of diarrhea

Psychological dependence: compulsion to use a substance to obtain a pleasurable experience

Ptosis: drooping of the upper eyelid

Purpura: condition characterized by various degrees of hemorrhaging into the skin and/or mucous membranes producing ecchymoses (bruises) and petechiae (small red patches) on the skin

QT interval: is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle (depolarization and repolarization) of the left and right ventricles. Dependent on the heart rate (the faster the heart rate the shorter the QT interval). A lengthened QT interval is a biomarker for ventricular tachyarrhythmias like torsades de pointes and a risk factor for sudden death.

Remission: periods of partial or complete disappearance of signs and symptoms

Retinitis: inflammation of the retina of the eye

Reye's syndrome: acute and potentially fatal disease of childhood; associated with a previous viral infection

Rheumatic fever: a disease associated with a delayed response to a prior streptococcal infection in the body and characterized by fever and pain in the joints

Rheumatoid arthritis: a type of arthritis marked by inflammation, degeneration, and derangement of the joints and related structures resulting in contractures and deformities of the joints

Rhinitis: inflammation of the nasal passages resulting in increased nasal secretions

Sedative: a drug producing a relaxing, calming effect

Somatotropic hormone: growth hormone produced by the anterior pituitary gland

Somnolence: prolonged drowsiness; sleepiness

Sprue: a disease characterized by weakness, anemia, weight loss, and malabsorption of essential nutrients

Status epilepticus: an emergency situation characterized by continual seizure activity

Stevens-Johnson syndrome: fever, cough, muscular aches and pains, headache, and lesions of the skin, mucous membranes and eyes. The lesions appear as red wheals or blisters, often starting on the face, in the mouth, or on the lips, neck, and extremities.

Stomatitis: inflammation of the mouth

Sublingual: under the tongue

Sulfonylurea: a type of drug used to lower blood sugar in persons with non-insulin-dependent diabetes

Superinfection: an overgrowth of bacterial or fungal microorganism not affected by the antibiotic being administered

Sympathomimetic: acting like the sympathetic nervous system

Synergistic: a drug interaction occurring when two drugs interact to produce an effect that is greater than the sum of their separate actions

Tachycardia: heart rate above 100 beats/minute

Tardive dyskinesia: rhythmic, involuntary movements of the tongue, face, mouth, jaw, and sometimes the extremities

Testosterone: the most prominent male sex hormone that acts to stimulate development of the male reproductive organ and the secondary sex characteristics

Tetany: nervous condition characterized by sharp flexion of the wrist and ankle joints, muscle twitching, cramps, and possible convulsions, usually caused by abnormal levels of calcium, vitamin D, and alkalosis

Thrombocytopenia: low platelet count

Thrombus: a blood clot (pl. Thrombi)

Thyroid storm: see thyrotoxicosis

Thrombocytopenia: low number of the platelets in the blood

Thyrotoxicosis: severe hyperthyroidism that is characterized by symptoms such as high fever, extreme tachycardia, and altered mental status (also called thyroid storm)

Tinnitus: ringing in the ears

Tolerance: decreased response to a drug, usually requiring an increase in the dosage to give the desired effect

Tonic-clonic seizure: generalized seizure consisting of alternate contraction (tonic) and relaxation of muscles (clonic)

Toxicity: poisonous or harmful

Toxoid: an attenuated toxin that is capable of stimulating the formation of antitoxins

Transient ischemic attack (TIA): temporary interference with blood supply to the brain causing symptoms related to the portion of the brain affected (ie, temporary blindness, aphasia, dizziness, numbness, difficulty swallowing or paresthesias); may last from a few moments to several hours, after which no residual neurologic

Tyramine: substance found in most cheeses and in beer, bean pods, yeast, wine, and chicken liver; individuals taking the antidepressant MAOs and eating foods containing tyramine may experience severe hypertension

Unlabelled (off-label or unapproved) Use: use of an approved product in a scenario that is not included or is disclaimed in the product information.

Urticaria: hives; itchy wheals on the skin resulting from contact with or ingestion of an allergic substance or food

Uveitis: a nonspecific term for any intraocular inflammatory disorder

Vaccine: substance with either weakened or killed antigens developed for the purpose of creating resistance to disease

Vasodilatation: an increase in the size of the blood vessels, which when widespread results in a rise in blood pressure

Vertigo: a feeling of a spinning or rotation-type motion

Vitamin: organic substance needed by the body in small amounts for normal growth and nutrition

APPENDIXES

APPENDIX I: Medicines Dose Calculation for Children

Age	Mean weight approximate % of	
Age	Body weight (Kg)	Adult dose
Newborn (full term)	3.5	12.5
2 months	4.5	15
4 months	6.5	20
1 year	10	25
3 years	15	33.3
7 years	23	50
10 years	30	60
12 years	39	75
14 years	50	80
16 years	58	90
Adult	68	100

N.B.: The percentage method is derived from the surface area formula for children. This table is to be used only for drugs with a high therapeutic index. The clinical response of the child, age- or disease-related changes in drug clearance and any adverse effects that might present should be given due consideration when calculating doses.

Approximate Measures

1 teaspoonful = 5ml

1 dessertspoonful = 10ml

1 tablespoonful = 15ml

Drugs Formulary for Health Centers

APPENDIX II: Body Weight to Surface Area

BODY SURFACE AREA IN CHILDREN

Body-weight under 40kg

Body-weight (kg)	Surface area (m ²)
1	0.10
1.5	0.13
2	0.16
2.5	0.19
3	0.21
3.5	0.24
4	0.26
4.5	0.28
5	0.30
5.5	0.32
6	0.34
6.5	0.36
7	0.38
7.5	0.40
8	0.42
8.5	0.44
9	0.46
9.5	0.47
10	0.49
11	0.53
12	0.56
13	0.59
14	0.62
15	0.65
16	0.68

Body-weight (kg)	Surface area (m ²)
17	0.71
18	0.74
19	0.77
20	0.79
21	0.82
22	0.85
23	0.87
24	0.90
25	0.92
26	0.95
27	0.97
28	1.0
29	1.0
30	1.1
31	1.1
32	1.1
33	1.1
34	1.1
35	1.2
36	1.2
37	1.2
38	1.2
39	1.3
40	1.3

APPENDIX III: Medicines Adverse Events

An adverse drug reaction (ADR) may be defined as ‘any response to a drug which is noxious, unintended and occurs at doses normally used for prophylaxis, diagnosis, or therapy. ADRs are therefore unwanted or unintended effects of a medicine, including idiosyncratic effects, which occur during its proper use. They differ from accidental or deliberate excessive dosage or drug maladministration. ADRs may be directly linked to the properties of the drug in use, the so-called ‘A’ type reactions. An example is hypoglycaemia induced by an antidiabetic drug. ADRs may also be unrelated to the known pharmacology of the drug, the ‘B’ type reactions including allergic effects, for example anaphylaxis with penicillins. Any drug may produce unwanted or unexpected adverse reactions. Detection and recording of these is of vital importance.

In Ethiopia we use passive form of reporting of ADR to pharmacovigilance center using pre-paid yellow postage which is available in every health facility. Any health professional who encountered any type of ADR can fill and send the case free of charge to **FMHACA** through nearby post office to:

Food, Medicine and Healthcare Administration and Control Authority (FMHACA) of Ethiopia

Pharmacovigilance Center, P.o.Box 5681; Addis Ababa

Fax. 251-115-521392

E-mail: regulatory@fmhaca.gov.et

Reporting format as shown below

Food, Medicine and Health Care Administration and Control Authority of Ethiopia (FMHACA)
Adverse Drug Event reporting form

Patient Name (abbreviation)	Card No.	Age, Date of birth	Sex	Weight	Height
Ethnic group		Substance of abuse			
Information on suspected drug/vaccine					
Drug name(s) including brand name batch no. and manufacturer	S/C	Dose/dosage form, route, frequency	Date drug taking was started (D/M/Y)	Date drug reaction started (D/M/Y)	Date drug taking was stopped (D/M/Y)
S-suspected drug			C-concomitantly used drugs		
Indication (Reason for drug use)					
Adverse drug event description (include all available laboratory test results)					
Reaction necessitated discontinuation of drug(s) <input type="checkbox"/> YES <input type="checkbox"/> No					
Hospitalization prolonged <input type="checkbox"/> YES <input type="checkbox"/> No					
Treatment of reaction					
Outcome: <input type="checkbox"/> Died due to the adverse event <input type="checkbox"/> Died, drug may be contributory <input type="checkbox"/> Not yet recovered <input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae <input type="checkbox"/> Unknown					
Sequelae					
Relevant medical conditions such as allergies, renal disease, liver disease, other chronic diseases, pregnancy etc.					
Reported by Name	Profession	Email address	Telephone		
Name of health institution	Date				

Product quality problem: Color change, separating of components, powdering, crumbling, caking, molding, change of odor, incomplete pack, suspected contamination, poor packaging/poor labeling, etc (Write if anything different than given above)

Drug trade name	Batch No.	Registration no.	Dosage form and strength	Size /type of package
For office use only				
Received on:		Registration no.:		
Key: D/M/Y ; Date /Month/Year	D/C Discontinue treatment	Y/YES	N/NO	
የፕላንቲፍ ስርዓት ለፍጥነት		what to report		
<ul style="list-style-type: none"> All suspected reactions to drugs Unknown or unexpected reactions Serious adverse drug reactions Unexpected therapeutic effects All suspected drug interactions Product quality problems Treatment failures Medication errors 				
<p>This ADE reporting form was prepared by FMHACA in collaboration with MSU/SPS and the financial support from USAID</p> <p>የፕላንቲፍ ስርዓት ለፍጥነት</p>				
<p>From _____</p> <p>የፕላንቲፍ ስርዓት ለፍጥነት ከዚህ በኋላ ይህን ደብዳቤ ይጻፉ</p> <p>Business Reply Service License No HQ2</p>				
<p>Postage prepaid</p>  <p>Food, Medicine and Health Care Administration and Control Authority of Ethiopia</p> <p>Regulatory Information Development and Dissemination Team P.O.Box 5081-Tel.0115-5213142 Addis Ababa, Ethiopia</p>				

APPENDIX IV: Medicines Storage Condition

	Terms used	Applications
1	Store frozen (in a deep freezer) (-20 ⁰ C	For products, such as certain vaccines, need to be transported within a cold chain.
2	"..in a refrigerator" or Store at 2 ⁰ C – 8 ⁰ C (36 ⁰ -46 ⁰ F)	For products which are very heat sensitive but must not be frozen. Appropriate of storing vaccines for a short period of time
3	in a cool/cold place	For products labeled to be kept between 8 ⁰ -15 ⁰ C (45 ⁰ 59 ⁰ F)
4	".. at room temperature"	For products labeled to be kept between 15 ⁰ -25 ⁰ C (59 ⁰ -77 ⁰ F)
5	Store at ambient temperature	Store at the surrounding temperature. It means "room temperature" or normal storage conditions, i.e. storage in a dry, clean, well-ventilated area room temperature between 15 ⁰ -25 ⁰ C (59 ⁰ - 77 ⁰ F) or up to 30 ⁰ C , depending on climatic conditions
	"..protect from heat"	not more than 30oc
	".. in a dry place"	relative humidity less than 5%

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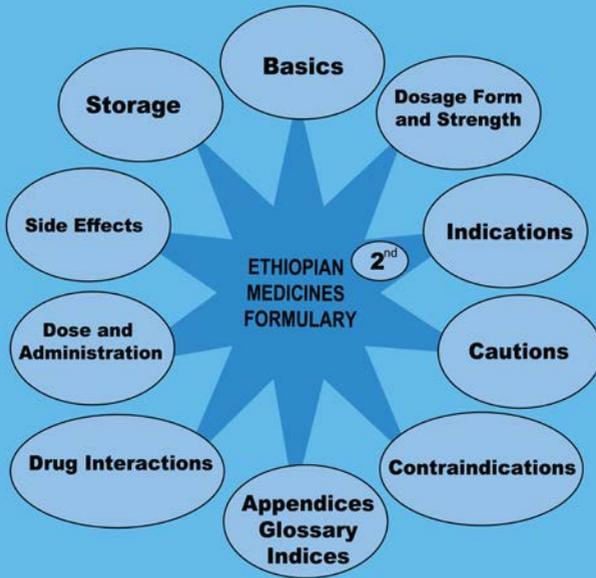
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