Food, Medicine and Healthcare Administration and Control Authority of Ethiopia

Standard Treatment Guidelines for Primary Hospital

Diseases

Clinical features

Investigations

Treatment

Referrals

Good Prescribing & Dispensing Practices for Better Health Outcomes

Third Edition, 2014

FOOD, MEDICINE AND HEALTHCARE ADMINISTRATION
AND CONTROL AUTHORITY OF ETHIOPIA

STANDARD TREATMENT GUIDELINES
FOR PRIMARY HOSPITAL

THIRD EDITION,2014

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ACRONYMS

ACD	Allergic contact dermatitis
ACEIs	Angiotensin converting enzyme inhibitors
ACS	Acute Coronary Syndrome
ADL	Acute adenolymphangitis
ADRs	Adverse Drug Reactions
AFB	Acid fast Bacilli
AIVR	Accelerated Idioventricular Rhythm
AKI	Acute kidney Injury
ALF	Acute liver failure
ARBs	Angiotensin receptor blockers
ART	anti-retroviral therapy
AV	Atrio ventricular
BID	Twice a day
BMI	body mass index
C/Is	Contraindications
CBC	Complete blood count
CDAD	Clostridium Difficille Associated Disease
CKD	Chronic kidney Injury
CL	Cutaneous leishmaniasis
CLL	Chronic lymphocytic leukemia
CML	Chronic Myelogenous Leukemia
CNS	Central nervous system
COPD	Chronic Obstructive Pulmonary Disease
CPR	Cardiopulmonary resuscitation
CRP	C-reactive protein
CSF	Cerebrospinal fluid
D/Is	Drug interactions
D/S	Dextrose in Saline solution
D/W	Dextrose in water solution
DBS	Dry Blood Spot
DEC	Diethylcarbamazine citrate
DKA	Diabetic Ketoacidosis
DLA	Dermatolymphangioadenitis

DMARD	Disease-modifying anti-rheumatic drugs
DST	Drug Susceptibility Testing
DVT	deep vein thrombosis,
ECG	electrocardiogram
ENL	Erythema Nodosum Leprosum
ENT	Ear, Nose and Throat
ESR	erythrocyte sedimentation rate
ESRD	End Stage Renal Disease
FH	Fulminant hepatitis
FMHACA	Food, Medicine and Health Care Administration and Control Authority
FPG	Fasting plasma glucose
G	Gram
GDM	Gestational Diabetes Mellitus
GERD	Gastro Esophageal Reflux Disease
GFR	Glomerular Filtration rate
GI	Gastrointestinal
GTD	Gestational Trophblastic diseases
GTN	Gestational Trophoblastic Neoplasia
HDL	high-density lipoprotein cholesterol
HHS	Hyperglycemic Hyperosmolar State
Hrs	Hours
ICD	Irritant Contact Dermatitis
IDU	Intravenous Drug Use
IHCP	Intra-hepatic cholestasis pregnancy
IM	Intramuascular
IOP	Intra-ocular pressure
IRIS	Immune Reconstitution Immune Syndrome
ITP	Immune Thrombocytopenic Purpura
IU	International Unit
IUGR	Intrauterine growth restriction
IV	Intravenous
IVDA	intravenous drug abuse endocarditic
LDL	low-density lipoprotein cholesterol

MAT	Multifocal Atrial Tachycardia
MDR	Multi Drug Resistance
MDT	Multi-drug therapy
Ml	Milliliter
MNT	Medical Nutrition Therapy
MOH	Ministry of Health
MSH	Management Sciences for Health
N/S	Normal saline solution
NNRTI	Nucleoside Reverse Transcriptase Inhibitors
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
NSVT	Non sustained ventricular tachycardia
NVE	native valve endocarditic
OGTT	Oral Glucose Tolerance Test
P.O	Per Os (mouth)
P/Cs	Precautions
PCP	Pneumocystis Carinni Pneumonia
PEP	Post-exposure prophylaxis
PI	Protease Inhibitors
PKDL	Post kala-azar Dermal Leishmaniasis
PMTCT	Prevention of mother-to-child transmission
PPH	Post-Partum Haemorrhage
PRN	As required
PROM	Premature Rupture Of Membranes
PSVT	Paroxysmal supra-ventricular tachycardia
PTE	Pulmonary thrombo-embolism
PTT	Placental trophoblastic tumour
PVE	Prosthetic Valve Endocarditits
QD	Once a day
QID	Four times a day
RA	Rheumatoid Arthritis
RBC	Reduction in red blood cell
RDT	Rapid Diagnostic Tests
RUTF	Ready to use therapeutic feeding
SBGM	Self-blood glucose monitoring

SBP	Prophylaxis for spontaneous bacterial peritonitis
SSIs	Surgical site infections
STG	Standard Treatment Guideline
STI	Sexually transmitted infections
TID	Three times a day
VT	Ventricular Tachycardia
VTE	Venous thromboembolism
WBC	White blood cell count
WPW	Wolff-Parkinson-White

PREFACE

In a healthcare system where multiple treatment options are available, the development and implementation of standard treatment guidelines (STGs) is a crucial strategy for ensuring effective and safe use of medicines, containing health care costs, and preventing antimicrobial resistance.

STGs promote therapeutically effective and economic use of medicines at different levels of health facilities, as they give clear guidance and recommendations about the treatment and management of each clinical condition. When properly developed and implemented, treatment guidelines enhance rational medicine use and improve the quality of care. These guidelines provide up-to-date information relevant to the prevention, diagnosis and treatment of common diseases in Ethiopia which helps to achieve provision of quality care to patients.

These STGs provide greater consistency and standards of care, improve diagnostic accuracy, and promote effective and safe use of medicines, and serves as a basis for improving treatment outcomes. It is also important to supply chain managers in improving the predictability of demand, and provide a standardized basis for forecasting, ordering, and purchasing of medicines. Health policy makers, health insurance agencies and planners will benefit from these STGs as it serves as an effective way to contain the cost of treatment for both patients and the health sector.

This 3rd edition includes a package of evidence based information on diseases conditions, clinical features, methods of investigations, treatment options and referral to the next level of care.Special emphasis is given to primary healthcare so as to address important public health needs in the country. EFMHACA has officially approved this treatment guidelines to be used as a guide for prescribers, dispensers and other health care providers operating at the level of Primery Hospital. Accordingly, health care providers shall comply with these guidelines unless there is aproven and specific treatment need for a patient that is supported by adequate evidence.

Finally, I would like to take this opportunity to acknowledge USAID/SIAPS, EFMHACA regulatory standard team, Bethel Teaching General Hospital and participants of the consultative workshop for their huge contributionsin the revision of these important guidelines.

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January 2014

INTRODUCTION

Irrational use of drugs has been one of the major problems in the Ethiopian health care system for a long time. Among the strategies devised to improve the situation, Medicine, Food and Healthcare Administration and Control Authority (FMHACA) of Ethiopia, was involved in the preparation and distribution of Standard Treatment Guidelines (STGs) for the different levels of health institutions in the country.

The 1st edition of the STGs was published in January 2004 after wide consultation with relevant stakeholders. There has been continuous demand since then for copies of the STGs, calling for several reprints and revision. The 2nd edition of the guidelines was published in 2010. The demand for these guidelines is increasing, perhaps because STGs are also being used as an alternative to fill the gap in reference materials.

Following the changes made to the national list of drugs and an increasing demand for incorporating new developments in diagnosis and treatment, it was found important to revise the 2nd edition of STGs.Accordingly, this edition of STGs was thoroughly revised by a panel of experts through contracting out to Bethel Teaching General Hospital with technical and financial support from USAID/SIAPS.

This third edition addresses common health problems in Ethiopia and it includes several new diseases as well as brief description of the diseases condition, clinical features, methods of investigation and non-pharmacologic and pharmacologic treatment options.Information on dosing, dosage forms, course of treatment, adverse reactions, contraindications and drug interactions are given for the first line and alternative drugs whenever applicable. Diseases have been classified into cardiovascular disorders, endocrine disorders, gastrointestinal tract and liver disorders, hematologic disorders, infectious diseases, kidney and genitourinary tract disorders, musculoskeletal disorders, neurological disorders, oncology, psychiatric disorders, respiratory disorders, emergency conditions, pediatric disorders, gynecology and obstetrics,

dermatological disorders, sexually transmitted infections, ophthalmological disorders and ear, nose and throat disorders.

EFMHACA believes that utmost care has been made by the panel of experts to ensure that the recommendations given are evidence-based. In addition, the draft STGs documents were reviewed in a national consultative workshop where relevant experts are involved. Above all, this document will undergo continuous improvement through the inputs of users including prescribers, dispensers, academia and researchers, supply chain managers, policy makers and other relevant stakeholders. Users are, therefore, encouraged to send their feedbacks, supporting itwith scientific evidences, to the following address:

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CHAPTER I: GOOD PRESCRIBING AND DISPENSING PRACTICES

General

Rational use of medicines is a mechanism through which safe, effective and economic medication is provided. It is promoted through the collaborative efforts of prescribers, dispensers, patient and policymakers. Rational prescribing ensures adherence to treatment and protects medicine consumers from unnecessary adverse medicine reactions. The prescriber could be a physician, a nurse or health officer or any health professional authorized to prescribe . Rational dispensing, on the other hand, promotes the safe, effective and economic use of medicines. The dispenser could be a pharmacist, or pharmacy technician. Prior to prescribing or dispensing of any Medicines, the prescriber or dispenser should make sure that it is within his/her scope of practice.

Medicines should only be prescribed when necessary, and the benefit-risk ratio of administering the medicine should always be considered prior to prescribing and dispensing. Irrational prescribing leads to ineffective, unsafe and uneconomical treatment. Thus it is very important that steps are taken to promote rational medicine use in order to effectively promote the health of the public especially given limited resources. One way of promoting rational medicine use is throught the development and use of standard treatment guidelines.

Rational approaches to therapeutics requires careful evaluation of health problems and selecting appropriate therapeutic strategies. Making the right diagnosis is the cornerstone for choosing the right kinds of therapy. Based on the diagnosis, health workers may select more than one treatment and the patient should agree with the selected treatment. The treatment could be non-pharmacologic or pharmacologic. It is important to consider the total cost of treatment in the selection process. The process should also consider efficacy, safety and suitability. Medicine treatment should be individualized to the needs

of each patient as much as possible. The concept of good clinical practice has to be incorporated within rational prescribing

Prescription writing

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 medicine consumer pertaining to treatment or prophylaxis.

A prescription should be written on a standard prescription blank legibly and clearly in ink and in generic names of the medicine(s).

A prescription should contain

- 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 medcines. 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 infront of the decimal point.

- prescriber's name, signature and address.
- **See Annex 17 for Standard Prescription form**

Good Dispesing Practice

Good dispensing practices ensure that the correct medicine 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 medicine.

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 medcines 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 medicines.

Patient adherence

Patient compliance is the extent to which the patient follows the prescribed drug regime, while adherence is participation of patients in their care plan resulting in understanding, consent and partnership with the provider. There are different factors which contribute to patients' non-adherence. These factors include:

- nature of treatment, which in turn depends on the
  - complexity of the regime (more frequency of administration and more number of drugs prescribed)
  - adverse effects
- 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 pharmacy

- unable to pay prescription charges
- inconvenience of taking medicines 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 and dispensors
  - not winning confidence of patients
  - irrational prescribing and dispensing
  - giving inadequate information on the treatment
  - poor attitude to patients
  - negligence
  - poor perception to team work

Patient adherence can be improved by

- supervising medicine administration
- simplifying therapeutic regime
- educating patients on the importance of adhering to the prescribed medication
- improving the attitudesa of prescribers and dispensors

Adverse drug/Medicines reactions

Adverse drug/medicine reactions (ADRs) are noxious unwanted effects that occur at the rapeutic doses. They could be mild (where no intervention is required), moderate (where switch to another drug is necessary), severe (where antidote should be employed to alleviate the situation), or lethal. They could also be predicted (extensions of pharmacological effects) or unpredicted (bizarre reactions which are not expected in all patients taking the drug, such as hypersensitivity and idiosyncratic reaction). ADRs are different from toxic reactions for the later occur at doses higher than therapeutics. They are also different from side effects as the latter have broad concept, i.e., include both beneficial and all unwanted effects which may not necessarily be noxious. The two extreme age groups, i.e., pediatric and geriatric patients are more susceptible to ADRs due to physiological and pathological factors.

Special precaution should be taken for coexisting illnesses, such as kidney and liver disease, as they could contribute to ADRs development

Monitoring ADRs

Pre-marketing clinical trials cannot be exhaustive as far as detection of all ADRs is concerned due to

- Recruitment of small population(< 2500 patients)
- The remote chance of low incidence reactions to be picked up before marketing
- Shorter duration of assessment
- Exclusion of patients who may take the medicine after marketing

Only the most common ADRs could be detected during pre-marketing trials. It is, therefore, important to devise methods for quick detecting ADRs. This could be carried out by post-marketing surveillance, i.e., ADRs monitoring. Hence, all health professionals have the responsibility to report any unique ADR observed to Food, Medicine and Health Care Control and Administration Agency (FMHACA).

Drug /Medicine Interactions

Though some drug/medicine interactions could be beneficial most are harmful. Hence it is always important to note the possible medicine interactions prior to concomitant medicine/food or drink administration.

Drug/medicine interactions could occur at different levels including:

- Pharmaceutics, which are physicochemical interactions in an IV 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 medicine induced disease alters the response to another medicine.

Drug/medicine interactions could be additive (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 medicines), or

antagonism (the effect of the agonist is blocked by the antagonist when given together). Medicne interactions are some of the most common causes of adverse reactions. As medicine reactions could also occur between a medicine and food or a medicine and drink. We should always inform our patients the type of food or drink which they have to avoid while taking the drug.

Prescribing for pregnant women

The kinetics of a medicine 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, organogesis 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 medicine 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.

Prescribing for breast feeding women

Most medicines 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 breast feeding and 3-4

Hours before the nex t 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.Medicines 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 breast feeding mothers can be detected in breast milk. e.g., tetracycline and chloramphenichol. Most sedative hypnotics achieve concentrations in breast milk. Opioids also achieve concentrations in breast milk. Antineoplastic medicines are contraindicated in breast feeding. So it is worth noting not to prescribe medicines 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. All the four parameters of kinetics are, therefore, affected in children: Gastric acid secretion begins soon after birth and increases gradually over several hours in full term infants. In premature infants, however, the secretion is slower, with the highest concentration occurring on the fourth day. So medicines, 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 acids so that absorption of lipid soluble drugs is less. Gastric emptying time is prolonged in the first day. So medicines, 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 medicines, 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.

Dose adjustment in pediatrics:

The most reliable pediatric doses are those given by the manufacturer. If no such information is given, the dose can be calculated using formulae based on age, weight or surface area. Calculations of doses based on age or weight are conservative and tend to underestimate the required dose. Doses based on surface area are more likely to be adequate. This is available in form of chart. Pediatric doses can be calculated as follow:

Dose calculations based on Age:

$$\text{Dose} = \text{adult dose} \times \frac{\text{age (years)}}{\text{Age} + 12}$$

Dose calculations based on weight

$$\text{Dose} = \text{adult dose} \times \frac{\text{weight (kg)}}{70}$$

Prescribing for elderly patients

There is no major alteration in medicine absorption in elderly patients. However, Conditions associated with age may alter the rate of absorption of some medicines. Such conditions include altered nutritional habits, alteration in gastric emptying, which is often slower and the concurrent administration of other medicines. 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. Phase I reactions are more affected in elderly patients than phase II. 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 medicines in aged people. The quality and quantity of life in elderly patients can be improved by careful use of drugs. Adherence to the doses is absolutely required in these patients. Unfortunately patient nonadherence 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.

Prescribing in renal failure

Many drugs are excreted through the kidneys and impairment of renal function alters the excretion of these medicines and may result in renal as well as non-renal toxicity unless doses are adjusted on the basis of the degree of renal impairment. There are two principal pathways for drug excretion by the kidneys; glomerular filtration and tubular excretion. Glomerular filtration plays a major role in the excretion of small, non-protein bound molecules whereas protein bound molecules that are excreted in urine are eliminated by secretion into the proximal tubules.

For dose adjustment in renal failure it may occasionally be necessary to measure drug levels and adjust doses accordingly, but generally doses are adjusted on the basis of the estimated glomerular filtration rate (GFR). Among the various formulae used to estimate the GFR from the serum creatinine, the Cockcroft Gault formula is the easiest to use although not the most accurate one. The GFR in the C&G formula is calculated as follows:

$$GFR = \frac{(140-age) \times \text{lean body weight(kg)}}{\text{Serum creatinine (mg/dl)} \times 72}$$

The value is multiplied by 0.85 in women to account for the smaller muscle mass.

Factors that potentiate renal dysfunction and contribute to the nephrotoxic potential of renally excreted medicines include;

a. intravascular volume depletion either due to external losses or fluid sequestration (as in ascites or edema)
b. concomitant use of 2 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

1. Avoid potentially nephrotoxic drugs and use alternative drugs that are excreted through other routes.
2. If there are no alternative drugs to use calculate the GFR and adjust the dose on the basis of the estimated GFR. (Many textbooks, formularies have tables showing dose adjustment on the basis of estimated GFR).Dose adjustment may be accomplished in three different ways i) Decreasing each individual dose and maintaining the same dose frequency ii) Maintaining the same individual dose but administering each dose less frequently and iii) Modifying both individual doses and the frequency of administration, which is a combination method.
3. Avoid concomitant use of 2 or more potentially nephrotoxic agents.
4. Insure that the patient is adequately hydrated.

5. 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.
6. Serially monitor kidney function.

Prescribing in liver disease

The liver is a site for the metabolism and elimination of many medicines but it is only in severe liver disease that changes in medicines 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 terms drug prescription should be kept to a minimum in all patients with severe liver disease as liver disease may alter the response to drugs in several ways. 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.

Prescribing and pain management in Palliative Care

Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Focus lies in four main domains: 1) control of pain and other physical symptoms; 2) mental or psychological symptoms; 3) social needs; and 4) spiritual needs. This requires careful assessment of the symptoms and needs of the patient by a multidisciplinary team. The family should be included in the care of terminally ill patients.

OR

Enoxaparin 40mg, SC, daily

(For ADRs, C/Is, P/Cs, D/Is and dosage forms, see page 53)

D. Pharmacologic treatment of chronic heart failure with depressed lef ventricular systolic function-

- **Diuretics**
- **ACEI or ARBS** } **+/- Spironolactone and Digoxin**
- **Beta blockers**

Table 5- Drugs for the treatment of Chronic Systolic Heart failure

Drugs	Initial dose	Maximum dose	Comments
Diuretics			
Furosemide	20–40 mg qd or bid	400 mg/d	Dose depends on fluid overload Followfor hypokalemia
Angiotensin-Converting Enzyme Inhibitors (ACEI)			
Captopril	6.25 mg tid	50 mg tid	Increase dose to target gradually Follow RFT and serum K^+
Enalapril	2.5 mg bid	10 mg bid	
Lisinopril	2.5–5 mg qd	20–35 mg qd	
Angiotensin Receptor Blockers(ARBs)- alternative to ACEI			
Valsartan	40 mg bid	160 mg bid	Increase dose to target gradually Follow RFT and serumK^+ Do not combine with ACEI
Candesartan	4 mg qd	32 mg qd	
Losartan	12.5 mg qd	50 mg qd	
Beta Blockers			
Carvedilol	3.125 mg bid	25–50 mg bid	- Start when patient is stable - Increase dose gradually(≥2wks)
Metoprolol succinate CR	12.5–25 mg qd d	Target dose 200 mg qd	
Additional Therapies			
Spironolactone	12.5–25 mg qd	25–50 mg qd	To be added if HF remains poorly controlled despite optimal therapy with the above class of drugs
Digoxin	0.125 mg qd	0.25 mg qd	

4. Hypertension

Hypertension is a state of elevated systemic blood pressure that causes marked increment of cardiovascular risk. It is one of the major but preventable risk factors of coronary artery disease, hemorrhagic and ischemic stroke, heart failure and chronic kidney disease. In 90-95% of cases, the cause is unknown

and it is called essential hypertension. Secondary hypertension refers to hypertension caused by other systemic illness as part of their manifestation. The common causes are renal parenchymal disease (e.g. glomerulonephritis, chronic kidney disease of any cause), renovascular disease (renal artery stenosis), endocrine (e.g. Cushing syndrome, primary hyperaldosteronism, Pheochromocytoma), coarctation of the aorta, obstructive sleep apnea and drug induced (e.g. corticosteroid, oral contraceptive pills).

Although the risk of cardiovascular and renal disease continuously rises over the entire range of blood pressure; based on the level of blood of blood pressure hypertension is defined a systolic blood pressure $\geq$140mmHg and/or diastolic blood pressure $\geq$ 90mmHg.

Clinical features

- Hypertension is generally **ASYMPTOMATIC.**
- Clinical evaluation (history and physical examination) should focus on proper blood pressure measurement , looking for other cardiovascular risk factors(Diabetes Mellitus, Dyslipidemia, Obesity , Smoking and family history of coronary heart disease) , looking for evidence of end organ damage and searching for possible secondary causes.

Table 6. Category of blood pressure according to the USA Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)

	Blood pressure in mm Hg		
Category	**Systolic**		**Diastolic**
Normal	<120	AND	<80
Prehypertension	120-139	OR	80-89
Hypertension	≥140	OR	≥90

Table 7 . Category of stage of hypertension according to the USA Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)

Stage of hypertension	Systolic		Diastolic
Stage1	140-159	OR	90-99
Stage 2	≥160	OR	≥100

N.B These definitions apply to adults on no antihypertensive treatment and who are not acutely ill. If there is a disparity in the category between the systolic and diastolic pressures, the higher value determines the severity of hypertension**.**

1) **Hypertensive Emergencies-** are acute, life-threatening, and usually associated with marked increases in blood pressure (BP), generally ≥180/120 mmHg **.**These are situations that require immediate (within minutes) blood pressure reduction to prevent or limit target organ damage.
   The conditions include ypertensive encephalopathy, intracranial hemorrhage, unstable angina, acute myocardial infarction, acute kidney injury, pulmonary edema and dissecting aortic aneurysm, and eclampsia.
2) **Hypertensive Urgency-** is a situation in which there is asymptomatic severe hypertension with no target organ damage.Tthe goal of management is to reduce the blood pressure to ≤160/100 mmHg over several **hours to days, not rapidly.** This is based on the adverse effects observed with faster correction and/or lower achieved blood pressure.

Investigations

- Urinalysis
- Blood chemistry potassium, sodium, creatinine/estimated glomerular filtration rate
- Fasting blood glucose
- Fasting total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides
- Standard 12 lead electrocardiogram (ECG)

Treatment Objectives

- Detection and management of other cardiovascular risk factors
- Detection and management of target organ damage

- Prevention of target organ damage
- Decrease the side effects of medications
- Achieve target blood pressure (< 140/90mmHg, in patients having diabetes with proteinuria and chronic kidney disease < 130/80 mmHg)

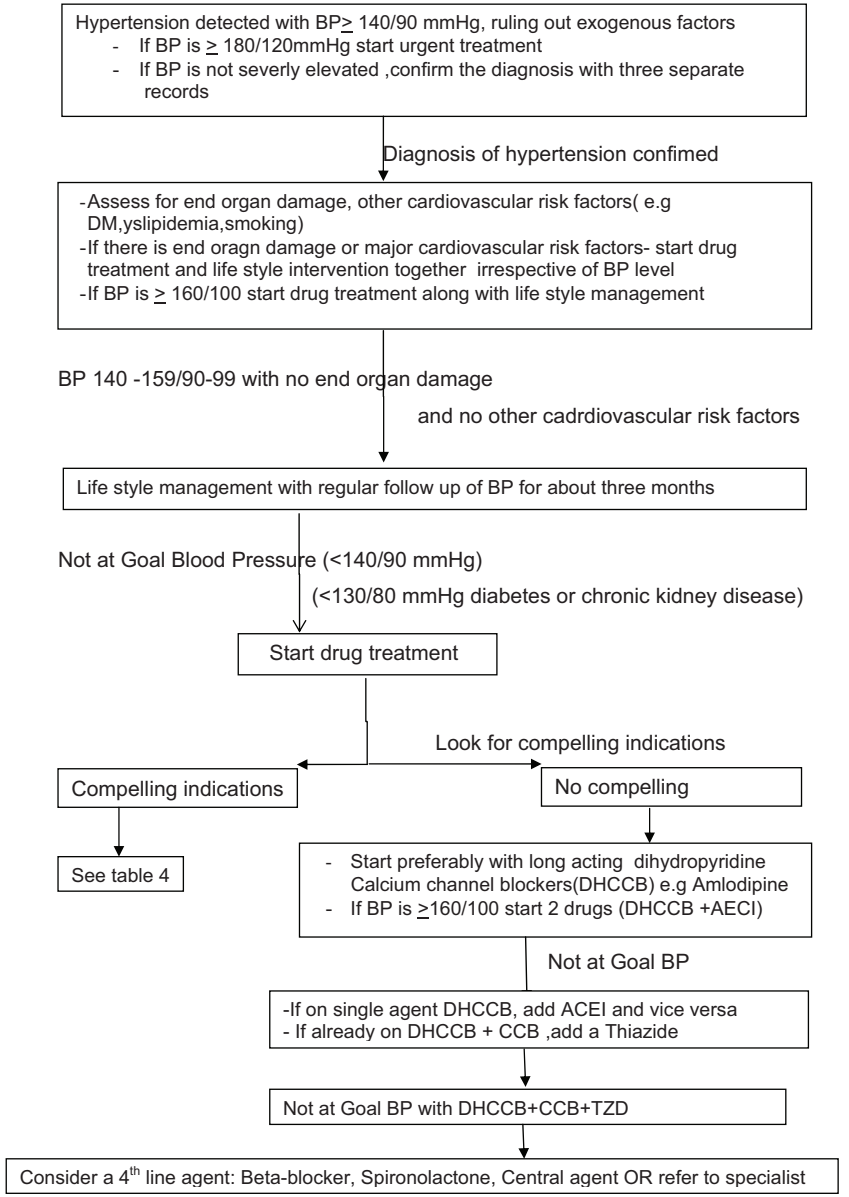
Non pharmacologic

- **Smoking cessation**: Complete cessation of smoking
- **Physical activity**: At least 30 minutes of moderate intensity activity 5-7 days per week
- **Weight reduction**: BMI 18-24 kg/m2, waist circumference < 102 men, < 88 cm women
- **Dietary recommendations**: emphasize fruits, vegetables, low-fat dairy products, fibre, whole grains, and protein sources that are reduced in saturated fats and cholesterol
- **Reduce salt intake**: about1 tsp of table salt. Do not forget hidden salt in home prepared spices .
- **Alcohol consumption**: limited to two drinks or less per day.**(One standard drink)**
    - 1 bottle (341 mL) of 5% beer or 1 glass (150 mL) of 12% wine or, 1.5 oz (45 mL) of 40% spirit

Pharmacologic

- The first-line drugs are roughly equally effective as mono therapy although there is inter-patient variability.
- Beta blockers are not considered as first line in the absence of a compelling indication.
- Start with a single agent among the first lines, two drugs can be started at the beginning in stage 2 hypertension if the BP is hiher than 20/10 mmHg from the target.
- If BP target is not achieved by a single agent add a second agent rather than increasing the dose of the first drug to maximum dose.
- If two drug combinations are started, start with a long acting ACEI (e.g Lisinopril) and long acting dihydropyridine calcium channel blocker(e.g Amlodipine)

Fig1: Algorithm for the Treatment of Essential Algorithm



Non -Emergency conditions

First line (in the absence of compelling indications**)**

Calcium channel blockers - Amlodipine, Nifedipine (extended or slow release),

Felodipine

ACE inhibitors - Lisinopril, Enalapril and captopril

Thiazide diuretics- Hydrochlorothiazide

Angiotensin receptor blockers (ARBs) – Candesartan, Valsartan, Losartan

(For dose regimens, ADRs, C/Is, P/Cs, D/Is and dosage forms, see page 34)

Alternatives

Beta blockers- Atenolol, Metoprolol, Carvedilol, propranolol

Central alpha-2 agonist – methyldopa

(For dose regimens, ADRs, C/Is, P/Cs, D/Is and dosage forms, see page35)

Table 8– Dose, frequency and ADRs of antihypertensive medications available

Class	Drug	Dose range (mg/d)	Frequency (Per day)	Common ADRs
ACEI	Enalapril	5 - 40	1-2	-Dry cough, hyperkalemia, AKI, angioedema
	Lisinopril	10 - 40	1	
	Captopril	25 -100	2-3	
Thiazide diuretics	Hydrochlorothiazide	12.5 - 25	1	Frequent urination, hyperglycemia, hyperlipidemia, hyperuricemia
Dihydropyrdine CCB	Amlodipine	2.5 - 10	1	Pedal edema and headache
	Nifedipine (extended release)	20 - 120	1-2	
	Felodipine	2.5 - 20	1	
Beta blockers	Atenolol	25 - 100	1	Fatigue, bronchospasm,bradycardia, AV block hyperglycemia, sexual dysfunction
	Propranolol	40 - 160	2-3	
	Metoprolol succinate	25 - 100	1	
	Carvedilol	12.5 - 50	2	
ARBS	Candesartan	8 -32	1	Hyperkalemia and AKI
	Valsartan	80- 320	1 - 2	
	Losartan	25 - 100	1 - 2	

Class	Drug	Dose range (mg/d)	Frequency (Per day)	Common ADRs
Non-dihydropyrdine CCB	Verapamil	120–360	1-2	Constipation (verapamil), headache (diltiazem), bradyacrdia
	Diltiazem	180-420	1	
Central α agonists	Methyl dopa	250 - 1000	2	Sedation, dry mouth, rebound hypertension, sexual dysfunction

Table 9- Compelling indication/co-morbidities in hypertension treatment

Compelling condition	First line	Second line
Coronary heart disease	ACE inhibitors/ARB Beta blockers	Calcium channel blocker
Heart failure	ACE inhibitor/ARB Metoprolol/Carvedilol	Diuretics
Diabetes with proteinuria	ACE inhibitor/ARB	Thiazide Calcium channel blockers
Left ventricular hypertrophy	ACE inhibitor/ARB	Thiazide
Chronic kidney disease	ACE inhibitor/ARB	Loop diuretics, cacium channel blocker

1. Treatment of Hypertensive Emergencies:

Optimal therapy varies with the type of hypertensive emergency. Hydralazine, 5-10 mg initial dose, repeated every 20 to 30 minutes (with maximum dose of 20 mg) should be given until the mean arterial blood pressure is reduced by 25% (within minutes to 2 hours), then towards 160/100 mm Hg within 2-6 hours.

2. Hypertensive Urgency

- **For previously treated patients** - adjust existing medication regimen, or reinstituting their medications (if nonadherent).

- **For previously untreated patients** – start either a low dose of a calcium channel blocker (Nifedipine slow release 30) or ACE inhibitor (captopril or Enalapril) or Beta blocker.
- **Furosemide 20 -40mg** (PO or IV) can be added to the above agents
- If patient is reliable follow up can be made every one to two day. If not reliable admit.
- Avoid rapid drop in blood pressure

Table 10. Drugs used in the treatment of hypertensive emergency

Drug	Route	Initial dose	Dose Range	Onset peak Effects	Duration
Nitroprusside	I.V	0.5 μg/kg /min	0.5 to 10 μg/kg /min	1 to 2 min	2 to 3 min
Nitroglycerin	IV	5 μg/min IV infusion	5–100 μg/min IV infusion	2–5 min	5–10 min
Hydralazine	I.V	5-10 mg	5 to 20 mg	5 to 15min	2 to 6 hr
Captopril	P.O	6.25 to 12 .5 mg	12.5 - 50 mg , TID	30 to 90 min	4 to 6 hr

5. Ischaemic Heart Disease

Clinically Ischemic Heart Disease comprises of stable angina pectoris, acute coronary syndromes and ischemic cardiomyopathy.

Stable angina pectoris

Stable angina pectoris refers to recurrent characteristic/atypical chest pain induced by physical activity or emotional stress and relieved by rest or nitrates. Atherosclerosis with narrowing of the coronary blood vessels of the vessels leading to reduction in blood supply to the myocardium is the cause. Risk factors of stable angina are that of atherosclerotic vascular disease, the major risk factors include diabetes mellitus, hypertension, cigarette smoking, dyslipidemia, obesity, a family history of ischemic heart disease or sudden death, old age, male gender and elevated markers of inflammation such as C-reactive protein.