

Central Administration of Pharmaceutical Care  
General Administration for Drug Utilization and Pharmacy Practice

# Egyptian National Drug Formulary Guideline

## Cardiovascular Chapter

### 2024

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## Preface

The Egyptian Drug Formulary is published by the Egyptian Drug Authority, the Central Administration of Pharmaceutical Care, by the General Administration of Drug Utilization and Pharmacy Practice. It has been discussed within the Committee for Pharmacy Practice Guidelines and National Drug Lists.

The Egyptian Drug Formulary aims to provide pharmacists and other healthcare professionals with accessible and reliable information about the available medications in the Egyptian drug database for making the right clinical decisions.

The Egyptian Drug Formulary is a guide that should be interpreted in light of professional knowledge. The developers work to ensure that the information is as accurate and up-to-date as possible at the date of publication but knowledge and best practice change regularly. No responsibility for the work team for errors or omissions.

# Egyptian Drug Formulary (Cardiovascular Chapter) Manual

The Egyptian Drug Formulary (Cardiovascular Chapter) contains a list of medicines registered in the Egyptian drug database included in the essential medicines list or widely used on the Egyptian pharmaceutical market. It is designed as drug monographs classified pharmacologically and arranged alphabetically. There is a pharmacologically classified drug index at the beginning of the document and another alphabetically classified index at the end.

The Egyptian Drug Formulary (Cardiovascular Chapter) presents detailed practical information for healthcare providers about each medicine.

Each monograph includes:

1. Generic name
2. Dosage form/strengths available in Egypt from the EDA database
3. Route of administration
4. Pharmacological category and ATC code
5. Indications: labeled indications
6. Dosage regimens for adults and children
7. Dosage adjustments if needed.
8. Contraindications
9. Adverse drug reaction
10. Monitoring parameters
11. Drug Interactions: that imply avoidance or considering modifications.
12. Pregnancy and lactation
13. Administration: detailed administration information for all routes  
[parenteral (preparation concentrations, compatibility with diluents, infusion rate, precautions during administration), Oral (food correlation)].

Refer to the manufacturer Leaflet if there are other specific considerations.

#### 14. Warnings/Precautions

#### 15. Storage:

- For reconstituted vials or diluted solutions, apply mentioned storage conditions only if prepared in aseptic techniques and ISO-controlled conditions according to USP standards, otherwise discard immediately if not used.
- USP develops standards for compounding medications to help ensure patient benefit and reduce risks such as contamination, infection, or incorrect dosing.

Refer to manufacturer PIL (Patient Information Leaflet) and SPC (Summary of product characteristics) if there are other specific considerations.

### Cardiovascular System Formulary:

This document includes medications that affect cardiovascular system or contribute in management of disorders that involve heart and blood vessels.

Therapeutic classes include Adrenoreceptor antagonists (Alpha-blockers, Beta-Blockers, and Alpha and Beta Blockers), Angiotensin II Receptor Antagonists, Angiotensin-Converting Enzyme (ACE) Inhibitor, Antianginals (Cardioprotective agents and Vasodilators), Antiarrhythmic agents, Antihypertensive (Centrally acting agents and Vasodilators), Antiplatelet drugs, Calcium-Channel Blockers (Dihydropyridine and Non-dihydropyridine), Cardiac glycoside, Diuretics (Loop, Osmotic, Potassium-sparing, and Thiazides), Fibrinolytics Agents, Lipid modifying agents (Bile acid sequestrants, Cholesterol absorption inhibitors, Fibrates, and Statins), Selective Sinus Node I(f) Inhibitors, Sodium-glucose cotransporter 2 (SGLT2) Inhibitors, and Sympathomimetics.



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## Disclaimer

**Any information about drugs mentioned inside this formulary is general, and does not cover all data of the medications included. The content is not intended for use as medical advice for individual problems or for evaluating the risks and benefits of taking a particular drug. Generally, all knowledge and best practices are subject to frequent changes and updates.**

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## List of Abbreviations

Abbreviation	Meaning
ECG	Electrocardiogram
ACE inhibitors	Angiotensin-Converting-Enzyme Inhibitors
AERD	Aspirin Exacerbated Respiratory Disease
AKI	Acute Kidney Injury
ALT	Alanine Transaminase
AMI	Acute Myocardial Infarction
ANA	Antinuclear Antibody
ARBs	Angiotensin II Receptor Blockers
ASCVD	Atherosclerotic Cardiovascular Disease
AST	Aspartate Aminotransferase
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CAD	Coronary Artery Disease
CBC	Complete Blood Count
CHF	Congestive Heart Failure
CPK	Creatine Phosphokinase
CrCl	Creatinine Clearance
CVA	Cerebral Vascular Accident
D5W	Dextrose 5% In Water
DKA	Diabetic Ketoacidosis
ER	Extended Release
G6PD	Glucose-6-Phosphate Dehydrogenase
GIT	Gastrointestinal Tract
HbA1c	Glycosylated Hemoglobin
HDL	High-Density Lipoprotein
HMG-CoA	Hydroxymethylglutaryl- Coenzyme A
INR	International Normalised Ratio
IR	Immediate Release
LDL	Low-Density Lipoprotein
LFT	Liver Function Test
NS	Normal Saline (Sodium Chloride 0.9% Solution)
PO	Orally
PPI	Proton Pump Inhibitor
PR	Pulse Rate
PT	Prothrombin Time
PVC	Polyvinyl Chloride
PVD	Peripheral Vascular Disease

Abbreviation	Meaning
PVOD	Pulmonary Veno-Occlusive Disease
SGLT2	Sodium-Glucose Co-Transporter-2
SI	International System of Units
ULN	Upper Limit Normal

## Alpha- blockers

## Alfuzosin

<b>Generic Name</b>	<b>Alfuzosin</b>
<b>Dosage form/strengths</b>	Prolonged release tablets: 5mg, 10mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha 1 Blocker ATC: G04CA01
<b>Indications</b>	<b>Benign prostatic hyperplasia:</b> Treatment of benign prostatic hyperplasia.
<b>Dosage Regimen</b>	<i>Extended release:</i> 10 mg once daily or 5 mg twice daily.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> Modified release: Avoid in severe renal impairment (CrCl <30 mL/minute). <b>Dosage: Hepatic Impairment: Adult</b> Modified release: Mild hepatic impairment: Use caution, not studied. Moderate or severe hepatic impairment: Use is contraindicated.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Alfuzosin or any component of the formulation.</li> <li>• Moderate or severe hepatic impairment.</li> <li>• History of micturition syncope.</li> <li>• History of postural hypotension</li> <li>• Concurrent use with potent CYP3A4 inhibitors (e.g. Itraconazole, Ketoconazole)</li> </ul>
<b>Adverse Drug Reactions</b>	<b>1% to 10%:</b> Gastrointestinal: Abdominal pain 2%, constipation 2%, dyspepsia 2%, nausea 2% Genitourinary: Impotence 2% Nervous system: Dizziness 6%, fatigue 3%, headache 3%, pain 2% Respiratory: Bronchitis 2%, pharyngitis 2%, sinusitis 2%, upper respiratory tract infection 3%
<b>Monitoring Parameters</b>	Blood pressure. Heart rate.
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Alpha1-Blockers, Strong CYP3A4 Inhibitors (e.g. Clarithromycin, Itraconazole, Ketoconazole, Posaconazole), Fexinidazole, Fusidic Acid (Systemic)
<b>Pregnancy and Lactation</b>	This medicine is not intended for use in women.
<b>Administration</b>	Oral: Administer immediately following a meal at the same time each day. Swallow tablet whole; do not crush or chew. Refer to manufacturer PIL if there are specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Floppy iris syndrome:</b> Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha<sub>1</sub>-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> <li>• <b>Orthostatic hypotension/syncope:</b> May cause significant orthostatic hypotension with or without syncope, especially with first dose, if dosage is rapidly increased, or if another antihypertensive drug is co-administered.; First-dose" orthostatic hypotension may occur few hours after dosing; may be dose</li> </ul>

related. Vertigo and dizziness due to orthostatic hypotension may occur. Patients should be cautioned about performing hazardous tasks or driving when starting new therapy or adjusting dosage upward. Elderly are at higher risk.

- **Hepatic or renal impairment:** Use with caution in patients with mild hepatic impairment; contraindicated in moderate-to-severe impairment. Caution in patients with severe renal impairment (CrCl <30 mL/minute).
- **Prostate cancer:** It is recommended to rule out prostatic carcinoma before beginning therapy
- **Heart disease:** Use with caution in patients with histories of tachyarrhythmia or with certain cardiovascular conditions, such as myocardial ischemia. Discontinue if symptoms of angina occur or worsen. Alfuzosin has been shown to prolong the QT interval alone (minimal) and with other drugs with comparable effects on the QT interval (additive). Use with caution in patients with known QT prolongation (congenital or acquired).

#### Storage

Store between 15°C to 30°C. Protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.



## Doxazosin

<b>Generic Name</b>	<b>Doxazosin</b>
<b>Dosage form/strengths</b>	Tablets: 1mg, 2mg, 4mg, 8mg Modified Release Film Coated Tablets: 4mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha 1 Blocker; Antihypertensive ATC: C02CA04
<b>Indications</b>	<b>Benign prostatic hyperplasia:</b> Treatment of benign prostatic hyperplasia. <b>Hypertension:</b> Management of hypertension.
<b>Dosage Regimen</b>	<b>Adult dosing:</b> <b>Hypertension:</b> <i>Immediate-release medicines:</i> initial 1mg once daily increased by doubling in 1-2 weeks' interval up to 16 mg. <i>Modified-release medicines:</i> 4mg once daily, may be increased to 8mg after 4 weeks. <b>Benign prostatic hyperplasia:</b> <i>Immediate-release medicines:</i> initial 1mg once daily increased by doubling in 1-2 weeks' interval up to 8 mg. usual maintenance dose: 2-4mg daily. <i>Modified-release medicines:</i> 4mg once daily, may be increased to 8mg after 4 weeks.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> No adjustments necessary. <b>Dosing: Hepatic Impairment: Adult</b> Mild to moderate impairment: use with caution. Severe impairment: Use is not recommended.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Doxazosin, other Quinazolines (e.g. Prazosin, Terazosin), or any component of the formulation.</li> <li>• History of micturition syncope (in patients with benign prostatic hypertrophy).</li> <li>• History of postural hypotension.</li> <li>• Monotherapy in patients with overflow bladder or anuria.</li> <li>• Concurrent use with potent CYP3A4 inhibitors (eg, Itraconazole, Ketoconazole).</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> <b>Floppy iris syndrome:</b> with current or prior use of alpha-1 blockers undergoing cataract surgery. <b>Orthostatic hypotension:</b> Dose related. Onset after initial dose or after few months. <b>&gt;10%:</b> Nervous system: Dizziness ( $\leq 19\%$ ), fatigue ( $\leq 12\%$ ), malaise ( $\leq 12\%$ ), vertigo ( $\leq 16\%$ ) <b>1% to 10%:</b> Cardiovascular: Edema ( $\leq 3\%$ ), hypotension ( $\leq 2\%$ ), orthostatic hypotension (2%) Gastrointestinal: Abdominal pain (2%), dyspepsia (1%), nausea (2%), xerostomia (1%) Genitourinary: Urinary tract infection (1%) Nervous system: Asthenia (4%), drowsiness (1%), headache (6%) Neuromuscular and skeletal: Myalgia ( $\leq 1\%$ ) Renal: Polyuria (2%)

	Respiratory: Dyspnea (1% to 3%), respiratory tract infection (5%), rhinitis (3%)
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Alpha1-Blockers, Bromperidol</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Obinutuzumab, Phosphodiesterase 5 Inhibitors</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> No evidence of teratogenicity; Animal Data Suggest Moderate Risk. Use only when potential benefit outweighs risk.</p> <p><b>Lactation:</b> Accumulates in milk in animal studies. Potential Toxicity. Better to avoid.</p>
<b>Administration</b>	<p><b>Oral:</b> <i>Immediate release:</i> Administer without regard to meals at the same time each day. <i>Extended release:</i> Swallow tablets whole; do not crush or divide. Administer with morning meal. Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Floppy iris syndrome:</b> Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha<sub>1</sub>-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> <li>• <b>Orthostatic hypotension/syncope:</b> May cause significant orthostatic hypotension with or without syncope, especially with first dose, if dosage is rapidly increased, or if another antihypertensive drug is co-administered.; First-dose” orthostatic hypotension may occur few hours after dosing; may be dose related. Vertigo and dizziness due to orthostatic hypotension may occur. Patients should be cautioned about performing hazardous tasks, driving, or operating heavy machinery when starting new therapy or adjusting dosage upward. Elderly are at higher risk.</li> <li>• <b>Hepatic impairment:</b> Use with caution in patients with mild to moderate impairment; monitor blood pressure and for symptoms of hypotension. Not recommended in severe impairment as extensively metabolized.</li> <li>• <b>Prostate cancer:</b> It is recommended to rule out prostatic carcinoma before starting therapy.</li> <li>• <b>Heart disease:</b> Use with caution in patients with heart failure, angina pectoris, or recent acute myocardial infarction (within the last 6 months). If symptoms of angina pectoris appear or worsen, discontinue use.</li> <li>• <b>Hematologic effect:</b> Leukopenia and thrombocytopenia rarely occur and reversible after discontinuation.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.</p>

## Silodosin

<b>Generic Name</b>	Silodosin
<b>Dosage form/strengths</b>	Capsules: 4mg, 8mg Scored tablet: 8mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha1 blocker ATC Code: G04CA04
<b>Indications</b>	Treatment of benign prostatic hyperplasia. N.B not indicated for the treatment of hypertension.
<b>Dosage Regimen</b>	<b>Oral:</b> 8 mg once daily with a meal.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> CrCl >50 mL/minute: No dosage adjustment necessary. CrCl 30-50 mL/minute: 4 mg once daily. CrCl <30 mL/minute: Use is contraindicated. <b>Dosing: Hepatic Impairment: Adult</b> Mild-to-moderate impairment: No dosage adjustment necessary. Severe impairment: Use is contraindicated.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Severe renal or hepatic impairment.</li> <li>• Hypersensitivity to silodosin or any ingredient of the formulation.</li> <li>• Concurrent use with potent CYP3A4 inhibitors (eg, Itraconazole, Ketoconazole).</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><b>Floppy iris syndrome:</b> with current or prior use of alpha-1 blockers undergoing cataract surgery.</p> <p><b>Orthostatic hypotension:</b> Dose related. Onset after initial dose or after few months.</p> <p><b>&gt;10%:</b> Genitourinary: Retrograde ejaculation (28%)</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Orthostatic hypotension (3%; increased in elderly ≥65 years up to 5%)</p> <p>Central nervous system: Dizziness (3%), headache (2%), insomnia (1%)</p> <p>Gastrointestinal: Diarrhea (3%), abdominal pain (1%)</p> <p>Genitourinary: Prostate specific antigen increased (1%)</p> <p>Neuromuscular and skeletal: Weakness (1% to 2%)</p> <p>Respiratory: Nasal congestion (2%), rhinorrhea (1%), sinusitis (1%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Alpha1-Blockers, Strong CYP3A4 Inhibitors (e.g. Clarithromycin, Itraconazole, Ketoconazole, Posaconazole), Fexinidazole, Fusidic Acid (Systemic)
<b>Pregnancy and Lactation</b>	Not indicated for women.

<b>Administration</b>	<p><b>Oral:</b> Administer Silodosin with a meal, at about the same time every day.</p> <ul style="list-style-type: none"> <li>• Swallow the capsule intact; do not chew or crush.</li> <li>• Do not subdivide capsule contents.</li> <li>• The dose should be swallowed immediately (within 5 minutes) without chewing and followed by 240 mL glass of cool water.</li> </ul> <p>Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Floppy iris syndrome:</b> Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha<sub>1</sub>-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> <li>• <b>Orthostatic hypotension/syncope:</b> May cause significant orthostatic hypotension with or without syncope, especially with first dose, if dosage is rapidly increased, or if another antihypertensive drug is co-administered.; First-dose” orthostatic hypotension may occur few hours after dosing; may be dose related. Vertigo and dizziness due to orthostatic hypotension may occur. Patients should be cautioned about performing hazardous tasks, driving, or operating heavy machinery when starting new therapy or adjusting dosage upward. Elderly are at higher risk.</li> <li>• <b>Hepatic or renal impairment:</b> Use with caution in patients with mild-to-moderate impairment; contraindicated with severe hepatic or renal impairment.</li> <li>• <b>Prostate cancer:</b> It is recommended to rule out prostatic carcinoma before beginning therapy.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.</p>

## Tamsulosin

<b>Generic Name</b>	Tamsulosin
<b>Dosage form/strengths</b>	Modified Release Hard Gelatin Capsule: 0.4mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha 1 Blocker ATC: G04CA02
<b>Indications</b>	<b>Benign prostatic hyperplasia:</b> Treatment of benign prostatic hyperplasia. N.B. Not indicated for the treatment of hypertension
<b>Dosage Regimen</b>	<b>Oral:</b> Modified release capsule: 0.4 mg daily.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> CrCl $\geq$ 10 mL/minute: No dosage adjustment necessary. CrCl <10 mL/minute: Has not been studied; use with caution.  <b>Hemodialysis, Peritoneal dialysis:</b> Highly protein bound. Has not been studied; use with caution.  <b>Dosing: Hepatic Impairment: Adult</b> Mild-to-moderate impairment: No dosage adjustment is necessary. Severe impairment: Has not been studied. Avoid.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Tamsulosin or any component of the formulation.</li> <li>• History of micturition syncope.</li> <li>• History of postural hypotension.</li> <li>• Concurrent use with potent CYP3A4 inhibitors (eg, Itraconazole, Ketoconazole)</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><b>Floppy iris syndrome:</b> with current or prior use of alpha-1 blockers undergoing cataract surgery.</p> <p><b>Orthostatic hypotension:</b> Dose related. Onset after initial dose or after few months.</p> <p><b>&gt;10%:</b></p> <p>Cardiovascular: Orthostatic hypotension (by orthostatic testing: first dose: 6% to 7%, chronic use: 16% to 19%; symptomatic: &lt;1%)</p> <p>Genitourinary: Ejaculation failure (8% to 18%)</p> <p>Infection: Infection (9% to 11%)</p> <p>Nervous system: Dizziness (15% to 17%), headache (19% to 21%)</p> <p>Respiratory: Rhinitis (13% to 18%)</p> <p><b>1% to 10%:</b></p> <p>Endocrine and metabolic: Decreased libido (2%)</p> <p>Gastrointestinal: Diarrhea (6%), nausea (4%)</p> <p>Nervous system: Asthenia (8% to 9%), drowsiness (3% to 4%), insomnia (1% to 2%),</p>

	vertigo (1%) Neuromuscular and skeletal: Back pain (7% to 8%) Ophthalmic: Blurred vision ( $\leq 2\%$ ) Respiratory: Increased cough (3% to 5%), pharyngitis (6%), sinusitis (4%)
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure.</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Alpha1-Blockers, Bromperidol, Strong CYP3A4 Inhibitors (e.g. Clarithromycin, Itraconazole, Ketoconazole, Posaconazole), Fexinidazole, Fusidic Acid (Systemic).</p> <p><b>Risk D: Consider therapy modification</b>                  Amifostine Obinutuzumab</p> <p><b>Risk C: Monitor therapy</b>                  Ajmaline, Alpha-/Beta-Agonists, Alpha1-Agonists, Amisulpride, Antipsychotic Agents (Second Generation [Atypical]), Arginine, Artemether and Lumefantrine, Barbiturates, Benperidol, Blood Pressure Lowering Agents, Brimonidine, Cimetidine, Clofazimine, CYP2D6 Inhibitors, CYP3A4 Inhibitors (Moderate), Dapoxetine, Diazoxide, Duloxetine, Herbal Products with Blood Pressure Lowering Effects, Hypotension-Associated Agents, Levodopa-Foslevodopa, Lormetazepam, Molsidomine, Nicorandil, Peginterferon Alfa-2b, Pentoxifylline, Pholcodine, Phosphodiesterase 5 Inhibitors, Prostacyclin Analogues, Quinagolide, Rilmenidine.</p>
<b>Pregnancy and Lactation</b>	Tamsulosin is not indicated in women.
<b>Administration</b>	<p><b>Administration: Oral</b>                  Administer capsules as a whole at the same time each day, with or without food.                  N.B. Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Floppy iris syndrome:</b> Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha<sub>1</sub>-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> <li>• <b>Orthostatic hypotension/syncope:</b> May cause significant orthostatic hypotension with or without syncope, especially with first dose, if dosage is rapidly increased, or if another antihypertensive drug is co-administered.; First-dose" orthostatic hypotension may occur few hours after dosing; may be dose related. Vertigo and dizziness due to orthostatic hypotension may occur. Patients should be cautioned about performing hazardous tasks, driving, or operating heavy machinery when starting new therapy or adjusting dosage upward. Elderly are at higher risk.</li> <li>• <b>Hepatic or renal impairment:</b> Use with caution in patients with severe renal impairment; avoid in severe hepatic impairment</li> <li>• <b>Prostate cancer:</b> It is recommended to rule out prostatic carcinoma before beginning therapy.</li> <li>• <b>Sulfonamide allergy:</b> Rarely, patients with a sulfa allergy have also developed an allergic reaction to Tamsulosin; avoid use when previous reaction has been</li> </ul>

	<p>severe or life-threatening.</p> <ul style="list-style-type: none"> <li>• <b>Heart disease:</b> Tamsulosin has been determined to be an agent that may exacerbate underlying myocardial dysfunction with moderate magnitude. Discontinue if symptoms of angina occur or worsen.</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.</p>



## Terazosin

Generic name	Terazosin
Dosage form/strengths	- Soft Gelatin Capsules: 1 mg, 2.4 mg, 6 mg - Tablets: 1 mg, 2 mg, 5 mg, 10 mg
Route of administration	Oral
Pharmacologic category	Alpha 1 Blocker; Antihypertensive ATC: G04CA03
Indications	-Benign prostatic hyperplasia -Hypertension
Dosage Regimen	<b>-Adult:</b> <b>-Benign prostatic hyperplasia:</b> Initial: 1 mg once daily at bedtime; titrate slowly every few weeks according to response and tolerability; usual dose: 5-10 mg once daily. Maximum dose: 20 mg per day.  <b>-Hypertension:</b> Initial: 1 mg once daily at bedtime. Titrate gradually according to response and tolerability. Maximum dose: 20 mg per day.
Dosage adjustment	<b>-Renal Impairment:</b> No dosage adjustment necessary  <b>-Hepatic Impairment:</b> Start with the lowest initial dosage (1 mg once daily). Monitor closely and adjust dosage based on clinical response. Metabolized by liver.
Contra-indications	-Hypersensitivity to terazosin or any component of the formulation. -In benign prostatic hyperplasia: History of micturition syncope, history of postural hypotension.
Adverse Drug Reactions	<b>-&gt;10%:</b> Nervous system: Asthenia ( $\leq 11\%$ ), dizziness (9% to 19%), fatigue ( $\leq 11\%$ ), lassitude ( $\leq 11\%$ )  <b>-1% to 10%:</b> -Cardiovascular: Orthostatic hypotension (1% to 5%), palpitations (4%), peripheral edema (6%), tachycardia (2%) -Gastrointestinal: Nausea (2% to 4%) -Genitourinary: Impotence (2%) -Nervous system: Drowsiness (4% to 5%), paresthesia (3%), vertigo (1%) -Neuromuscular and skeletal: Back pain (2%), limb pain (4%) -Ophthalmic: Amblyopia ( $\leq 1\%$ ), blurred vision ( $\leq 2\%$ ) -Respiratory: Dyspnea (2% to 3%), nasal congestion ( $\leq 6\%$ ), rhinitis ( $\leq 2\%$ ), sinusitis (3%)
Monitoring Parameters	Blood Pressure. Heart rate.



<b>Drug Interactions</b>	<p><b>Category X avoid combination:</b> Alpha1-Blockers, Bromperidol.</p> <p><b>Category D consider modification therapy:</b> Amifostine, Obinutuzumab, Phosphodiesterase 5 Inhibitors (eg. Sildenafil, Tadalafil, Vardenafil, and Avanafil).</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b> No Human Data. Agents other than Terazosin may be preferred in chronic hypertension. Terazosin should be used during pregnancy only if the benefits to the mother outweigh the risks to the fetus.</p> <p><b>-Lactation:</b> -It is not known if terazosin is present in breast milk. Caution if used.</p>
<b>Administration</b>	<p><b>-Oral:</b> -Terazosin may be administered without regard to meals. Food may delay the time to peak concentrations. -Administer at the same time each day. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Orthostatic hypotension/syncope:</b> May cause significant orthostatic hypotension with or without syncope, especially with first dose, if dosage is rapidly increased, or if another antihypertensive drug is co-administered.; First-dose” orthostatic hypotension may occur few hours after dosing; may be dose related. Vertigo and dizziness due to orthostatic hypotension may occur. Patients should be cautioned about performing hazardous tasks, driving, or operating heavy machinery when starting new therapy or adjusting dosage upward. Elderly are at higher risk.</li> <li>• <b>Floppy iris syndrome:</b> Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha<sub>1</sub>-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C; protect from light and moisture. Refer to manufacturer PIL if there are specific considerations.</p>

## Alpha and Beta Blockers

## Carvedilol

<b>Generic Name</b>	Carvedilol
<b>Dosage form/strengths</b>	Tablets: 3.125 mg, 6.25mg, 12.5mg, 25mg Carvedilol phosphate: Extended release capsule: 10mg, 20mg, 40mg, 80mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha- And Beta-Adrenoceptor Blockers ATC: C07AG02
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Chronic heart failure</li> <li>• Left ventricular dysfunction following myocardial infarction.</li> <li>• Angina</li> <li>• Hypertension</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Hypertension</b>  <i>-Immediate release:</i> Initially 6.25 mg twice daily for 2 days, then increased if necessary in week intervals up to 25 mg once or twice daily.                      Elderly: Initially 12.5 mg daily, initial dose may provide satisfactory control  <i>-Extended release: Oral:</i> Initial: 20 mg once daily; titrate in intervals of more than a week as needed according to response; usual dosage range: 20 to 80 mg/day.</p> <p><b>Angina:</b>  <i>-Immediate release: Oral:</i> Initial: 12.5 mg twice daily; increase dose if tolerable up to 25 mg once or twice daily.</p> <p><b>Chronic heart failure (adjunct therapy)</b>  <i>-Immediate release:</i> Initially 3.125 mg twice daily, then increased by doubling at intervals of at least 2 weeks.                      Maximum doses:                      ≤85 kg or severe heart failure patients: 25 mg twice daily.                      &gt;85 kg: 50 mg twice daily.  <i>-Extended release: Oral:</i> Initial: 10 mg once daily; then increased by doubling at intervals of 1-2 weeks. Maximum 80 mg daily.</p> <p><b>Left ventricular dysfunction following myocardial infarction:</b>                      Start at 6.25 mg twice daily and increase by doubling after intervals of 3 to 10 days.</p> <p><b>Pediatric use:</b>                      Effectiveness in patients younger than 18 years has not been established.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b>                      No dosage adjustment necessary</p> <p><b>Dosing: Hepatic Impairment:</b>                      Moderate impairment: may need dose adjustment.                      Severe impairment: Avoid use.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Acute heart failure</li> <li>• Bronchial asthma</li> <li>• AV block</li> <li>• Severe bradycardia (unless permanent pacemaker is used)</li> <li>• Cardiogenic shock</li> <li>• Severe hepatic disease</li> <li>• Sick sinus syndrome</li> <li>• Acute or decompensated heart failure requiring intravenous inotropes.</li> <li>• History of serious hypersensitivity reaction</li> </ul>

**Adverse Drug Reactions**
**Significant Adverse Reactions:**

Bradyarrhythmias  
 Bronchospasm  
 Potentiation/masking of hypoglycemia  
 Abrupt Withdrawal symptoms

**>10%:**

Cardiovascular: Hypotension ( $\leq 20\%$ ), orthostatic hypotension ( $\leq 20\%$ )  
 Endocrine and metabolic: Hyperglycemia (5% to 12%), weight gain (10% to 12%)  
 Gastrointestinal: Diarrhea (1% to 12%)  
 Nervous system: Dizziness (2% to 32%), fatigue (24%)  
 Neuromuscular and skeletal: Asthenia (11%)

**1% to 10%:**

*Cardiovascular:* Angina pectoris (6%), atrioventricular block (2%), bradycardia ( $\leq 10\%$ ), dependent edema (5% to 6%), edema (5% to 6%), exacerbation of angina pectoris (2%), hypertension (2%), lower extremity edema (2%), palpitations (2%), peripheral edema (1% to 7%), peripheral ischemia ( $\leq 1\%$ ), peripheral vascular disease (2%), syncope ( $\leq 8\%$ ), tachycardia ( $\leq 1\%$ )

*Dermatologic:* Diaphoresis ( $\leq 1\%$ ), erythematous rash ( $\leq 1\%$ ), maculopapular rash ( $\leq 1\%$ ), pruritus ( $\leq 1\%$ ), psoriasiform eruption ( $\leq 1\%$ ), skin photosensitivity ( $\leq 1\%$ )

*Endocrine and metabolic:* Albuminuria (2%), decreased libido ( $\leq 1\%$ ), diabetes mellitus (2%), hypercholesterolemia (4%), hyperkalemia (2%), hypertriglyceridemia ( $\leq 1\%$ ), hyperuricemia (2%), hypervolemia (2%), hypoglycemia (2%), hypokalemia ( $\leq 1\%$ ), hyponatremia (2%), hypovolemia (2%), increased nonprotein nitrogen (6%), weight loss (2%)

*Gastrointestinal:* Gastrointestinal pain (2%), melena (2%), nausea (2% to 9%), periodontitis (2%), vomiting (6%), xerostomia ( $\leq 1\%$ )

*Genitourinary:* Glycosuria (2%), hematuria (2%), impotence (2%), urinary frequency ( $\leq 1\%$ )

*Hematologic and oncologic:* Hypoprothrombinemia (1% to 3%), leukopenia ( $\leq 1\%$ ), purpuric disease (2%), thrombocytopenia (2%)

*Hepatic:* Hyperbilirubinemia ( $\leq 1\%$ ), increased gamma-glutamyl transferase (2%), increased liver enzymes ( $\leq 1\%$ ), increased serum alanine aminotransferase (2%), increased serum alkaline phosphatase (2%), increased serum aspartate aminotransferase (2%)

*Hypersensitivity:* Hypersensitivity reaction (2%)

Nervous system: Abnormality in thinking ( $\leq 1\%$ ), cerebrovascular accident (2%), depression (2%), drowsiness (2%), emotional lability ( $\leq 1\%$ ), exacerbation of depression ( $\leq 1\%$ ), headache (5% to 8%), hypoesthesia (2%), hypotonia (2%), insomnia (1% to 2%), lack of concentration ( $\leq 1\%$ ), malaise (2%), nervousness ( $\leq 1\%$ ), nightmares ( $\leq 1\%$ ), paranoid ideation ( $\leq 1\%$ ), paresthesia (2%), sleep disorder ( $\leq 1\%$ ), vertigo (2%)

*Neuromuscular and skeletal:* Arthralgia (6%), arthritis (2%), gout (2%), hypokinesia ( $\leq 1\%$ ), muscle cramps (2%)

*Ophthalmic:* Blurred vision (2%), visual disturbance (5%)

*Otic:* Tinnitus ( $\leq 1\%$ )

*Renal:* Increased blood urea nitrogen ( $\leq 6\%$ ), increased serum creatinine (2%), renal insufficiency (2%)

*Respiratory:* Asthma ( $\leq 1\%$ ), dyspnea ( $> 3\%$ ), flu-like symptoms (2%), increased cough (5%), nasal congestion (1%), nasopharyngitis (4%), paranasal sinus congestion (1%),

	rales (4%) <i>Miscellaneous:</i> Fever (2%)
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• ECG, heart rate, blood pressure.</li> <li>• Kidney function; liver function</li> <li>• Blood glucose in patients with diabetes.</li> <li>• Signs and symptoms of bronchospasm in patients with existing bronchospastic disease.</li> <li>• Mental alertness.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Beta2-Agonists, Bilastine, Bromperidol, Doxorubicin (Conventional), Etofylline, Fexinidazole, Pazopanib, Rivastigmine, Sirolimus (Protein Bound), Topotecan, Vincristine (Liposomal), White Birch Allergen Extract.</p> <p><b>Risk D: Consider therapy modification</b>                  Afatinib, Alpha2-Agonists, Amifostine, Berostralstat, Ceritinib, Colchicine, Dronedarone, Fingolimod, Grass Pollen Allergen Extract, Lefamulin, Obinutuzumab, Patiromer, Ponesimod, Pralsetinib, Relugolix, Rimegepant, Siponimod, Sirolimus (Conventional), Talazoparib, Tasimelteon, Ubrogapant, Venetoclax.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Insufficient data. Use of beta-blockers in 3rd Trimesters, may induce risk in neonates. If carvedilol is used close to delivery, infants should be monitored for signs of alpha and beta -blockade.</p> <p><b>Lactation:</b> Infants should be monitored as there is a risk of possible toxicity due to alpha and beta blockade.</p>
<b>Administration</b>	Oral: Should be taken with food to minimize the risk of orthostatic hypotension. Refer to manufacturer PIL if there are specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Anaphylactic reactions: Use caution in patients with history of severe anaphylaxis; patients taking beta-blockers may become more sensitive to allergens and unresponsive to usual doses of epinephrine used for treatment.</li> <li>• Bradycardia: Reduce dosage if heart rate drops below 55 beats/minute.</li> <li>• Floppy iris syndrome: Intraoperative floppy iris syndrome is observed in cataract surgery patients who have been treated with alpha1-blockers; no benefit to discontinue therapy prior to surgery. Instruct patients to inform ophthalmologist of alpha-blocker use before eye surgery.</li> <li>• Hypotension or syncope may occur, usually within the first 30 days of therapy; close monitor patients especially in initial or change dosing; gradual dose increase, and administration with food may help to decrease the occurrence of hypotension or syncope. Avoid driving or other hazardous tasks during initiation of therapy.</li> <li>• Angina: Use caution in patients that may have vasospastic angina.</li> <li>• Bronchospastic disease: Patients with bronchospastic disease should not use beta-blockers; if used, should be used cautiously with close monitoring.</li> <li>• Diabetes: <math>\beta</math>-blockers may potentiate insulin-induced hypoglycemia and mask symptoms of hypoglycemia e.g. tachycardia. Also, in patients with heart failure and diabetes, carvedilol may worsen hyperglycemia.</li> <li>• Heart failure with reduced ejection fraction: Worsening heart failure or fluid retention may occur during up-titration of carvedilol. Gradual titration and adjustments of other medications instead of increasing carvedilol dosing is required.</li> <li>• Peripheral vascular disease (PVD): May precipitate or aggravate symptoms of arterial insufficiency in patients with PVD; use with caution and monitor for</li> </ul>

	<p>progression of arterial obstruction.</p> <ul style="list-style-type: none"> <li>• Pheochromocytoma (untreated): Use with caution; adequate alpha-blockade should be initiated prior to use of any beta-blocker.</li> <li>• Thyroid disease: <math>\beta</math>-adrenergic blockade may mask clinical signs of hyperthyroidism, such as tachycardia. Abrupt withdrawal may exacerbate symptoms of hyperthyroidism or precipitate thyroid storm.</li> <li>• Rarely, use of carvedilol in patients with heart failure has resulted in deterioration of renal function</li> <li>• Elderly: Bradycardia may be observed more frequently in elderly patients (&gt;65 years of age); dosage reductions may be necessary.</li> <li>• Abrupt withdrawal: Beta-blocker therapy should be gradually withdrawn to avoid acute tachycardia, hypertension, and/or ischemia. Severe exacerbation of angina, ventricular arrhythmias, and myocardial infarction (MI) have been reported following abrupt withdrawal of beta-blocker therapy.</li> <li>• Major surgery: Chronic beta-blocker therapy should not be routinely withdrawn prior to major surgery.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Protect from moisture and light. Refer to manufacturer PIL if there are specific considerations.

## Angiotensin II Receptor Antagonists

## Candesartan

<b>Generic Name</b>	<b>Candesartan</b>
<b>Dosage form/strengths</b>	Tablets: 4mg, 8mg, 16 mg, 32mg And in combinations
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA06
<b>Indications</b>	<ul style="list-style-type: none"> <li>Heart failure with impaired left ventricular systolic function in conjunction with an ACE inhibitor or when ACE inhibitors are not tolerated</li> <li>Hypertension.</li> </ul>
<b>Dosage Regimen</b>	<p><b>Dosing: Adult Hypertension:</b> Initial and usual dose: 8mg. May need to increase by doubling dose in 4-week intervals up to 32mg.</p> <p><b>Heart failure with impaired left ventricular systolic function in conjunction with an ACE inhibitor or when ACE inhibitors are not tolerated:</b> Initial dose: 4mg. May need to increase by doubling dose in 2-week intervals up to 32mg.</p> <p><b>Dosing: Pediatric Hypertension</b> Child 6–17 years: Initially 4 mg once daily. May be adjusted up to 8mg in patients up to 50 kgs, or to 16 mg in patients over 50 kgs.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> CrCl &gt;30 mL/minute/1.73 m<sup>2</sup>: No dosage adjustment necessary. CrCl ≤30 mL/minute/1.73 m<sup>2</sup>: Start with a lower initial dose (eg. 4 mg once daily). Hemodialysis, intermittent (thrice weekly), Peritoneal dialysis: Not likely to be significantly dialyzed</p> <p><b>Dosing: Hepatic Impairment: Adult</b> Mild impairment: No initial dosage adjustment necessary. Moderate impairment: lower Initial dose. Severe impairment: Avoid in severe impairment or cholestasis. Candesartan has not been adequately studied in patients with severe hepatic insufficiency.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to candesartan or any component of the formulation</li> <li>Concomitant use with Aliskiren in patients with diabetes mellitus or with moderate to severe Kidney impairment.</li> <li>Pregnancy.</li> <li>Children &lt;1 year of age</li> <li>Rare hereditary problems of galactose intolerance, congenital lactase deficiency or glucose-galactose malabsorption.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Cardiovascular: Hypotension (19%) Renal: Renal function abnormality (13%)</p> <p><b>1% to 10%:</b></p>



	<p>Dizziness (4%), Hyperkalemia (6%), Back pain (3%), Upper respiratory tract infection (6%), pharyngitis (2%), rhinitis (2%)</p> <p><b>Frequency not defined:</b></p> <p>Central nervous system: Headache</p> <p>Renal: Exacerbation of renal disease (children and adolescents), increased serum creatinine.</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Kidney function</li> <li>• Serum potassium</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Sparsentan.</p> <p><b>Risk D: Consider therapy modification</b> Aliskiren, Amifostine Angiotensin-Converting Enzyme Inhibitors, Antihepaciviral Combination Products, Lithium, Obinutuzumab.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Contraindicated. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> No human data. Potential for adverse effects in breastfed infant.</p>
<b>Administration</b>	<p><b>Oral:</b> May be administered without regard to meals</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium-sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal function.</li> <li>• <b>Aortic/mitral stenosis:</b> As with other vasodilators, use caution in patients with aortic/mitral stenosis.</li> <li>• <b>Pediatric:</b> Avoid use in infants &lt;1 year of age due to potential effects on the development of immature kidneys.</li> <li>• <b>Race/Ethnicity:</b> In Black patients, the antihypertensive effect may be lower.</li> <li>• <b>Pregnancy:</b> Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with</li> </ul>

	<p>reduced fetal renal function and increased fetal and neonatal morbidity and death.</p> <ul style="list-style-type: none"> <li>• <b>Renal impairment:</b> Use with caution with preexisting renal insufficiency. Monitor closely.</li> <li>• <b>Hypoglycemic effect:</b> ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.</li> <li>• <b>Hypotension:</b> May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.</li> <li>• Avoid use in Severe hepatic impairment, biliary cirrhosis or cholestasis.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Irbesartan

<b>Generic Name</b>	<b>Irbesartan</b>
<b>Dosage form/strengths</b>	Tablets: 75mg, 150mg, 300mg Scored tablet: 300mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA04
<b>Indications</b>	<ul style="list-style-type: none"> <li>Hypertension</li> <li>Renal disease in hypertensive type 2 diabetes mellitus.</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Hypertension</b></p> <ul style="list-style-type: none"> <li>Adult 18-74 years: Initially 150 mg once daily, may be increased (after 2-4 weeks) if necessary to 300 mg once daily.</li> <li>Adult 75 years and over or patients receiving hemodialysis: Initially 75-150 mg once daily, may be increased (after 2-4 weeks) if necessary to 300 mg once daily.</li> </ul> <p><b>Renal disease in hypertensive type 2 diabetes mellitus</b></p> <ul style="list-style-type: none"> <li>Adult 18–74 years: Initially 150 mg once daily, increased if tolerated to 300 mg once daily.</li> <li>Adult 75 years and over or patients receiving hemodialysis: Initially 75–150 mg once daily, increased if tolerated to 300 mg once daily.</li> </ul> <p><b>Pediatric dosing:</b> Efficacy and safety in children has not been established.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> No dosage adjustment necessary for kidney dysfunction unless the patient is also volume-depleted. Volume depletion should be corrected before administration.</p> <p><b>Dosing: Hepatic Impairment: Adult</b> Mild to moderate hepatic disease: No dosage adjustment needed. Severe liver disease: Irbesartan has not been studied.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to Irbesartan or any component of the formulation</li> <li>Concomitant use with Aliskiren in patients with diabetes mellitus or with moderate to severe renal impairment</li> <li>Pregnancy</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Endocrine and metabolic: Hyperkalemia (diabetic nephropathy: 19%)</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Orthostatic hypotension (diabetic nephropathy: 5%) Gastrointestinal: Diarrhea (3%), dyspepsia (≤2%), heartburn (≤2%) Nervous system: Dizziness (diabetic nephropathy: 10%), fatigue (4%), orthostatic dizziness (diabetic nephropathy: 5%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Baseline and periodic BP</li> <li>Electrolytes</li> <li>Kidney function</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b> Aliskiren, Amifostine, Angiotensin-Converting Enzyme Inhibitors, Lithium, Obinutuzumab</p>

<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Contraindicated. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> No human data. Potential for serious adverse reactions in the breastfeeding infant.</p>
<b>Administration</b>	<p>Oral: May be administered without regard to food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal function.</li> <li>• <b>Aortic/mitral stenosis:</b> As with other vasodilators, use caution in patients with aortic/mitral stenosis.</li> <li>• <b>Race/Ethnicity:</b> In Black patients, the antihypertensive effect may be lower.</li> <li>• <b>Pregnancy:</b> Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.</li> <li>• <b>Renal impairment:</b> Use with caution with preexisting renal insufficiency. Monitor closely.</li> <li>• <b>Hypoglycemic effect:</b> ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.</li> <li>• <b>Hypotension:</b> May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Losartan

<b>Generic Name</b>	Losartan
<b>Dosage form/strengths</b>	Tablets: 25mg, 50mg, 100mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA01
<b>Indications</b>	<ul style="list-style-type: none"> <li>Chronic hypertension in adults and children <math>\geq 6</math> years of age.</li> <li>Treatment of diabetic nephropathy in type 2 diabetes mellitus.</li> <li>Treatment of chronic heart failure in adult patients (alternative agent).</li> </ul>
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b>  <b>Chronic hypertension, diabetic nephropathy in type 2 diabetes mellitus:</b>  <b>Oral:</b> Initial: 25 to 50 mg once daily; increase dose gradually according to blood pressure after several weeks if needed up to 100 mg/day in 1 to 2 divided doses. If additional blood pressure control is needed, consider combination therapy.  <b>Chronic heart failure:</b> Initial: 12.5 mg once daily. The dose is increased gradually weekly up to a maximum dose of 150 mg once daily.  <b>Dosing: elderly:</b>                      Start with lower dose (25 mg) in patients over 75 years.</p> <p><b>Dosing: Pediatric</b>  <b>Hypertension:</b>                      Children <math>\geq 6</math> years and Adolescents <math>\leq 16</math> years: Oral:  <math>\geq 20</math> kg to <math>&lt; 50</math> kg: Initial: 25 mg once daily; titrate to desired effect; maximum dose: 50 mg/day.  <math>\geq 50</math> kg: Initial: 50 mg once daily; titrate to desired effect; maximum dose: 100 mg/day.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b>  <b>Adult:</b> Mild to severe impairment and Hemodialysis: No dosage adjustment necessary.  <b>In pediatric</b>  <math>CrCl &lt; 30</math> mL/minute/<math>1.73</math> m<sup>2</sup>: Not recommended for use.  <b>Dosing: Hepatic Impairment:</b>                      Mild to severe hepatic impairment, or a history of hepatic impairment: Initial: 25 mg once daily.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to losartan or any component of the formulation;</li> <li>Concomitant use with Aliskiren in patients with diabetes mellitus or renal impairment.</li> <li>Pregnancy</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions:</b>  <b>1% to 10%:</b>                      Orthostatic hypotension, vertigo, dizziness, anemia, renal impairment, renal failure, asthenia, fatigue, increase in blood urea, serum creatinine, and serum potassium, hypoglycaemia</p>

<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Baseline and periodic BP</li> <li>• Electrolytes</li> <li>• Kidney function</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b> Aliskiren, Amifostine, Angiotensin-Converting Enzyme Inhibitors, Antihepaciviral Combination Products, Strong CYP3A4 Inducers, Lithium, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue losartan as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> No human data. Potential for serious adverse reactions in the breastfeeding infant. It is recommended to discontinue either breastfeeding or the drug.</p>
<b>Administration</b>	<p>Administer without regard to meals; however, administer consistently with regard to dietary intake at nearly the same time every day.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal function.</li> <li>• <b>Race/Ethnicity:</b> In Black patients, the antihypertensive effect may be lower.</li> <li>• <b>Aortic/mitral stenosis:</b> As with other vasodilators, use caution in patients with aortic/mitral stenosis.</li> <li>• <b>Pregnancy:</b> Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.</li> <li>• <b>Renal impairment:</b> Use with caution with preexisting renal insufficiency. Monitor closely.</li> <li>• <b>Hypoglycemic effect:</b> ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.</li> <li>• <b>Hypotension:</b> May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to</li> </ul>

	<p>administration.</p> <ul style="list-style-type: none"> <li>• Avoid use in patients with ascites; otherwise, monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>



## Olmesartan

<b>Generic Name</b>	<b>Olmesartan</b>
<b>Dosage form/strengths</b>	Tablets: 10 mg 20 mg 40 mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA08
<b>Indications</b>	<b>Hypertension, chronic:</b> Management of hypertension in adults and pediatric patients $\geq 6$ years of age.
<b>Dosage Regimen</b>	<b>Dosing: Adult Hypertension</b> Adult: Initially 10 mg daily, increased if necessary to 20 mg daily; maximum 40 mg per day <b>Dosing: Pediatric Hypertension</b> Child 6–18 years: Initially 10mg once daily. May be adjusted up to 20mg in patients up to 35 kgs, or to 40 mg in patients over 35 kgs.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> CrCl 20–60 mL/minute: Maximum 20 mg daily. CrCl less than 20 mL/minute: Avoid <b>Dosing: Hepatic Impairment: Adult</b> Mild impairment: No dosage adjustment necessary. Moderate: Caution. Maximum 20 mg daily. Severe: Avoid
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Concomitant use with Aliskiren in patients with diabetes mellitus and moderate to severe renal impairment.</li> <li>Hypersensitivity to Olmesartan or any component of the formulation</li> <li>Pregnancy.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>1% to 10%:</b> Hypertriglyceridemia, hyperuricaemia, dizziness, headache, bronchitis, pharyngitis, cough, rhinitis, gastroenteritis, diarrhoea, abdominal pain, nausea, dyspepsia, arthritis, back pain, skeletal pain, haematuria, urinary tract infection, pain, chest pain, peripheral oedema, influenza-like symptoms, fatigue, increased hepatic enzymes, blood urea increased, increased blood creatine phosphokinase.
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Blood pressure</li> <li>Kidney function</li> <li>Serum potassium</li> </ul>
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Bromperidol, Sparsentan <b>Risk D: Consider therapy modification</b> Aliskiren, Amifostine, Angiotensin-Converting Enzyme Inhibitors, Lithium, Obinutuzumab
<b>Pregnancy and Lactation</b>	<b>Pregnancy:</b> Contraindicated. Discontinue as soon as possible once pregnancy is detected. Risk of injury and death to fetus. <b>Lactation:</b> No human data. Potential for serious adverse reactions in the



	breastfeeding infant.
<b>Administration</b>	<p>Oral: May be administered with or without food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal function.</li> <li>• <b>Aortic/mitral stenosis:</b> As with other vasodilators, use caution in patients with aortic/mitral stenosis.</li> <li>• <b>Race/Ethnicity:</b> In Black patients, the antihypertensive effect may be lower.</li> <li>• <b>Pregnancy:</b> Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.</li> <li>• <b>Renal impairment:</b> Use with caution with preexisting renal insufficiency.</li> <li>• <b>Hypoglycemic effect:</b> ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.</li> <li>• <b>Hypotension:</b> May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.</li> <li>• Avoid use in Severe hepatic impairment, biliary cirrhosis or cholestasis.</li> <li>• <b>Pediatric:</b> Olmesartan has not been shown to be effective for hypertension in children &lt;6 years of age.</li> </ul>
<b>Storage</b>	<p>Store between 20°C to 25°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Sacubitril and Valsartan

<b>Generic Name</b>	Sacubitril and Valsartan
<b>Dosage form/strengths</b>	Tablets: <b>50mg</b> (Valsartan 25.7 mg + Sacubitril 24.3 mg ), <b>100mg</b> (Valsartan 51.4 mg + Sacubitril 48.6 mg), <b>200mg</b> (Valsartan 102.8 mg + Sacubitril 97.2 mg)
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Valsartan: Angiotensin II Receptor Blocker; Sacubitril: Neprilysin Inhibitor ATC: C09DX04
<b>Indications</b>	Symptomatic chronic heart failure with reduced ejection fraction  <b>N.B.</b> Sacubitril (a prodrug) inhibits the breakdown of natriuretic peptides which induces: increased diuresis, natriuresis, and vasodilation.
<b>Dosage Regimen</b>	<b>Dosing adult:</b> <i>In patients not currently on other agents (ACE inhibitor or angiotensin II receptor antagonist):</i> <ul style="list-style-type: none"> <li>- Initially 50 mg twice daily for 3–4 weeks, increased if tolerated by doubling with 3-4 weeks interval up to 200mg twice daily.</li> </ul> <i>In patients currently stabilized on other agents (ACE inhibitor or angiotensin II receptor antagonist):</i> <ul style="list-style-type: none"> <li>- Initially 100 mg twice daily for 3–4 weeks, increased if tolerated by doubling with 3-4 weeks interval up to 200mg twice daily.</li> <li>- In case of Systolic blood pressure less than 110 mmHg start with 50mg twice daily.</li> </ul>
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> <ul style="list-style-type: none"> <li>• Mild to moderate impairment: No dosage adjustments. Caution.</li> <li>• Severe impairment: Caution. Risk of hypotension. Start with 50mg twice daily.</li> <li>• Hemodialysis: Unlikely to be significantly dialyzed (valsartan and sacubitril are both highly protein bound).</li> <li>• CRRT, PIRRT: avoid use.</li> </ul> <b>Dosing: Hepatic Impairment: Adult</b> <ul style="list-style-type: none"> <li>• Mild impairment: No dosage adjustment.</li> <li>• Moderate impairment or if hepatic transaminases exceed 2 times the upper limit of normal: Caution. Initial: 50mg twice daily.</li> <li>• Severe impairment, biliary cirrhosis or cholestasis: Avoid (has not been studied).</li> </ul>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Concomitant use with an ACE inhibitor (do not initiate until at least 36 hours after discontinuing ACE inhibitor—risk of angioedema).</li> <li>• Concomitant use with an angiotensin II receptor antagonist.</li> <li>• History of angioedema related to previous ACE inhibitor or ARB (angiotensin receptor blocker) therapy.</li> <li>• Systolic blood pressure less than 100 mmHg.</li> <li>• Concomitant use of Aliskiren in patients with diabetes or renal disease.</li> <li>• Pregnancy; Lactation.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> <ul style="list-style-type: none"> <li>• Acute kidney injury</li> <li>• Angioedema: onset may occur at any time. Most reported cases are mild.</li> <li>• Hyperkalemia: less severe cases than with ARB alone. May occur within 1 week</li> </ul>

	<p>of use.</p> <ul style="list-style-type: none"> <li>Hypotension: rapid onset. Occurs at a higher rate than with angiotensin receptor blocker (ARB) therapy alone. Proactive reduction in diuretic dose or initiation at a lower dose may be required.</li> </ul> <p><b>&gt;10%:</b>                  Cardiovascular: Hypotension (18%)                  Endocrine and metabolic: Hyperkalemia (12%)                  Renal: Increased serum creatinine (17%)</p> <p><b>1% to 10%:</b>                  Cardiovascular: Orthostatic hypotension (2%)                  Hematologic and oncologic: Decreased hematocrit or hemoglobin (<math>\leq 7</math>)                  Hypersensitivity: Angioedema (Black patients: 2%; others: <math>&lt; 1\%</math>)                  Nervous system: Dizziness (6%), falling (2%)                  Renal: Acute kidney injury (<math>\leq 5\%</math>), renal failure syndrome (<math>\leq 5\%</math>)                  Respiratory: Cough (9%)</p> <p><b>Postmarketing:</b>                  Dermatologic: Pruritus, skin rash                  Hypersensitivity: Anaphylaxis</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Baseline and periodic BP</li> <li>Electrolytes</li> <li>Kidney function</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Angiotensin-Converting Enzyme Inhibitors, Bromperidol, Leniolisib, Sparsentan.</p> <p><b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Antihepaciviral Combination Products, Lithium, Obinutuzumab, Trofinetide.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Contraindicated. Toxicity with Sacubitril in animal studies. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> Not recommended due to the potential for serious adverse reactions.</p>
<b>Administration</b>	<p>Oral: Administer oral without regard to food.                  Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li><b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li><b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely. less severe cases than with ARB alone.</li> <li><b>Combination of ARBs and ACE inhibitors</b> is contraindicated.</li> <li>Patients should be closely monitored in case low systolic BP, low serum sodium, diabetes mellitus, and impaired kidney function.</li> <li><b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal</li> </ul>

function.

- **Aortic/mitral stenosis:** As with other vasodilators, use caution in patients with aortic/mitral stenosis.
- **Pregnancy:** Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.
- **Renal impairment:** Use with caution with preexisting renal insufficiency.
- **Hypoglycemic effect:** ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.
- **Hypotension:** May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.
- Avoid use in Severe hepatic impairment, biliary cirrhosis or cholestasis.

#### Storage

Store between 15°C to 30°C. Protect from moisture.  
N.B Refer to manufacturer PIL if there are specific considerations.

## Telmisartan

Generic name	Telmisartan
Dosage form/strengths	Telmisartan 40 , 80 mg tablets
Route of administration	Oral
Pharmacologic category	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA07
Indications	- Management of hypertension. -Prevention of cardiovascular events in atherosclerotic or diabetic nephropathy patients.
Dosage Regimen	<b>-Adults:</b> <b>-Hypertension:</b> Initially, 20-40 mg once daily in adults, increased if necessary after 4 weeks to 80mg.  <b>-Prevention of cardiovascular events in atherosclerotic or diabetic nephropathy patients</b> 80mg once daily or 40 mg once daily for 4 to 12 weeks, then increased to 80 mg once daily.
Dosage adjustment	<b>-Renal Impairment:</b> No dosage adjustment necessary. <b>-Hepatic Impairment:</b> -Initiate therapy with low dose (20 mg once daily); titrate slowly and monitor closely as Telmisartan is primarily eliminated by biliary excretion.
Contra-indications	- Hypersensitivity to Telmisartan or any component of the formulation - Biliary obstructive disorders, cholestasis - Concurrent use of aliskiren in patients with diabetes or renal impairment. - Pregnancy.
Adverse Drug Reactions	<b>-1% to 10%:</b> -Cardiovascular: Intermittent claudication (7%), chest pain ( $\geq 1\%$ ), hypertension ( $\geq 1\%$ ), peripheral edema ( $\geq 1\%$ ) -Central nervous system: Dizziness ( $\geq 1\%$ ), fatigue ( $\geq 1\%$ ), headache ( $\geq 1\%$ ), pain ( $\geq 1\%$ ) -Dermatologic: Dermal ulcer (3%) -Gastrointestinal: Diarrhea (3%), abdominal pain ( $\geq 1\%$ ), dyspepsia ( $\geq 1\%$ ), nausea ( $\geq 1\%$ ) -Genitourinary: Urinary tract infection ( $\geq 1\%$ ) -Neuromuscular and skeletal: Back pain (3%), myalgia ( $\geq 1\%$ ) -Respiratory: Upper respiratory tract infection (7%), sinusitis (3%), cough ( $\geq 1\%$ ), flu-like symptoms ( $\geq 1\%$ ), pharyngitis (1%)
Monitoring Parameters	-Blood pressure -Electrolytes - Kidney functions
Drug Interactions	<b>Risk X: Avoid combination</b> Bromperidol, Ramipril, Sparsentan <b>Risk D: Consider therapy modification</b> Aliskiren, Amifostine, Angiotensin-Converting Enzyme Inhibitors, Lithium, Obinutuzumab, Patiromer

<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> No human data. Potential for serious adverse reactions in the breastfeeding infant. It is recommended to discontinue either breastfeeding or the drug.</p>
<b>Administration</b>	<p><b>Oral:</b> May be administered without regard to meals N.B. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal function.</li> <li>• <b>Aortic/mitral stenosis:</b> As with other vasodilators, use caution in patients with aortic/mitral stenosis.</li> <li>• <b>Pregnancy:</b> Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.</li> <li>• <b>Renal impairment:</b> Use with caution with preexisting renal insufficiency.</li> <li>• <b>Hypoglycemic effect:</b> ARBs may enhance the hypoglycemic effects of antidiabetic agents by improving insulin sensitivity. Monitor blood glucose.</li> <li>• <b>Hypotension:</b> May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.</li> <li>• Avoid use in Severe hepatic impairment, biliary cirrhosis or cholestasis.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. N.B. Refer to manufacturer PIL if there are specific considerations.</p>



## Valsartan

<b>Generic Name</b>	Valsartan
<b>Dosage form/strengths</b>	Tablets 40mg, 80mg, 160mg, 320mg Capsules 80mg, 160mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin II Receptor Blocker; Antihypertensive ATC: C09CA03
<b>Indications</b>	<b>Heart failure</b> in adults. <b>Hypertension</b> in adults and pediatric patients $\geq 1$ year of age. <b>Post-myocardial infarction:</b> Reduction of cardiovascular mortality in patients with left ventricular dysfunction or failure following myocardial infarction (MI) in adults.
<b>Dosage Regimen</b>	<b>Dosing: Adult</b> <b>Heart failure (alternative agent):</b> <b>Oral:</b> Initial: 20 to 40 mg twice daily; increase dose after at least 2 weeks based on response and tolerability up to a 160 mg twice daily. <b>Hypertension, chronic:</b> <b>Oral:</b> Initial: 40 to 80 mg once daily; increase the dose if needed after 2 to 4 weeks up to a maximum of 320 mg once daily. If additional blood pressure control is needed, consider combination therapy. <b>left ventricular dysfunction or failure following myocardial infarction (MI):</b> <b>Oral:</b> Initial: 20 mg twice daily; may increase the dose as tolerated up to 160 mg twice daily under close monitoring to avoid hypotension. <b>Dosing: Pediatric</b> <b>Hypertension:</b> <b>Children and Adolescents 6 months to 16 years:</b> Oral: Initial: 1-2 mg/kg/dose once daily; maximum initial daily dose: 40 mg/day. Gradual increase if needed up to a maximum daily dose: 4 mg/kg/day not to exceed 160 mg/day. <b>Adolescents <math>\geq 17</math> years:</b> Oral: Initial: refer to adult dosing.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function:</b> CrCl $\geq 30$ mL/minute/1.73 m <sup>2</sup> : No dosage adjustment necessary. CrCl $< 30$ mL/minute/1.73 m <sup>2</sup> : Has not been studied; use with caution; monitor kidney function and potassium more closely. Dialysis: Not significantly removed. <b>Dosing: Hepatic Impairment:</b> Mild to moderate impairment: No initial dosage adjustment is necessary; use with caution. The maximum dose is 80mg. Severe impairment: Has not been studied; use with caution.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to valsartan or any component of the formulation;</li> <li>• Concomitant use with Aliskiren in patients with diabetes mellitus or renal impairment.</li> <li>• Biliary cirrhosis, cholestasis</li> <li>• Pregnancy, breastfeeding</li> </ul>
<b>Adverse Drug Reactions</b>	<b>&gt;10%:</b> Nervous system: Dizziness (17%; hypertension: 2% to 8%)

	<p>Renal: Increased blood urea nitrogen (&gt;50% increase: 17%)  <b>1% to 10%:</b>                  Cardiovascular: Hypotension (6% to 7%; hypertension: &lt;1%), orthostatic dizziness (2%), orthostatic hypotension (2%), syncope (&gt;1%; hypertension: &lt;1%)                  Endocrine and metabolic: Hyperkalemia (2%)                  Gastrointestinal: Abdominal pain (hypertension: 2%), diarrhea (5%), nausea (&gt;1%), upper abdominal pain (&gt;1%)                  Hematologic and oncologic: Neutropenia (2%)                  Infection: Viral infection (hypertension: 3%)                  Nervous system: Fatigue (3%; hypertension: 2%), headache (&gt;1%), vertigo (&gt;1%)                  Neuromuscular and skeletal: Arthralgia (3%), back pain (3%)                  Ophthalmic: Blurred vision (&gt;1%)                  Renal: Increased serum creatinine (4%), renal insufficiency (&gt;1%)                  Respiratory: Dry cough (hypertension: 3%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Baseline and periodic blood pressure</li> <li>• kidney functions.</li> <li>• Electrolyte panels</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Leniolisib, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Angiotensin-Converting Enzyme Inhibitors, Antihepaciviral Combination Products, Lithium, Obinutuzumab, Trofinetide.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> No human data. Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended.</p>
<b>Administration</b>	<p><b>Administration: Oral:</b> Administer with or without food.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• <b>Angioedema:</b> Angioedema has been reported rarely at any time during treatment with some angiotensin II receptor antagonists (ARBs). As angioedema results in obstruction of the airways, it is necessary to monitor the patient regularly, especially if the tongue, glottis, or larynx are involved. If angioedema develops, discontinue therapy immediately. An aggressive early management approach is essential. IM epinephrine may be necessary. ARBs should not be re-administered if angioedema occurred.</li> <li>• <b>Hyperkalemia:</b> May occur; risk factors include diabetes mellitus, renal dysfunction, concomitant use of potassium- sparing or supplements. Use cautiously, and monitor potassium closely.</li> <li>• <b>Combination of ARBs and ACE inhibitors</b> should be avoided, due to risk of dual blockade of the renin-angiotensin system. It is associated with higher risks of hypotension, hyperkalemia, and renal function disorders, including acute renal failure, compared to monotherapy. Closely monitor blood pressure, renal function, and electrolytes.</li> <li>• <b>Kidney function deterioration:</b> May be associated with deterioration of renal function, particularly in patients with renal artery stenosis or heart failure due to low renal blood flow. Small increases in serum creatinine may occur following initiation; Discontinue only with progressive or significant deterioration in renal</li> </ul>



function.

- **Aortic/mitral stenosis:** As with other vasodilators, use caution in patients with aortic/mitral stenosis.
- **Pregnancy:** Contraindicated. When used during the second and third trimesters, medications that affect the renin-angiotensin system have been associated with reduced fetal renal function and increased fetal and neonatal morbidity and death.
- **Renal impairment:** Use with caution with preexisting renal insufficiency.
- **Hypotension:** May occur early at initiation particularly in patients who are salt- or volume-depleted or concurrent diuretic; correct volume depletion prior to administration.
- **Ascites:** Generally, avoid use or monitor BP and kidney function carefully to avoid rapid development of kidney failure.

### Storage

Store between 15°C to 30°C. Protect from moisture.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Angiotensin-Converting Enzyme (ACE) Inhibitors

## Benazepril Hydrochloride

<b>Generic name</b>	<b>Benazepril Hydrochloride</b>
<b>Dosage form/strengths</b>	Tablets: 5mg, 10mg, 20mg, 40mg And in combinations
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin-Converting Enzyme (ACE) Inhibitor; Antihypertensive ATC: C09AA07
<b>Indications</b>	Management of chronic hypertension.
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b>  <b>Oral:</b> Initial: 10 mg once daily; evaluate response after 2 to 4 weeks and titrate dose (eg, increase the daily dose by doubling), as needed, up to 40 mg daily in 1 or 2 divided doses; if additional blood pressure control is needed, consider combination therapy.</p> <p><b>Dosing: Pediatric</b>                      Children <math>\geq 6</math> years and Adolescents:  <b>Oral:</b> Initial: 0.2 mg/kg/dose once daily as monotherapy.                      Maintenance: 0.1-0.6 mg/kg/dose once daily.                      Maximum initial dose: 10 mg/day; maximum daily dose: 40 mg/day</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b>                      CrCl <math>\geq 30</math> mL/minute/1.73m<sup>2</sup>: No dose adjustment necessary.                      CrCl <math>&lt; 30</math> mL/minute/1.73m<sup>2</sup>: Initial at lower dose 5 mg once daily. Pediatric use is not recommended.                      Hemodialysis: Use 25% to 50% of usual dose; No supplemental dose is necessary                      Peritoneal dialysis: Use 25% to 50% of usual dose; No supplemental dose is necessary</p> <p><b>Dosing: Hepatic Impairment: Adult</b>                      Use with caution, particularly in patients with ascites due to cirrhosis.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme inhibitors (ACE inhibitors) hypersensitivity</li> <li>• History of angioedema.</li> <li>• Concomitant use with Aliskiren in patients with diabetes mellitus or moderate to severe kidney impairment; coadministration with or within 36 hours of switching to or from a neprilysin inhibitor (eg, Sacubitril).</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant adverse Reactions:</b>                      Acute kidney injury                      Angioedema                      Cough                      Hyperkalemia  <b>1% to 10%:</b> Dizziness (4%), drowsiness (2%), headache (6%), orthostatic dizziness (2%)</p> <p><b>Frequency not defined:</b>                      Cardiovascular: Flushing, hypotension                      Dermatologic: Alopecia, diaphoresis, pemphigus, skin photosensitivity, Stevens-Johnson syndrome                      Endocrine and metabolic: Decreased libido                      Gastrointestinal: Constipation, gastritis, melena, nausea, vomiting                      Genitourinary: Impotence, urinary frequency, urinary tract infection                      Hematologic and oncologic: Hemolytic anemia, thrombocytopenia</p>

	Infection: Infection Nervous system: Anxiety, fatigue, hypertonia, insomnia, nervousness, paresthesia Neuromuscular and skeletal: Arthralgia, arthritis, asthenia, myalgia Respiratory: Asthma, bronchitis, cough, dyspnea, sinusitis
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Kidney functions</li> <li>• Serum potassium and sodium.</li> <li>• In case of patient has collagen vascular disease and/or kidney impairment, monitor CBC with differential</li> <li>• If angioedema is suspected, assess risk of airway obstruction</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Grass Pollen Allergen Extract, Sacubitril, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Angiotensin II Receptor Blockers, Lanthanum, Lithium, Obinutuzumab, Urapidil</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> Poor oral absorption. Considered acceptable for use in lactation unless high doses are required.</p>
<b>Administration</b>	Oral: May be administered without regard to food. Refer to manufacturer PIL if there are specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity reactions</li> <li>• Hypotension/syncope: close monitoring is needed. Although dose reduction may be needed, discontinuation is not necessary. Correct any volume depletion prior to initiation.</li> <li>• Caution when use in patients with ischemic heart disease, cerebrovascular disease, Collagen vascular disease or Kidney impairment.</li> <li>• Ascites: avoid use or monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> </ul> <p>In Black patients, the BP-lowering effects of ACE inhibitors may be less pronounced.</p> <ul style="list-style-type: none"> <li>• Diabetes: Use with caution, may be at increased risk for episodes of hypoglycemia.</li> <li>• Use with caution in patients with hypertrophic cardiomyopathy and left ventricular outflow tract obstruction, as reduction in afterload may worsen symptoms.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Protect from moisture. Refer to manufacturer PIL if there are specific considerations.

## Captopril

<b>Generic Name</b>	Captopril
<b>Dosage form/strengths</b>	Tablets: 25mg, 50mg Oral Solution: 5mg/5ml
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin-Converting Enzyme (ACE) Inhibitor; Antihypertensive ATC: C09AA01
<b>Indications</b>	<p><b>Acute coronary syndrome:</b> To improve survival following myocardial infarction (MI) in clinically stable patients.</p> <p><b>Treatment of heart failure with reduced ejection fraction.</b> Management of chronic hypertension.</p> <p><b>Proteinuric chronic kidney disease, diabetic:</b> Treatment of diabetic nephropathy (proteinuria &gt;500 mg/day) in patients with type 1 diabetes mellitus and retinopathy.</p>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Acute coronary syndrome:</b> <b>Oral:</b> Initial: 6.25-12.5mg 3 times daily; then gradually increase dose up to 50 mg 3 times daily as tolerated. Dose to be increased gradually at intervals of at least 2 weeks.</p> <p><b>Heart failure:</b> <b>Oral:</b> Initial: 6.25-12.5 mg 2 to 3 times daily; increase dose (eg, double) as tolerated every <math>\geq 1</math> to 2 weeks to a target dose of 50 mg 3 times daily.</p> <p><b>Hypertension, chronic:</b> <b>Oral:</b> Initial: 12.5 to 25 mg 2 times daily; then gradually increase dose up to 50 mg 3 times daily as tolerated. Dose to be increased gradually at intervals of at least 2 weeks; if additional BP control is needed, consider combination therapy.</p> <p><b>Proteinuric chronic kidney disease (in diabetic patients):</b> <b>Oral:</b> Initial: 25 mg 3 times daily; titrate dose as tolerated to achieve the desired BP response and a proteinuria goal of &lt;1 g/day.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> Reduce initial daily dose and titrate more gradually.</p> <p>CrCl 20–40 mL/minute: Initial dose not to exceed 25 mg daily, maintenance not exceed 100 mg daily.</p> <p>CrCl 10–20 mL/minute: Initial dose not to exceed 12.5 mg daily, maintenance not exceed 75 mg daily.</p> <p>CrCl less than 10 mL/minute: Initial dose not to exceed 6.25 mg daily, maintenance not exceed 37.5mg daily.</p> <p>Intermittent hemodialysis: Taken after hemodialysis on dialysis days</p> <p><b>Dosing: Hepatic Impairment: Adult</b> No dosage adjustments are recommended for captopril in hepatic impairment.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme inhibitors (ACE inhibitors) hypersensitivity.</li> <li>• History of angioedema.</li> <li>• Concomitant use with Aliskiren in patients with diabetes mellitus or moderate to severe kidney impairment; coadministration with or within 36 hours of switching to or from a neprilysin inhibitor (eg, Sacubitril).</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant adverse Reactions:</b> Acute kidney injury</p>

	<p>Angioedema Cough Hyperkalemia <b>1% to 10%:</b> Cardiovascular: Chest pain (1%), palpitations (1%), tachycardia (1%) Dermatologic: Alopecia (<math>\leq 2\%</math>), pruritus (2%), skin rash (4% to 7%) Gastrointestinal: Abdominal pain (<math>\leq 2\%</math>), ageusia (<math>\leq 4\%</math>), anorexia (<math>\leq 2\%</math>), aphthous stomatitis (<math>\leq 2\%</math>), constipation (<math>\leq 2\%</math>), diarrhea (<math>\leq 2\%</math>), dysgeusia (<math>\leq 4\%</math>; diminished taste perception), gastric irritation (<math>\leq 2\%</math>), nausea (<math>\leq 2\%</math>), peptic ulcer (<math>\leq 2\%</math>), vomiting (<math>\leq 2\%</math>), xerostomia (<math>\leq 2\%</math>) Genitourinary: Proteinuria (<math>\leq 1\%</math>) Hematologic and oncologic: Neutropenia (1%-4%) Nervous system: Dizziness (<math>\leq 2\%</math>), fatigue (<math>\leq 2\%</math>), headache (<math>\leq 2\%</math>), insomnia (<math>\leq 2\%</math>), malaise (<math>\leq 2\%</math>), paresthesia (<math>\leq 2\%</math>) Respiratory: Cough (<math>\leq 2\%</math>), dyspnea (<math>\leq 2\%</math>)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Kidney functions</li> <li>• Electrolytes (serum potassium, serum sodium)</li> <li>• CBC with differential during the first 3 months of therapy and periodically thereafter in patients with kidney impairment and/or collagen vascular disease</li> <li>• Assess risk of airway obstruction in case of angioedema is suspected</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Sacubitril, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b> Aliskiren, Antifungal Agents (Azole Derivatives, Systemic), Amifostine, Angiotensin II Receptor Blockers, Carbamazepine, Grass Pollen Allergen Extract, Lanthanum, Lithium, Obinutuzumab, Urapidil, Fosphenytoin, Macrolide Antibiotics, Phenytoin, Rifamycin Derivatives, Simvastatin</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> Avoid in first few weeks after delivery. May use for older infants with caution.</p>
<b>Administration</b>	<p><b>Oral:</b> Administer on an empty stomach. Preparation of aqueous solution for oral administration: mix prior to administration and use within 10 minutes. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Cholestatic jaundice: A rare toxicity; discontinue if marked elevation of hepatic transaminases or jaundice occurs.</li> <li>• Hypersensitivity reactions.</li> <li>• Hypotension/syncope: Close monitoring is needed. Although dose reduction may be needed, discontinuation is not necessary. Correct any volume depletion prior to initiation.</li> <li>• Caution when use in patients with ischemic heart disease, cerebrovascular disease, Collagen vascular disease or Kidney impairment.</li> <li>• Ascites: Avoid use or monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> </ul> <p>In Black patients, the BP-lowering effects of ACE inhibitors may be less pronounced.</p> <ul style="list-style-type: none"> <li>• Proteinuria: In most cases, proteinuria subsided or cleared within 6 months (whether or not captopril was continued).</li> </ul>

### Storage

Store between 15°C to 30°C; protect from moisture.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Enalapril

<b>Generic Name</b>	Enalapril
<b>Dosage form/strengths</b>	Tablets: 5mg, 10mg, 20mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin-Converting Enzyme (ACE) Inhibitor; Antihypertensive ATC: C09AA02
<b>Indications</b>	Heart failure Hypertension.
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Heart failure:</b> <b>Oral:</b> Initial: 2.5 mg twice daily; increase dose as tolerated to a target dose of 10 to 20 mg twice daily over 2-4 weeks.</p> <p><b>Hypertension, chronic:</b> <b>Oral:</b> Initial: 5 to 10 mg once daily; titrate dose if needed after 2-4 weeks up to 40 mg/day in 1 or 2 divided doses; if additional blood pressure control is needed, consider combination therapy.</p> <p><b>Dosing: Pediatric</b></p> <p><b>Note:</b> Use lower listed initial dose in patients with hyponatremia, hypovolemia, severe CHF, decreased renal function, or in those receiving diuretics.</p> <p><b>Hypertension:</b> Children under 12 years and over 20 KGs weight: <b>Oral:</b> Initial: 0.1 mg/kg once daily increased to 1mg/kg in 1-2 divided doses according to response with close monitoring. Children 12-17 years: : Initially 2.5 mg once daily, monitor blood pressure carefully for 1–2 hours, maintenance 10–20 mg daily in 1–2 divided doses</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> CrCl &gt;30 mL/minute: No dose adjustment necessary. CrCl 10 to 30 mL/minute: Initial dose: 2.5 mg once daily; Maximum recommended dose: 20 mg/day. CrCl &lt;10 mL/minute: Consider alternative therapy; risk of adverse effects or complications (eg, hyperkalemia, kidney failure). Initial: 2.5 mg every other day; Maximum recommended dose: 10 mg/day.</p> <p><b>Dosing: Hepatic Impairment: Adult</b> No dose adjustment necessary. Use with caution, particularly in patients with ascites due to cirrhosis.</p> <p><b>Dosing: Altered Kidney Function: Pediatric</b> Use in infants, children, and adolescents ≤16 years of age with GFR &lt;30 mL/minute/1.73 m<sup>2</sup> is not recommended; no dosing recommendations available.</p> <p><b>Dosing: Hepatic Impairment: Pediatric</b> No dosage adjustment necessary. Use with caution.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme inhibitors (ACE inhibitors) hypersensitivity.</li> <li>• History of angioedema.</li> </ul>



	<ul style="list-style-type: none"> <li>Concomitant use with aliskiren in patients with diabetes mellitus or moderate to severe kidney impairment; coadministration with or within 36 hours of switching to or from a neprilysin inhibitor (eg, Sacubitril).</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant adverse Reactions</b></p> <p>Acute kidney injury                  Angioedema                  Cough                  Hyperkalemia</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Hypotension (<math>\leq 7\%</math>), orthostatic hypotension (2%), syncope (<math>\leq 2\%</math>)                  Dermatologic: Skin rash (1%)                  Gastrointestinal: Diarrhea (2%), nausea (1%), vomiting (1%)                  Nervous system: Dizziness (8%), headache (2%), orthostatic dizziness (1%- 2%), vertigo (2%)                  Neuromuscular and skeletal: Asthenia (1% to 2%)                  Respiratory: Bronchitis (1%), cough (1% to 2%), dyspnea (1%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Blood pressure</li> <li>Kidney functions</li> <li>Serum potassium, Serum sodium</li> <li>CBC with differential during the first 3 months of therapy and periodically thereafter in patients with kidney impairment and/or collagen vascular disease</li> <li>Assess risk of airway obstruction in case of angioedema is suspected</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Sacubitril, Grass Pollen Allergen Extract</p> <p><b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Angiotensin II Receptor Blockers, Lanthanum, Lithium, Obinutuzumab, Urapidil</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> Avoid in first few weeks after delivery, may use in older infants with caution.</p>
<b>Administration</b>	<p><b>Administration: Oral:</b> Administer without regard to meals.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>Hypersensitivity reactions may occur</li> <li>Hypotension/syncope: close monitoring is needed. Although dose reduction may be needed, discontinuation is not necessary. Correct any volume depletion prior to initiation.</li> <li>Caution when use in patients with: Aortic stenosis, may reduce coronary perfusion resulting in ischemia.</li> <li>Avoid use in patients with ascites or monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> <li>Caution when use in patients with ischemic heart disease, cerebrovascular disease, Collagen vascular disease or Kidney impairment. Avoid rapid dose escalation.</li> <li>In Black patients, the BP-lowering effects of ACE inhibitors may be less</li> </ul>

	pronounced.
<b>Storage</b>	Store between 15°C to 30°C. Protect from moisture. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Lisinopril

<b>Generic Name</b>	Lisinopril
<b>Dosage form/strengths</b>	Tablets 5mg,10mg,20mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin-Converting Enzyme (ACE) Inhibitor; Antihypertensive ATC: C09AA03
<b>Indications</b>	<b>Heart failure with reduced ejection fraction:</b> Adjunctive therapy. <b>Chronic hypertension:</b> in adult and pediatric patients $\geq 6$ years of age. <b>ST-elevation myocardial infarction:</b> Treatment of acute MI within 24 hours in hemodynamically stable patients to improve survival.
<b>Dosage Regimen</b>	<b>Heart failure with reduced ejection fraction:</b> <b>Oral:</b> Initial: 2.5 to 5 mg once daily; increase dose as tolerated every $\geq 1$ to 2 weeks to a target dose of 20 to 40 mg once daily. <b>Chronic Hypertension:</b> <b>Oral:</b> Initial: 5 to 10 mg once daily; evaluate response after $\sim 2$ to 4 weeks and titrate dose as needed, up to 40 mg once daily; if additional blood pressure control is needed, consider combination therapy. <b>ST-elevation myocardial infarction:</b> <b>Oral:</b> Initial: 2.5 to 5 mg once daily initiated within 24 hours of presentation; titrate slowly up to 10 mg/day or higher as tolerated under close monitoring to avoid hypotension; maximum: 40 mg/day.
<b>Dosage adjustment</b>	<b>Dosing: Renal Impairment: Adult</b> CrCl $\geq 30$ mL/minute: No dosage adjustment necessary. CrCl 10 to $< 30$ mL/minute: Reduce initial recommended dose by 50% for adults (i.e., 5 mg once daily for hypertension, 2.5 mg PO once daily for heart failure and acute myocardial infarction). Max: 40 mg/day; titrate slowly. CrCl $< 10$ mL/minute: Consider alternative therapy; risk of adverse effects or complications (eg, hyperkalemia, kidney failure) is increased. If necessary, begin 2.5 mg once daily; titrate slowly. <b>Dosing: Hepatic Impairment: Adult</b> There are no dosage adjustments available. use with caution.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme inhibitors (ACE inhibitors) hypersensitivity</li> <li>• History of angioedema.</li> <li>• Concomitant use with Aliskiren in patients with diabetes mellitus or moderate to severe kidney impairment; coadministration with or within 36 hours of switching to or from a neprilysin inhibitor (eg, Sacubitril).</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant adverse Reactions:</b> Acute kidney injury Angioedema Cough Hyperkalemia <b>&gt;10%:</b> Cardiovascular: Hypotension (up to 11%)

	<p>Nervous system: Dizziness (up to 19%)  <b>1% to 10%:</b>                  Cardiovascular: Flushing, orthostatic hypotension, syncope, vasculitis                  Dermatologic: Alopecia, diaphoresis, erythema of skin, skin rash, pruritus, skin photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria                  Endocrine and metabolic: Hyperkalemia, diabetes mellitus, gout                  Gastrointestinal: Constipation, diarrhea, dysgeusia, flatulence, pancreatitis, xerostomia                  Genitourinary: Impotence                  Hematologic and oncologic: Bone marrow depression, leukocytosis, leukopenia, eosinophilia, hemolytic anemia, increased erythrocyte sedimentation rate, neutropenia, positive ANA titer, pseudolymphoma (cutaneous), thrombocytopenia                  Nervous system: Altered sense of smell, fatigue, paresthesia, vertigo                  Neuromuscular and skeletal: Arthralgia, arthritis, asthenia, myalgia                  Ophthalmic: Blurred vision, diplopia, photophobia, vision loss                  Otic: Tinnitus                  Renal: Increased blood urea nitrogen, increased serum creatinine, renal insufficiency                  Respiratory: Cough                  Miscellaneous: Fever</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Kidney function</li> <li>• Serum potassium, Serum Sodium</li> <li>• CBC with differential, in case of patient has collagen vascular disease and/or kidney impairment</li> <li>• If angioedema is suspected, assess risk of airway obstruction</li> <li>• Monitor for jaundice or signs of hepatic failure</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Sacubitril, Grass Pollen Allergen Extract, Sparsentan  <b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Angiotensin II Receptor Blockers, Lanthanum, Lithium, Obinutuzumab, Urapidil</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue losartan as soon as possible. Risk of injury and death to fetus.  <b>Lactation:</b> Avoid. Due to the potential for serious adverse reactions in the breastfed infant, it is recommended a decision be made whether to discontinue breastfeeding or to discontinue Lisinopril.</p>
<b>Administration</b>	<p><b>Administration: Oral</b>                  Administer as a single daily dose and without regard to meals.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hematologic effects: Patients with kidney impairment are at high risk of developing neutropenia.</li> <li>• Hypersensitivity reactions: Anaphylactic/anaphylactoid reactions can occur with angiotensin-converting enzyme (ACE) inhibitors.</li> <li>• Hypotension/syncope: close monitoring is needed. Although dose reduction may be needed, discontinuation is not necessary. Correct any volume depletion prior to initiation.</li> </ul>

	<ul style="list-style-type: none"> <li>• Caution when use in patients with: Aortic stenosis, may reduce coronary perfusion resulting in ischemia.</li> <li>• Avoid use in patients with ascites or monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> <li>• Caution when use in patients with ischemic heart disease, cerebrovascular disease, Collagen vascular disease, Hepatic impairment or Kidney impairment. Avoid rapid dose escalation.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from moisture.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Perindopril

<b>Generic Name</b>	Perindopril
<b>Dosage form/strengths</b>	Tablets Perindopril arginine preparations: 5mg, 10mg Perindopril erbumine preparations (Perindopril tert- butylamine): 2mg, 4mg, 8mg And in combinations
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Angiotensin-Converting Enzyme (ACE) Inhibitor; Antihypertensive ATC: C09AA04
<b>Indications</b>	<b>Hypertension, chronic:</b> Management of hypertension. <b>Stable coronary artery disease:</b> To reduce the risk of cardiovascular mortality or nonfatal myocardial infarction in patients with stable coronary artery disease.
<b>Dosage Regimen</b>	<b>Hypertension, chronic:</b> <b>Oral:</b> <ul style="list-style-type: none"> <li>- <i>Perindopril arginine:</i> Initial: 5 mg once daily daily (2.5mg in elderly or in combination with diuretic); may increase after 4 weeks to 10 mg once daily.</li> <li>- <i>Perindopril erbumine:</i> Initial: 4 mg once daily (2mg in elderly or in combination with diuretic); evaluate response after ~2 to 4 weeks and may increase dose up to 8 mg once daily; if additional blood pressure control is needed, consider combination therapy.</li> </ul> <b>Stable coronary artery disease:</b> <b>Oral:</b> <ul style="list-style-type: none"> <li>- <i>Perindopril arginine:</i> Initial: 5 mg (2.5mg in elderly) once daily for 2 weeks; then increase as tolerated to 10 mg once daily.</li> <li>- <i>Perindopril erbumine:</i> Initial: 4 mg (2mg in elderly) once daily for 2 weeks; then increase as tolerated to 8 mg once daily.</li> </ul>
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> <b>Altered kidney function: Oral:</b> <i>Perindopril erbumine:</i> CrCl >80 mL/minute: No dose adjustment necessary. CrCl ≥30 to ≤80 mL/minute: Initial: 2 mg/day; maximum maintenance dose: 8 mg/day. CrCl <30 mL/minute: Use is not recommended; however, an initial dose of 2 mg every 48 hours may be considered; cautious titration based on tolerability and response, not to exceed 4 mg/day. <i>Perindopril arginine:</i> CrCl ≥60 mL/minute: No dosage adjustment necessary. CrCl 30 to 60 mL/minute: Initial: 2.5 mg/day. CrCl 15 to 30 mL/minute: Initial: 2.5 mg every other day. <b>Hemodialysis, intermittent (thrice weekly):</b> Dialyzable <b>Oral:</b> <i>Perindopril erbumine:</i> Initial: 2 mg 3 times per week after dialysis on dialysis days; titrate cautiously based on tolerability and response, not to exceed 4 mg/day. <i>Perindopril arginine:</i> Initial: 2.5 mg on dialysis days (given after dialysis). <b>Peritoneal dialysis:</b> Use generally not recommended (has not been studied) <b>Dosing: Hepatic Impairment: Adult</b> Dosage adjustment is not required in patients with compensated hepatic

	cirrhosis. Adjust dosage based on clinical response. Severe hepatic disease has not been adequately studied. Use caution.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme inhibitors (ACE inhibitors) hypersensitivity.</li> <li>• History of angioedema.</li> <li>• Concomitant use with aliskiren in patients with diabetes mellitus or moderate to severe kidney impairment; coadministration with or within 36 hours of switching to or from a neprilysin inhibitor (eg, Sacubitril).</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant adverse Reactions:</b></p> <p>Acute kidney injury                  Angioedema                  Cough                  Hyperkalemia</p> <p><b>&gt;10%:</b></p> <p>Central nervous system: Headache (24%)                  Respiratory: Cough (12%; incidence higher in women, 3:1)</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Edema, chest pain, ECG abnormality, palpitations                  Central nervous system: Hypertonia, sleep disorder, depression, paresthesia, drowsiness, nervousness                  Dermatologic: Skin rash                  Endocrine and metabolic: Increased serum triglycerides, menstrual disease                  Gastrointestinal: Diarrhea, abdominal pain, dyspepsia, nausea, vomiting, flatulence                  Genitourinary: Urinary tract infection, proteinuria, sexual disorder                  Hepatic: Increased serum ALT                  Hypersensitivity: Seasonal allergy                  Infection: Viral infection                  Neuromuscular and skeletal: Weakness, back pain, leg pain, arm pain, arthralgia, arthritis, myalgia, neck pain                  Otic: Tinnitus, otic infection                  Respiratory: Upper respiratory tract infection, sinusitis, rhinitis, pharyngitis                  Miscellaneous: Fever</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Kidney function</li> <li>• Serum potassium, serum sodium</li> <li>• Monitor CBC with differential periodically, if patient has collagen vascular disease and/or kidney impairment</li> <li>• If angioedema is suspected, assess risk of airway obstruction</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Grass Pollen Allergen Extract, Sacubitril, Sparsentan</p> <p><b>Risk D: Consider therapy modification</b>                  Aliskiren, Amifostine, Angiotensin II Receptor Blockers, Lanthanum, Lithium, Obinutuzumab, Urapidil</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid. When pregnancy is detected, discontinue as soon as possible. Risk of injury and death to fetus.</p> <p><b>Lactation:</b> Due to the potential for adverse reactions in the breastfed infant, consider using another agent particularly when high doses are needed.</p>
<b>Administration</b>	Oral: Administer orally once or twice daily without regard to meals. In clinical studies, administration in 2 divided doses was only slightly more effective than once-daily



	dosing. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Angioedema: Rare cases. At any time during treatment (especially following first dose).</li> <li>• Cough: A dry, nonproductive cough that usually occurs within the first few months of treatment. Generally, resolve within a month after discontinuation of the ACE inhibitor. Exclude other causes of cough prior to discontinuation.</li> <li>• Hyperkalemia: Risk factors include diabetes mellitus, renal impairment or concomitant use of potassium-sparing or potassium supplements products. Caution. Monitor potassium closely.</li> <li>• Hypersensitivity reactions: Anaphylactic reactions can occur with ACE inhibitors.</li> <li>• Cholestatic jaundice: A rare toxicity associated; discontinue if marked elevation of hepatic transaminases or jaundice occurs.</li> <li>• Hypotension/syncope: close monitoring is needed. Although dose reduction may be needed, discontinuation is not necessary. Correct any volume depletion prior to initiation.</li> <li>• Renal function deterioration: May be associated with transient elevation of renal function and/or increases in BUN and serum creatinine. Consider discontinuation only in patients with progressive and/or significant deterioration in renal function.</li> <li>• Caution when use in patients with: Aortic stenosis, may reduce coronary perfusion resulting in ischemia.</li> <li>• Avoid use in patients with ascites or monitor BP and kidney function carefully to avoid rapid development of kidney failure.</li> <li>• Caution when use in patients with ischemic heart disease, cerebrovascular disease, Collagen vascular disease, Hepatic impairment or Kidney impairment.</li> <li>• Renal artery stenosis: Use with caution. If unstented unilateral or bilateral, use is generally avoided due to the elevated risk of deterioration in renal function unless possible benefits outweigh risks.</li> </ul> Special populations: <ul style="list-style-type: none"> <li>• Pregnancy: Drugs that act on the renin-angiotensin system can cause injury and death to the developing fetus. Discontinue as soon as possible once pregnancy is detected.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Protect from moisture. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.



## Antianginal, Cardioprotective agents

## Trimetazidine

<b>Generic Name</b>	Trimetazidine
<b>Dosage form/strengths</b>	Tablets: 20mg Modified Release Tablets: 35 mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Cardio protective Anti-ischemic agent ATC: C01EB15
<b>Indications</b>	<ul style="list-style-type: none"> <li>Prevent angina attacks as an add-on to existing treatments in patients who are not adequately controlled by or intolerant to other medicines for angina pectoris.</li> </ul>
<b>Dosage Regimen</b>	Immediate release tablet: Initial and maximum dose: 20 mg 3 times daily Modified release tablet: Initial and maximum dose: 35 mg twice daily
<b>Dosage Adjustment</b>	<p><b>Renal impairment functions:</b></p> <p>CrCl 30-60 mL/minute: Immediate release tablet: Initial and maximum dose: 20 mg twice daily Modified release tablet: Initial and maximum dose: 35 mg once daily (preferably in the morning)</p> <p>CrCl &lt;30 mL/minute: Use is contraindicated</p> <p><b>Elderly patients</b> older than 75 years old: Dose should be reduced.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to component of the formulation.</li> <li>Parkinson disease or and other related movement disorders</li> <li>Severe reduced kidney function (creatinine clearance &lt; 30ml/min)..</li> </ul>
<b>Adverse Drug Reactions</b>	Nausea and vomiting. Very rarely: Reversible parkinsonian symptoms after stopping treatment.
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Kidney disease.</li> <li>Symptoms of Parkinson.</li> </ul>
<b>Drug Interactions</b>	No available data.
<b>Pregnancy and Lactation</b>	No data, so not recommended to use during pregnancy and lactation.
<b>Administration</b>	Oral: at mealtime. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>Trimetazidine should be discontinued permanently in patients who develop movement disorders such as Parkinsonian symptoms. If Parkinsonian symptoms persist for more than four months after discontinuation, a neurologist's opinion</li> </ul>

	should be sought.
<b>Storage</b>	<p>Store between 15<sup>o</sup> C to 30<sup>o</sup> C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Antianginal, Vasodilators

## Isosorbide dinitrate

<b>Generic Name</b>	Isosorbide dinitrate
<b>Dosage form/strengths</b>	Sublingual Tablet 5mg, 10mg Capsules: 20mg, 40mg Tablet 5mg, 10mg, Tablet 20mg, 40mg (in combination) Sustained Release Capsule 20 mg, 40mg Lentocaps 40mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antianginal Agent; Vasodilator ATC: C01DA08
<b>Indications</b>	Prevention of angina pectoris due to coronary artery disease.
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b>  <b>Angina pectoris, prevention:</b>  <b>Note:</b> For prevention of recurrent angina, may use in combination with other anti-anginal therapy (eg, beta-blocker).  <b>Oral:</b>                      Immediate release: Initial: 5 to 20 mg 2 to 3 times daily; maintenance dose: 10 to 40 mg 2 to 3 times daily; allow for a 14-hour nitrate-free period after the evening dose and before the morning dose to minimize risk of tolerance.                      Sustained release:  <ul style="list-style-type: none"> <li>20 mg: Initial: 20 mg twice daily; may increase to 20 mg 3 times daily (ensure at least a 12-hour nitrate-free interval to minimize the risk of tolerance).</li> <li>40 mg tablets/capsules: 40 to 160 mg/day; once daily dosing allows for an 18-hour nitrate-free period to minimize the risk of tolerance; maximum dose: 160 mg/day.</li> </ul> <b>Sublingual:</b> 5 to 10 mg every 2 to 4 hours; consider supplementing with 5 to 10 mg prior to activities that may provoke angina.</p> <p>The safety and effectiveness of isosorbide dinitrate in children have not been established.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b>                      No dose adjustments are needed.</p> <p><b>Dosing: Hepatic Impairment: Adult</b>                      Specific dosage adjustments in hepatic impairment are not available; however, because isosorbide dinitrate plasma concentrations are elevated in patients with cirrhosis, cautious use of isosorbide dinitrate in this population may be prudent.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to Isosorbide dinitrate or any component of the formulation</li> <li>Concurrent use with phosphodiesterase inhibitors (Sildenafil, Tadalafil, Vardenafil, or Avanafil)</li> <li>Severe anemia</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Frequency not defined.</b>                      Cardiovascular: Hypotension, rebound hypertension, syncope, unstable angina pectoris                      Central nervous system: Headache</p>

<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Phosphodiesterase 5 Inhibitors, Riociguat</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> FDA pregnancy risk category C. Animal studies have shown no hazard at doses approximating usual human dosage. Human data are limited. Safety in pregnancy however, has not been established.</p> <p><b>Lactation:</b> It is not known whether isosorbide dinitrate or its metabolites are excreted in human milk. Caution should be exercised when isosorbide dinitrate is administered to a woman who is breast-feeding.</p>
<b>Administration</b>	<p><b>Administration: Oral</b></p> <p>Do not administer around the clock to prevent tolerance to nitrate effect; allow nitrate-free interval <math>\geq 14</math> hours (immediate-release products) and <math>&gt;12</math> to 18 hours (sustained-release products). Do not chew or crush sublingual tablets or sustained-release formulations.</p> <p><b>Immediate release products:</b> For twice daily dosing, consider administering at 8 AM and 1 PM. For 3 times daily dosing, consider 8 AM, 1 PM, and 6 PM.</p> <p><b>Sustained-release products:</b></p> <ul style="list-style-type: none"> <li>• 20 mg tablets: For twice daily dosing, the second dose should be administered 6 to 8 hours after the first dose of the day.</li> <li>• 40 mg tablets/capsules: Consider once daily in morning or twice-daily dosing at 8 AM and between 1 PM and 2 PM.</li> </ul> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hypotension/bradycardia</li> <li>• Intracranial pressure increased</li> <li>• Cardiovascular disease: Not recommended in patients with acute MI or HF (cannot easily reverse effects if adverse events develop).</li> <li>• Hypertrophic cardiomyopathy (HCM)</li> <li>• Tolerance: Appropriate dosing intervals are needed to minimize tolerance development.</li> </ul>
<b>Storage</b>	<p>Oral: Store between 15°C to 30°C. Protect from light.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Isosorbide Mononitrate

<b>Generic Name</b>	Isosorbide Mononitrate
<b>Dosage form/strengths</b>	Tablets 20mg, 40mg, 60mg Capsule 25mg, 50mg Retard Film Coated Tablet: 100mg Modified release capsule: 50mg, 60mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antianginal Agent; Vasodilator ATC: C01DA14
<b>Indications</b>	<b>Angina pectoris, prevention:</b> Treatment (immediate-release only) and prevention of angina pectoris caused by coronary artery disease. <b>Note:</b> The onset of action of oral isosorbide mononitrate is not sufficiently rapid for this product to be useful in aborting an acute anginal episode.
<b>Dosage Regimen</b>	<b>Dosing: Adult</b> <b>Angina pectoris:</b> <b>Immediate release:</b> 20 mg twice daily with the 2 doses given 7 hours apart (eg, 8 AM and 3 PM) to decrease tolerance development. According to some international product labels, dosages up to 40 mg 2 to 3 times daily may be considered; however, twice daily administration is generally required to prevent nitrate tolerance and provide sustained benefit. <b>Note:</b> Tolerance to nitrate effects develops with chronic exposure. Tolerance can only be overcome by short periods of nitrate absence from the body. Recommended twice daily dosage regimens incorporate this interval. Short periods of nitrate withdrawal may help minimize tolerance. <b>Extended release:</b> Oral: Initial: 25 to 60 mg once daily in the morning; may titrate after several days to 120 mg once daily; rarely, 240 mg once daily may be required.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> No dose adjustment necessary. <b>Dosing: Hepatic Impairment: Adult</b> No dose adjustment necessary.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Isosorbide dinitrate or any component of the formulation</li> <li>• Concurrent use with phosphodiesterase inhibitors (Sildenafil, Tadalafil, Vardenafil, or Avanafil)</li> <li>• Severe anemia</li> </ul>
<b>Adverse Drug Reactions</b>	<b>&gt;10%:</b> Central nervous system: Headache ( $\leq 57\%$ ), dizziness ( $\leq 11\%$ ) <b>1% to 10%:</b> Cardiovascular: Abnormal heart sounds ( $\leq 5\%$ ), atrial arrhythmia ( $\leq 5\%$ ), atrial fibrillation ( $\leq 5\%$ ), bradycardia ( $\leq 5\%$ ), bundle branch block ( $\leq 5\%$ ), cardiac arrhythmia ( $\leq 5\%$ ), cardiac failure ( $\leq 5\%$ ), chest pain ( $\leq 5\%$ ), ECG abnormality (Q wave: $\leq 5\%$ ), edema ( $\leq 5\%$ ), exacerbation of angina pectoris ( $\leq 5\%$ ), extrasystoles ( $\leq 5\%$ ), flushing ( $\leq 5\%$ ), heart murmur ( $\leq 5\%$ ), hypertension ( $\leq 5\%$ ), hypotension ( $\leq 5\%$ ), intermittent claudication ( $\leq 5\%$ ), myocardial infarction ( $\leq 5\%$ ), palpitations ( $\leq 5\%$ ), tachycardia ( $\leq 5\%$ ), varicose veins ( $\leq 5\%$ ), ventricular tachycardia ( $\leq 5\%$ ), cardiovascular toxicity (2%)

	<p>Central nervous system: Anxiety (<math>\leq 5\%</math>), confusion (<math>\leq 5\%</math>), depression (<math>\leq 5\%</math>), drowsiness (<math>\leq 5\%</math>), fatigue (<math>\leq 5\%</math>), hypoesthesia (<math>\leq 5\%</math>), insomnia (<math>\leq 5\%</math>), lack of concentration (<math>\leq 5\%</math>), malaise (<math>\leq 5\%</math>), migraine (<math>\leq 5\%</math>), myasthenia (<math>\leq 5\%</math>), nervousness (<math>\leq 5\%</math>), neuritis (<math>\leq 5\%</math>), nightmares (<math>\leq 5\%</math>), paresis (<math>\leq 5\%</math>), paresthesia (<math>\leq 5\%</math>), rigors (<math>\leq 5\%</math>), vertigo (<math>\leq 5\%</math>), pain (4%), emotional lability (2%)</p> <p>Dermatologic: Abnormal hair texture (<math>\leq 5\%</math>), acne vulgaris (<math>\leq 5\%</math>), diaphoresis (<math>\leq 5\%</math>), leg ulcer (<math>\leq 5\%</math>), pruritus (<math>\leq 5\%</math>), skin rash (<math>\leq 5\%</math>)</p> <p>Endocrine and metabolic: Decreased libido (<math>\leq 5\%</math>), hot flash (<math>\leq 5\%</math>), hyperuricemia (<math>\leq 5\%</math>), hypokalemia (<math>\leq 5\%</math>)</p> <p>Gastrointestinal: Abdominal pain (<math>\leq 5\%</math>), constipation (<math>\leq 5\%</math>), diarrhea (<math>\leq 5\%</math>), dyspepsia (<math>\leq 5\%</math>), flatulence (<math>\leq 5\%</math>), gastric ulcer (<math>\leq 5\%</math>), gastric ulcer with hemorrhage (<math>\leq 5\%</math>), gastritis (<math>\leq 5\%</math>), glossitis (<math>\leq 5\%</math>), hemorrhoids (<math>\leq 5\%</math>), loose stools (<math>\leq 5\%</math>), melena (<math>\leq 5\%</math>), nausea (<math>\leq 5\%</math>), vomiting (<math>\leq 5\%</math>), xerostomia (<math>\leq 5\%</math>)</p> <p>Genitourinary: Atrophic vaginitis (<math>\leq 5\%</math>), impotence (<math>\leq 5\%</math>), mastalgia (<math>\leq 5\%</math>), urinary tract infection (<math>\leq 5\%</math>)</p> <p>Hematologic and oncologic: Hypochromic anemia (<math>\leq 5\%</math>), nonthrombocytopenic purpura (<math>\leq 5\%</math>), thrombocytopenia (<math>\leq 5\%</math>)</p> <p>Hepatic: Increased serum alanine aminotransferase (<math>\leq 5\%</math>), increased serum aspartate aminotransferase (<math>\leq 5\%</math>)</p> <p>Hypersensitivity: Hypersensitivity reaction (2%)</p> <p>Infection: Bacterial infection (<math>\leq 5\%</math>), candidiasis (<math>\leq 5\%</math>), viral infection (<math>\leq 5\%</math>)</p> <p>Neuromuscular and skeletal: Arthralgia (<math>\leq 5\%</math>), asthenia (<math>\leq 5\%</math>), back pain (<math>\leq 5\%</math>), musculoskeletal pain (<math>\leq 5\%</math>), myalgia (<math>\leq 5\%</math>), myositis (<math>\leq 5\%</math>), shoulder stiffness (frozen shoulder: <math>\leq 5\%</math>), tendinopathy (<math>\leq 5\%</math>), torticollis (<math>\leq 5\%</math>), tremor (<math>\leq 5\%</math>)</p> <p>Ophthalmic: Blepharoptosis (<math>\leq 5\%</math>), conjunctivitis (<math>\leq 5\%</math>), photophobia (<math>\leq 5\%</math>), visual disturbance (<math>\leq 5\%</math>)</p> <p>Otic: Otagia (<math>\leq 5\%</math>), perforated tympanic membrane (<math>\leq 5\%</math>), tinnitus (<math>\leq 5\%</math>)</p> <p>Renal: Nephrolithiasis (<math>\leq 5\%</math>), polyuria (<math>\leq 5\%</math>)</p> <p>Respiratory: Bronchitis (<math>\leq 5\%</math>), bronchospasm (<math>\leq 5\%</math>), cough (<math>\leq 5\%</math>), dyspnea (<math>\leq 5\%</math>), flu-like symptoms (<math>\leq 5\%</math>), increased bronchial secretions (<math>\leq 5\%</math>), nasal congestion (<math>\leq 5\%</math>), pharyngitis (<math>\leq 5\%</math>), pneumonia (<math>\leq 5\%</math>), pulmonary infiltrates (<math>\leq 5\%</math>), rales (<math>\leq 5\%</math>), rhinitis (<math>\leq 5\%</math>), sinusitis (<math>\leq 5\%</math>), upper respiratory infection (1% to 4%), increased cough (2%)</p> <p>Miscellaneous: Fever (<math>\leq 5\%</math>), nodule (<math>\leq 5\%</math>)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Blood pressure</li> <li>Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Sildenafil, Tadalafil, Vardenafil, Avanafil, Riociguat</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Adverse events have been observed in some animal reproduction studies.</p> <p><b>Lactation:</b> No human data. Caution should be exercised when administering Isosorbide mononitrate to nursing women.</p>
<b>Administration</b>	<p><b>Administration: Oral</b></p> <p>Do not administer around-the-clock. Immediate release tablet should be scheduled twice daily with doses 7 hours apart.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>CNS depression: May cause CNS depression, which may impair physical or mental</li> </ul>



- abilities.
- Hypotension/bradycardia: Severe hypotension can occur; paradoxical bradycardia and increased angina pectoris can accompany hypotension. Orthostatic hypotension can also occur.
  - Intracranial pressure maybe increased
  - Cardiovascular disease: Not recommended for use in patients with acute myocardial infarction (MI) or heart failure (has not been studied). Use with caution in volume depletion and moderate hypotension, and with extreme caution with inferior wall MI and suspected right ventricular infarctions.
  - Hypertrophic cardiomyopathy with left ventricular outflow tract obstruction: Avoid use.
  - Phosphodiesterase -5 inhibitors: Avoid concurrent use with Sildenafil, Tadalafil, Vardenafil.
  - Appropriate use: Extended-release: Not intended for the immediate relief of acute attacks of angina pectoris.
  - Tolerance: Appropriate dosing intervals are needed to minimize tolerance development. Tolerance can only be overcome by short periods of nitrate absence from the body. Dose escalation does not overcome this effect.

**Storage**

Store between 15°C to 30°C. Protect from moisture.  
**N.B.** Refer to manufacturer PIL for specific considerations.

## Nicorandil

<b>Generic Name</b>	Nicorandil
<b>Dosage form/strengths</b>	Tablets: 10mg, 20mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antianginal Agent; Vasodilator, Potassium-channel openers ATC: C01DX16
<b>Indications</b>	Prophylaxis and treatment of stable angina (second-line)
<b>Dosage Regimen</b>	<b>Adult dosing:</b> <b>Prophylaxis and treatment of stable angina (second-line)</b> Oral: usual dose 10–20 mg twice daily Initially 5–10 mg twice daily, then increased if necessary and tolerated up to 40 mg twice daily. Not recommended for pediatric patients.
<b>Dosage Adjustment</b>	No dose adjustments required in liver or renal impairment
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypovolaemia or severe hypotension</li> <li>• Shock (including cardiogenic shock)</li> <li>• Acute pulmonary oedema</li> <li>• Left ventricular dysfunction with low filling pressure or cardiac decompensation</li> <li>• Hypersensitivity reactions to any component of the formulation.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> Nicorandil may cause serious ulcers at skin, mucosa, and eye; including GIT ulcers, which may progress to perforation, hemorrhage, fistula or abscess. Discontinue treatment if ulceration occurs and consider an alternative agent. <b>&gt;1%: Common or very common</b> Asthenia, dizziness, haemorrhage, headache (transient, at initiation), nausea, vomiting
<b>Monitoring Parameters</b>	cardiac function, Blood pressure
<b>Drug Interactions</b>	<b>Risk X avoid combination:</b> Aspirin, Corticosteroids, NSAIDs, phosphodiesterase type-5 inhibitors (eg. Sildenafil, Vardenafil, Tadalafil). <b>Risk D consider modify therapy</b> Hypotensive agents, Dapoxetine
<b>Pregnancy and Lactation</b>	<b>Pregnancy:</b> No data available. Use only if potential benefit outweighs risk. <b>Lactation:</b> No data available. Not recommended.
<b>Administration</b>	Oral: Without regard to food intake. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• May affect performance of driving or operating machinery.</li> <li>• Diverticular disease (risk of fistula formation or bowel perforation).</li> <li>• G6PD deficiency patients: Caution as may cause methemoglobinemia.</li> <li>• Heart failure: Caution in patients with heart failure.</li> </ul>

	<ul style="list-style-type: none"><li>Hyperkalaemia: Severe cases have been reported. Caution with potassium increasing medicines especially in moderate to severe kidney impairment.</li></ul>
<b>Storage</b>	Protect from moisture. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Nitroglycerin (Glyceryl Trinitrate)

<b>Generic Name</b>	Nitroglycerin (Glyceryl Trinitrate)
<b>Dosage form/strengths</b>	Sustained Release Capsules: 2.5mg, 6.5mg, 9mg Transdermal Therapeutic System: 5mg, 10mg Oral Spray: 0.4mg /dose Transdermal Patch: 22.4 mg, 44.8 mg, 18.7 mg, 37.4 mg Lyophilized Powder: 25mg, 50mg/10ml, Solution for I.V Infusion: 50mg/50ml Rectal Ointment: 400 mg/100gm
<b>Route of administration</b>	IV, Oral, Transdermal, topical
<b>Pharmacologic category</b>	Antianginal Agent; Antidote, Extravasation; Vasodilator ATC: Topical, local: C05AE01, other routes: C01DA02
<b>Indications</b>	<b>Oral administration:</b> Treatment or prevention of angina pectoris. <b>IV administration:</b> <ul style="list-style-type: none"> <li>• Treatment of angina pectoris</li> <li>• Acute decompensated heart failure</li> <li>• Perioperative hypertension</li> <li>• Induction of intraoperative hypotension.</li> </ul> <b>Rectal administration (ointment):</b> Treatment of moderate to severe pain associated with chronic anal fissure.
<b>Dosage Regimen</b>	<b>Dosing: Adult</b> <b>Acute decompensated heart failure (adjunctive therapy):</b> <i>Continuous IV infusion:</i> Initial: 5 to 10 mcg/minute; titrate as needed based on response and tolerability in increments of 5 to 10 mcg/minute every 3 to 5 minutes up to a maximum of 200 mcg/minute. <b>Acute angina:</b> <i>Sustained release capsule, oral:</i> Initial: 2.5 to 6.5 mg 3 to 4 times daily; increase dose as needed based on response and tolerability to 26 mg 4 times daily. Include a nitrate-free interval of ~10 to 12 hours each day to minimize the risk of tolerance. <i>Continuous IV infusion:</i> Initial: 5 to 10 mcg/minute with continuous cardiac monitoring; titrate as needed to relieve angina symptoms in increments of 5 mcg/minute every 5 to 10 minutes up to 20 mcg/minute; if angina persists at a dose of 20 mcg/minute, may increase by 10 to 20 mcg/minute every 3 to 5 minutes to a maximum dose of 400 mcg/minute. Tachyphylaxis develops within 24 to 48 hours of continuous nitrate administration. <b>Prevention of angina:</b> Topical patch, transdermal: one patch (5 or 10mg) to be applied to lateral chest wall, upper arm, tight abdomen, thigh or shoulder. Increase to two 10 patch if necessary to be replaced every 24 hours. <b>Hypertension, perioperative (alternative agent):</b> <b>Continuous IV infusion:</b> Initial: 5 to 10 mcg/minute; increase based on BP response and tolerability in increments of 5 mcg/minute every 3 to 5 minutes up to 20 mcg/minute; if no response at a dose of 20 mcg/minute, may increase by 10 to 20 mcg/minute every 3 to 5 minutes to a maximum dose of 200 mcg/minute. Lower

	<p>doses primarily produce venous dilation; however, arterial vasodilation may occur at high doses. Tachyphylaxis develops within 24 to 48 hours of continuous nitrate administration; if vasodilator requirements continue longer than 24 to 48 hours, transition to an alternative IV or oral vasodilator.</p> <p><b>Dosing: Pediatric</b>  <b>Heart failure; cardiogenic shock</b>  <i>Infants and Children:</i> Continuous IV infusion: Initial: 0.25 to 0.5 mcg/kg/minute; titrate by 1 mcg/kg/minute every 15 to 20 minutes as needed; faster titration may be necessary in some patients; in adolescents, titration every 3 to 5 minutes has been suggested; usual dose range: 1 to 5 mcg/kg/minute; usual maximum dose: 10 mcg/kg/minute  <i>Adolescents:</i> Continuous IV infusion: Initial: 5 to 10 mcg/minute; titrate every 3 to 5 minutes as needed to maximum rate of 200 mcg/minute</p>
<b>Dosage adjustment</b>	No dose adjustment required for renal or hepatic patients
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Nitrate hypersensitivity</li> <li>• Acute myocardial infarction, cardiomyopathy</li> <li>• Constrictive pericarditis</li> <li>• Increased intracranial pressure</li> <li>• Shock</li> <li>• Severe anemia</li> <li>• Acute circulatory failure or shock</li> <li>• Concurrent use with phosphodiesterase-5 (PDE-5) inhibitors (Avanafil, Sildenafil, Tadalafil, or Vardenafil)</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Nervous system: Headache (patch, ointment: 50% to 64%; sublingual powder, lingual spray: &gt;2%)</p> <p><b>1% to 10%:</b>                      Cardiovascular: Hypotension (<math>\leq 4\%</math>), peripheral edema (lingual spray: <math>\leq 2\%</math>), syncope (<math>\leq 4\%</math>)                      Gastrointestinal: Abdominal pain (lingual spray: <math>\leq 2\%</math>)                      Nervous system: Dizziness (&gt;2% to 6%), paresthesia (&gt;2%)                      Neuromuscular and skeletal: Asthenia (all sublingual forms: <math>\leq 2\%</math>)                      Respiratory: Dyspnea (<math>\leq 2\%</math>), pharyngitis (lingual spray: <math>\leq 2\%</math>), rhinitis (lingual spray: <math>\leq 2\%</math>)</p>
<b>Monitoring Parameters</b>	Blood pressure, heart rate; consult individual institutional policies and procedures
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                      Bromperidol, Avanafil, Sildenafil, Tadalafil, Vardenafil, Riociguat</p> <p><b>Risk D: Consider therapy modification</b>                      Amifostine, Ergot Derivatives, Apomorphine, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Insufficient data regarding the use of nitroglycerin during pregnancy to determine a drug-associated risk of major birth defects or miscarriage. Nitroglycerin should be given to a pregnant woman only if clearly needed.</p> <p><b>Lactation:</b> No human data. The decision to continue or discontinue breastfeeding during therapy should take into account the benefit and risk ratio.</p>

<b>Administration</b>	<p><b>Administration: Oral</b> ER capsule: Swallow whole. Do not chew, break, or crush. Administer with a full glass of water.</p> <p><b>Administration: Topical</b> Rectal ointment: Using a finger covering (eg, plastic wrap, surgical glove, finger cot), place finger beside 1 inch measuring guide on the box and squeeze ointment the length of the measuring line directly onto covered finger. Topical patch, transdermal: Application site should be clean, dry, and hair free. Rotate patch sites. Dispose of any used or unused patches by folding adhesive ends together, replace in pouch or sealed container and discard properly in trash, away from children and pets.</p> <p><b>Parenteral:</b> Continuous IV infusion: Vials (concentrated solution): Not for direct injection; must be diluted prior to administration. Administer via infusion pump. Adsorption to soft plastic (eg, PVC) occurs; special administration sets intended for nitroglycerin (nonpolyvinyl chloride) must be used; some inline IV filters also adsorb nitroglycerin; use of these filters should be avoided.</p> <p><b>Preparation for Administration:</b> Vial (concentrated solution): Dilute in D<sub>5</sub>W or NS to a maximum concentration of 400 mcg/mL; prepare in glass bottles, EXCEL or PAB containers (adsorption to soft plastic [eg, PVC] occurs).</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Headache: Dose-related headaches may occur, especially during initial dosing.</li> <li>• Hypotension/bradycardia: Severe hypotension and shock may occur (even with small doses); paradoxical bradycardia and increased angina pectoris may accompany hypotension. Orthostatic hypotension may also occur; ethanol may accentuate this. Use with caution in volume depletion, preexisting hypotension, constrictive pericarditis, aortic or mitral stenosis, and extreme caution with inferior wall myocardial infarction (MI) and suspected right ventricular involvement.</li> <li>• Increased intracranial pressure: Use is contraindicated in patients with increased intracranial pressure.</li> </ul> <p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Hypertrophic cardiomyopathy with left ventricular outflow tract obstruction: Avoid use in patients with hypertrophic cardiomyopathy with left ventricular outflow tract obstruction; nitrates may reduce preload, exacerbating obstruction and cause hypotension or syncope and/or worsening of heart failure.</li> </ul> <p><b>Dosage form specific issues:</b></p> <ul style="list-style-type: none"> <li>• Rectal ointment: Use caution when treating rectal anal fissures with nitroglycerin in patients with suspected or known significant cardiovascular disorders (eg, cardiomyopathies, HF, acute MI); intra-anal nitroglycerin administration may decrease systolic BP and decrease arterial vascular resistance.</li> <li>• Long-acting agents: Avoid use of long-acting agents in acute MI or acute HF; cannot easily reverse effects if adverse events develop.</li> <li>• Transdermal patches: May contain conducting metal (eg, aluminum); remove patch prior to magnetic resonance imaging.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Tolerance: May occur; cross tolerance to other nitro compounds have been reported. Appropriate dosing is needed to minimize tolerance development.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Protect from moisture.

Nitroglycerin diluted in D<sub>5</sub>W or NS in glass containers is physically and chemically stable for 48 hours at room temperature and for 7 days in refrigerator. In D<sub>5</sub>W or NS in EXCEL/PAB containers, it is physically and chemically stable for 24 hours at room temperature.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Antiarrhythmic Agents



## Amiodarone

<b>Generic Name</b>	Amiodarone
<b>Dosage form/strengths</b>	Tablet: 100mg, 200mg
<b>Route of administration</b>	IV, Oral
<b>Pharmacologic category</b>	Antiarrhythmic Agent, Class III ATC: C01BD01
<b>Indications</b>	Management of arrhythmias particularly when other agents are ineffective or contraindicated
<b>Dosage Regimen</b>	<p><b>-Adult Dosing:</b></p> <p><b>Arrhythmias:</b></p> <p>-Oral: 200 mg 3 times a day for 1 week, reduced to twice daily for the second week, then a maintenance dose of 200-400 mg daily.</p> <p>-IV: initially 5mg/kg over 20-120 minutes then subsequent infusions as required. Maximum dose 1.2 gm/day.</p>
<b>Dosage adjustment</b>	<p><b>-Renal Impairment:</b></p> <p>No dosage adjustment necessary. Hemodialysis, Peritoneal dialysis: Not dialyzable; supplemental dose is not necessary</p> <p><b>-Hepatic Impairment:</b></p> <p>Dosage adjustment is probably necessary in substantial hepatic impairment. If hepatic enzymes exceed 3 times normal or double in a patient with an elevated baseline, consider decreasing the dose or discontinuing amiodarone.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>-Hypersensitivity to amiodarone, iodine, or any component of the formulation</li> <li>-Sick sinus syndrome</li> <li>-Second- or third-degree atrioventricular block</li> <li>-Bradycardia leading to syncope without a functioning pacemaker</li> <li>-Cardiogenic shock</li> <li>- Thyroid dysfunction</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions:</b></p> <p><b>Hepatotoxicity:</b> Severe, acute hepatotoxicity has been associated with IV administration. Chronic toxicity may take the form of micronodular hepatic cirrhosis, hepatic fibrosis, or (less commonly) cholestasis. Hepatotoxicity may be irreversible in some cases</p> <p><b>Bradycardia/hypotension</b></p> <p><b>Proarrhythmic effects</b></p> <p><b>Pulmonary toxicity</b></p> <p><b>Thyroid effects</b></p> <p><b>&gt;10%:</b></p> <p>Cardiovascular: Hypotension (refractory in rare cases) Gastrointestinal: Nausea, vomiting (oral: &gt;10%; IV: &lt;2%) Ophthalmic: Epithelial keratopathy (98% to 99%) Respiratory: Pulmonary toxicity (including hypersensitivity pneumonitis and interstitial/alveolar pneumonitis: ≤17%)</p> <p><b>1% to 10%:</b></p>

	<p>Cardiovascular: Bradycardia (2% to 4%), cardiac arrhythmia, cardiac failure (IV, oral), edema, exacerbation of cardiac arrhythmia (2% to 5%), flushing, prolonged QT interval on ECG (associated with worsening arrhythmia), shock (IV: &lt;2%), sinus node dysfunction, torsades de pointes (IV: &lt;2%), ventricular fibrillation (IV: &lt;2%)</p> <p>Dermatologic: Skin photosensitivity, solar dermatitis, Stevens-Johnson syndrome (&lt;2%)</p> <p>Endocrine and metabolic: Decreased libido, hyperthyroidism (2%), hypothyroidism</p> <p>Gastrointestinal: Abdominal pain, altered salivation, anorexia, constipation, diarrhea (IV: &lt;2%), dysgeusia</p> <p>Hematologic and oncologic: Disorder of hemostatic components of blood</p> <p>Hepatic: Abnormal hepatic function tests (IV, oral), hepatic disease</p> <p>Nervous system: Abnormal gait, altered sense of smell, ataxia, dizziness, fatigue, headache, insomnia, involuntary body movements, malaise, paresthesia, sleep disorder</p> <p>Neuromuscular and skeletal: Tremor</p> <p>Ophthalmic: Blurred vision, visual disturbance, visual halos around lights</p> <p>Renal: Renal insufficiency (IV: &lt;2%)</p> <p>Respiratory: Acute respiratory distress syndrome (IV, oral: ≤2%; incidence may be higher in patients following anesthesia with high FiO<sub>2</sub> exposure), pulmonary fibrosis</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>-Blood pressure</li> <li>-Heart rate (ECG) and rhythm throughout therapy</li> <li>-Assessment for signs of lethargy, edema of the hands or feet, weight loss</li> <li>-Pulmonary toxicity (baseline pulmonary function tests and chest X-ray; continue monitoring chest X-ray annually during therapy)</li> <li>-Liver function tests (semiannually)</li> <li>-Serum electrolytes, especially potassium and magnesium.</li> <li>-Thyroid function tests before initiation of treatment and then periodically thereafter (every 3 to 6 months)</li> <li>-Regular ophthalmic exams</li> <li>-Pacing or defibrillation thresholds with initiation of amiodarone and during treatment in patients with implantable cardiac devices</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Abametapir, Agalsidase Alfa, Aminolevulinic Acid, Atazanavir, Bilastine, Cimetidine, Citalopram, Clarithromycin, Conivaptan, Daclatasvir, Domperidone, Doxorubicin (Conventional), Entrectinib, Erythromycin, Fexinidazole, Fingolimod, Flupentixol, Fusidic Acid (Systemic), Gemifloxacin, Grapefruit Juice, Idelalisib, Indinavir, Lefamulin, Levofloxacin, Levoketoconazole, Lofepamine, Lopinavir, Moxifloxacin, Nelfinavir, Nilotinib, Pazopanib, Pimozide, Piperaquine, Posaconazole, Probuco, Propafenone, Quetiapine, Ribociclib, Rimegepant, Ritonavir, Saquinavir, Sertindole, Sirolimus (Protein Bound), Sodium Iodide, Sparfloxacin, Thioridazine, Tipranavir, Topotecan, Vincristine (Liposomal), Voriconazole</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Afatinib, Agalsidase Beta, Amifostine, Amisulpride (Oral), Azithromycin, Berotralstat, Bile Acid Sequestrants, Bromperidol, Carbetocin, Cardiac Glycosides, Ceritinib, Chloroquine, Clofazimine, Clomipramine, Clozapine, Colchicine, CYP3A4 Inhibitors (Strong), Dabrafenib, Dasatinib, Doxepin, Droperidol, Encorafenib, Escitalopram, Etelcalcetide, Flecainide, Fluorouracil, Gadobenate Dimeglumine, Gilteritinib, Halofantrine, Haloperidol, Imipramine, Inotuzumab Ozogamicin, Lemborexant, Lofexidine, Lomitapide, Lonafarnib, Loratadine, Lovastatin, Meglumine Antimoniate,</p>

	<p>Methadone, Midostaurin, Mifepristone, Mitotane , Obinutuzumab, Olanzapine, Ondansetron, Osimertinib, Pentamidine, Pilsicainide, Ponesimod, Propafenone, QT-Prolonging Class IA Antiarrhythmics, QT-Prolonging Class III Antiarrhythmics, QT-Prolonging Inhalational Anesthetics, QT-Prolonging Kinase Inhibitors, QT-prolonging Miscellaneous Agents, QT-prolonging Moderate CYP3A4 Inhibitors, Quizartinib, Rimegepant, Relugolix, Risperidone, Simvastatin, Siponimod, Sirolimus, Sofosbuvir, Sunitinib, Talazoparib, Terbutaline, Toremfene, Ubrogapant, Vemurafenib, Venetoclax, Vitamin K Antagonists</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy</b> Possible risk of neonatal goitre; use only if no alternative.  <b>Lactation:</b> Avoid; present in milk in significant amounts; theoretical risk of neonatal hypothyroidism from release of iodine</p>
<b>Administration</b>	<p><b>Administration: Oral</b>                  Administer consistently with regard to meals. Take in divided doses with meals if GI upset occurs. If GI intolerance occurs with single-dose therapy, use twice daily dosing.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Amiodarone is intended for use only in patients with indicated life-threatening arrhythmias because its use is accompanied by substantial toxicity.</li> <li>• Amiodarone can cause pulmonary toxicity (hypersensitivity pneumonitis or interstitial/alveolar pneumonitis) that has resulted in clinically manifest disease at rates as high as 17% in some series of patients.</li> <li>• Amiodarone can cause hepatotoxicity, which can be fatal. Obtain baseline and periodic liver transaminases and discontinue or reduce dose if the increase exceeds 3 times normal or doubles in a patient with an elevated baseline. Discontinue amiodarone if the patient experiences signs or symptoms of clinical liver injury.</li> <li>• Amiodarone can exacerbate arrhythmias. Initiate amiodarone in a clinical setting where continuous ECGs and cardiac resuscitation are available.                      Extravasation: May be a vesicant; ensure proper needle or catheter placement prior to infusion. Avoid extravasation.</li> <li>• Ocular effects: Regular ophthalmic examination is recommended. May cause optic neuropathy and/or optic neuritis resulting in visual impairment at any time during therapy; permanent blindness has occurred. Corneal refractive laser surgery is generally contraindicated in amiodarone users (from manufacturers of surgical devices).</li> <li>• Photosensitivity: Avoid excessive exposure to sunlight; may cause photosensitivity. May be related to cumulative dose and duration of therapy.</li> <li>• Cardiac devices (eg, implanted defibrillators, pacemakers): Chronic administration of antiarrhythmic drugs may affect defibrillation or pacing thresholds. Assess when initiating amiodarone and during therapy.</li> <li>• Electrolyte imbalance: Correct electrolyte disturbances, especially hypokalemia, hypomagnesemia, or hypocalcemia, prior to use and throughout therapy.</li> <li>• Myocardial infarction: In the setting of acute myocardial infarction (MI), beta-blocker therapy should be initiated even though concomitant amiodarone therapy provides beta-blockade.</li> <li>• Wolff-Parkinson-White (WPW) syndrome: Amiodarone should not be used in patients with WPW syndrome and preexcited atrial fibrillation/flutter since ventricular fibrillation may result.</li> <li>• Discontinuation of therapy: Patients may still be at risk for amiodarone-related</li> </ul>

	adverse reactions or drug interactions after the drug has been discontinued.
<b>Storage</b>	Store between 15°C to 30°C; protect from light. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Lidocaine

<b>Generic Name</b>	Lidocaine
<b>Dosage form/strengths</b>	Solution for injection: 50mg Or 20mg or 10 mg/ml (1%), 40mg or 20mg or 20 mg/ml or 1 gm/50ml (2%) Solution for I.M Injection 20mg (1%), 50mg (1%) Solution for S.C injection: 34.610 mg/2ml, Solution for I.M or S.C injection: 20mg Solution for IM, IV and SC injection: 1gm, 400mg Solution for I.M or slow I.V Injection 20mg/ml Oral gel: 0.330 gm/100g Oral spray: 10gm/100gm (10%) Lozenges: 8 mg Topical Ointment: 50mg/1gm, 5 gm/100g Topical Spray: 10%, 40 mg/ml, 10gm, 10mg Topical Gel: 2 %, 4%, 5% 0.05gm Topical Patch: 700 mg/Patch Topical Cream: 0.02gm, 4%, 5% topical aerosol powder spray 10gm And in combinations.
<b>Route of administration</b>	<i>IM, IV, SC, Topical, oral</i>
<b>Pharmacologic category</b>	Systemic: Antiarrhythmic Agent, Class Ib; Local Anesthetic Topical: Analgesic, Topical; Local Anesthetic ATC: parentral antiarrhythmic C01BB01 ATC: Local for hemorrhoids C05AD01 ATC: Local for anesthetics D04AB01, N01BB02 ATC: Throat preparations R02AD02
<b>Indications</b>	<p><b>Systemic:</b> Ventricular Arrhythmias that occur following acute myocardial infarction MI or during cardiac manipulative procedures such as cardiac surgery.</p> <p><b>Local:</b> <b>Topical:</b> Relief of local pain. <b>Oral:</b> Topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract. <b>Note:</b> Not approved for relief of teething pain and discomfort in infants and children; serious adverse effects have been reported</p>
<b>Dosage Regimen</b>	<p><b>Systemic:</b> <b>Adult dosing:</b> <b>Ventricular tachycardia, hemodynamically stable:</b> IV: 1 to 1.5 mg/kg; repeat with 0.5 to 0.75 mg/kg every 5 to 10 minutes as necessary (maximum cumulative dose: 3 mg/kg). Follow with continuous infusion of 1 to 4 mg/minute or 20 to 50 mcg/kg/minute. <b>Note:</b> For prolonged infusion (after 24 hours), reduce the rate of infusion by approximately one-half to compensate for the reduced elimination rate. Administer under constant ECG monitoring.</p>

	<p><b>Anesthesia, local injection:</b> Varies with procedure, degree of anesthesia needed, vascularity of tissue, duration of anesthesia required, and physical condition of patient.</p> <p><i>Cutaneous infiltration:</i> Maximum: 4.5 mg/kg/dose not to exceed 300 mg; do not repeat within 2 hours.</p> <p><b>Pediatric dosing:</b></p> <p><b>Ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), shock-refractory:</b> Infants, Children, and Adolescents:</p> <p>IV: Initial:</p> <p>Loading dose: 1 mg/kg/dose; follow with continuous IV infusion; may administer second bolus if delay between initial bolus and start of infusion is &gt;15 minutes. Continuous IV infusion: 20 to 50 mcg/kg/minute. Do not exceed 20 mcg/kg/minute in patients with shock, hepatic disease, cardiac arrest, or congestive heart failure.</p> <p><b>Anesthesia, local injection:</b> Dose varies with procedure, degree of anesthesia needed, vascularity of tissue, duration of anesthesia required, and physical condition of patient.</p> <p><i>Cutaneous infiltration:</i> Children and Adolescents: Typically, solutions with concentration &lt;2% should be used (allow for larger volumes); maximum dose: 5 mg/kg/dose not to exceed the recommended adult maximum dose of 300 mg/dose; do not repeat within 2 hours</p> <p><b>Local:</b> Refer to PIL or SPC of product due to different concentrations and considerations.</p>
<p><b>Dosage adjustment</b></p>	<p><b>Systemic:</b></p> <p><b>Dosing: Altered Kidney Function:</b> eGFR &lt;30 mL/minute/1.73 m<sup>2</sup>: Administer lower maintenance infusion rate with close monitoring for toxicity.</p> <p><b>Dosing: Hepatic Impairment:</b> Administer lower maintenance infusion rate with close monitoring for toxicity. For pediatrics consider alternative therapy. Maximum rate of continuous IV infusion: 20 mcg/kg/minute</p> <p><b>Local:</b></p> <p><b>Dosing: Altered Kidney Function:</b> There are no dose adjustments needed.</p> <p><b>Dosing: Hepatic Impairment:</b> There are no dose adjustments needed. Use caution in patients with severe hepatic disease.</p>
<p><b>Contra-indications</b></p>	<ul style="list-style-type: none"> <li>• Hypersensitivity to lidocaine or to another local anesthetic of the amide type</li> <li>• Adam-Stokes syndrome</li> <li>• Wolff-Parkinson-White syndrome</li> <li>• Severe degrees of sinoatrial, atrioventricular, or intraventricular heart block (except in patients with a functioning artificial pacemaker)</li> <li>• In local dosage forms: bacterial, viral or fungal infection at the site of application</li> </ul>
<p><b>Adverse Drug Reactions</b></p>	<p><b>Systemic:</b></p> <p><b>1% to 10%:</b></p> <p>Central nervous system: Headache (positional headache following spinal anesthesia:</p>

	<p>3%), shivering (following spinal anesthesia: 2%), radiculopathy (<math>\leq 2\%</math>; transient pain; subarachnoid administration)</p> <p><b>Frequency not defined:</b></p> <p>Cardiovascular: Bradycardia, cardiac arrhythmia, circulatory shock, coronary artery vasospasm, edema, flushing, heart block, hypotension (including following spinal anesthesia), local thrombophlebitis, vascular insufficiency (periarticular injections)</p> <p>Central nervous system: Agitation, anxiety, apprehension, cauda equina syndrome (following spinal anesthesia), coma, confusion, disorientation, dizziness, drowsiness, euphoria, hallucination, hyperesthesia, hypoesthesia, intolerance to temperature, lethargy, loss of consciousness, metallic taste, nervousness, paresthesia, peripheral neuropathy (following spinal anesthesia), psychosis, seizure, slurred speech, twitching</p> <p>Gastrointestinal: Nausea (including following spinal anesthesia), vomiting</p> <p>Hypersensitivity: Anaphylactoid reaction, anaphylaxis, hypersensitivity reaction</p> <p>Neuromuscular and skeletal: Tremor, weakness</p> <p>Otic: Tinnitus</p> <p>Respiratory: Bronchospasm, dyspnea, respiratory depression, respiratory insufficiency (following spinal anesthesia)</p> <p><b>Local:</b></p> <p><b>&gt;10%:</b></p> <p>Dermatologic: Erythema (intradermal powder: adults - 67%; children and adolescents - 53%)</p> <p>Hematologic and oncologic: Petechia (intradermal powder: 44% to 46%)</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Edema</p> <p>Dermatologic: Pruritus</p> <p>Gastrointestinal: vomiting</p>
<p><b>Monitoring Parameters</b></p>	<p><b>Systemic:</b></p> <p>Liver function tests</p> <p>ECG</p> <p>Lidocaine concentrations, in patients requiring drug &gt;24 hrs, blood level monitoring recommended</p> <p><b>Reference Range</b></p> <p>Therapeutic: 1.5 to 5.0 mcg/mL (SI: 6 to 21 micromole/L)</p> <p>Potentially toxic: &gt;6 mcg/mL (SI: &gt;26 micromole/L)</p> <p>Toxic: &gt;9 mcg/mL (SI: &gt;38 micromole/L)</p> <p><b>Local:</b> Assess for signs of systemic toxicity. Assess skin for signs of hypersensitivity</p>
<p><b>Drug Interactions</b></p>	<p><b>Systemic:</b></p> <p><b>Risk X: Avoid combination</b></p> <p>Fexinidazole, Fusidic Acid (Systemic), Saquinavir</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Bupivacaine</p>
<p><b>Pregnancy and Lactation</b></p>	<p><b>Pregnancy</b> category B. Reproductive studies conducted in rats have not demonstrated lidocaine-induced fetal harm; however, animal studies are not always predictive of human response. There are no adequate or well controlled studies of lidocaine in pregnant women.</p> <p><b>Lactation</b> :Available guidelines consider lidocaine to be compatible with lactation when used as an antiarrhythmic or local anesthetic or locally. Use caution.</p>



<b>Administration</b>	<p><b>Usual Infusion Concentrations: Pediatric</b> IV infusion: 8000 mcg/mL</p> <p><b>Usual Infusion Concentrations: Adult</b> IV infusion: 1000 mg in 250 mL (concentration: 4 mg/mL) or 2000 mg in 250 mL (concentration: 8 mg/mL) of D5W</p> <p><b>Administration: IV</b> <b>Bolus:</b> May administer at 25 to 50 mg/minute. <b>Continuous infusion:</b> After initial bolus dosing, may administer as a continuous infusion; refer to indication-specific infusion rates in dosing for detailed recommendations. Local thrombophlebitis may occur in patients receiving prolonged IV infusions.</p> <p><b>Preparation for Administration:</b> <b>IV:</b> <b>Bolus:</b> Preparation dependent upon product; solutions containing 40 to 200 mg/mL must be diluted prior to use to a concentration not to exceed 20 mg/ml. The injectable solution of 20 mg/mL may be administered undiluted. <b>Continuous IV infusion:</b> Dilute in D5W or other compatible solution to a concentration of 1,000 to 8,000 mcg/mL (1 to 8 mg/mL) <b>Local infiltration:</b> Buffered lidocaine for injectable local anesthetic may be prepared: Add 2 mL of sodium bicarbonate 8.4% to 18 mL of lidocaine 1%. <b>Local:</b> Cream, gel: For external use only; avoid contact with eyes. Oral: Do not eat or chew gum for 60 minutes following use. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Intra-articular infusion related chondrolysis: Continuous intra-articular infusion of local anesthetics after arthroscopic or other surgical procedures is not an approved use;</li> <li>• Methemoglobinemia: clinically significant methemoglobinemia requires immediate treatment along with discontinuation of the anesthetic and other oxidizing agents. Onset may be immediate or delayed (hours) after anesthetic exposure. signs and symptoms of methemoglobinemia are cyanosis, headache, rapid pulse, shortness of breath, lightheadedness, fatigue.</li> </ul> <p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Hepatic dysfunction: Use extreme caution in patients with severe hepatic dysfunction; may have increased risk of lidocaine toxicity.</li> <li>• Pseudocholinesterase deficiency: Use caution in patients with pseudocholinesterase deficiency; may have increased risk of lidocaine toxicity</li> </ul> <p><b>Dosage-form specific issues:</b></p> <ul style="list-style-type: none"> <li>• Injectable anesthetic: Follow appropriate administration techniques so as not to administer any intravascularly. Solutions containing antimicrobial preservatives should not be used for epidural or spinal anesthesia. Some solutions contain a bisulfite; avoid in patients who are allergic to bisulfite. Resuscitative equipment, medicine and oxygen should be available in case of emergency. Use products containing epinephrine cautiously in patients with significant vascular disease, compromised blood flow, or during or following general anesthesia (increased risk of arrhythmias). Adjust the dose for the elderly, pediatric, acutely ill, and debilitated patients.</li> <li>• Intravenous: Constant ECG monitoring is necessary during IV administration. Use cautiously in hepatic impairment, HF, marked hypoxia, severe respiratory</li> </ul>



depression, hypovolemia, history of malignant hyperthermia, or shock. Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy. Correct any underlying causes of ventricular arrhythmias. Monitor closely for signs and symptoms of CNS toxicity. The elderly may be prone to increased CNS and cardiovascular side effects. Reduce dose in hepatic dysfunction and CHF.

**Local:**

**Concerns related to adverse effects:**

- Familial malignant hyperthermia: Many drugs used during the conduct of anesthesia may trigger familial malignant hyperthermia; not known whether amide-type local anesthetics trigger this reaction. Early unexplained signs of tachycardia, tachypnea, labile blood pressure, and metabolic acidosis may precede temperature elevation.
- Hypersensitivity allergic reactions may occur.
- Local effects: Irritation, sensitivity and/or infection may occur at the site of application; discontinue use and institute appropriate therapy if local effects occur.
- Methemoglobinemia: Has been reported with local anesthetics; clinically significant methemoglobinemia requires immediate treatment along with discontinuation of the anesthetic and other oxidizing agents. Onset may be immediate or delayed (hours) after anesthetic exposure. Patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, exposure to oxidizing agents or their metabolites, or infants <6 months are more susceptible and should be closely monitored for signs and symptoms of methemoglobinemia (eg, cyanosis, headache, rapid pulse, shortness of breath, lightheadedness, fatigue).
- Systemic adverse effects: Potentially life-threatening side effects (eg, irregular heartbeat, seizures, coma, respiratory depression, death) have occurred when used prior to cosmetic procedures. Excessive dosing for any indication (eg, application to large areas, use above recommended dose, application to denuded or inflamed skin, or wearing of device for longer than recommended), smaller patients, and/or impaired elimination may lead to increased absorption and systemic toxicity; patient should adhere strictly to recommended dosage and administration guidelines; serious adverse effects may require the use of supportive care and resuscitative equipment; lidocaine toxicity may occur at blood concentrations above 5 mcg/mL.

**Disease-related concerns:**

- Bleeding tendencies/platelet disorders: Intradermal injection: Use with caution; may have a higher risk of superficial dermal bleeding.
- Cardiovascular disease: Use with caution in patients with severe shock or heart block.
- Dermal integrity reduced: Application to broken or inflamed skin may lead to increased systemic absorption; use caution.
- Familial malignant hyperthermia: May potentially trigger malignant hyperthermia; follow standard protocol for identification and treatment.
- Hepatic impairment: Use caution in patients with severe hepatic disease due to diminished ability to metabolize systemically-absorbed lidocaine.
- Pseudocholinesterase deficiency: Use with caution; these patients have a greater risk of developing toxic plasma concentrations of lidocaine.
- Sepsis/severely traumatized mucosa: Use with extreme caution in the presence of sepsis and/or severely traumatized mucosa due to an increased risk of rapid systemic absorption at application site.

***Dosage form specific issues:***

- Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.
- Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Caution. Hypersensitivity reactions, usually a delayed reaction, occurred following exposure to products containing polysorbate 80 in certain individuals. Symptoms in premature neonates include Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure.
- Topical cream, liquid, lotion, gel, and ointment: Do not leave on large body areas for >2 hours. Not for ophthalmic use. Some products are not recommended for use on mucous membranes; consult specific product labeling.
- Topical oral solution/viscous: When used in mouth or throat, topical anesthesia may impair swallowing and increase aspiration risk. Avoid food for ≥60 minutes following oral or throat application. This is especially important in the pediatric population. Numbness may increase the danger of tongue/buccal biting trauma; ingesting food or chewing gum should be avoided while mouth or throat is anesthetized. Excessive doses or frequent application may result in high plasma levels and serious adverse effects; strictly adhere to dosing instructions. Use measuring devices to measure the correct volume, if applicable, to ensure accuracy of dose.
- Topical patch: Apply only on intact skin. Do not use around or in the eyes. To avoid accidental ingestion by children, store and dispose of products out of the reach of children. Avoid exposing application site to external heat sources (eg, heating pad, electric blanket, heat lamp, hot tub).

***Special populations:***

- Acutely ill patients: Use with caution; acutely ill patients should be given reduced doses commensurate with their age and physical status.
- Elderly and debilitated patients: Use with caution; elderly and debilitated patients should be given reduced doses commensurate with their age and physical status.
- Oral topical solution/viscous: Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients <3 years of age have been reported with use of lidocaine 2% viscous solution when it was not administered in strict adherence to the dosing and administration recommendations. Use of topical anesthetics for teething is discouraged by guidelines.
- Pediatric: Use with caution; children should be given reduced doses commensurate with their age and physical status.

***Other warnings/precautions:***

- Topical application: the lowest amount of anesthetic necessary for pain relief should be applied.

**Storage**

Injection: Store between 15°C and 30°C.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Propafenone

<b>Generic Name</b>	Propafenone
<b>Dosage form/strengths</b>	Tablets 150mg, 300mg Ampoule 70mg/20ml
<b>Route of administration</b>	Oral, IV
<b>Pharmacologic category</b>	Antiarrhythmic Agent, Class Ic
<b>Indications</b>	<p><b>Oral:</b> Treatment of life-threatening ventricular arrhythmias; to prolong the time to recurrence of paroxysmal atrial fibrillation/flutter (PAF) or paroxysmal supraventricular tachycardia (PSVT) in patients with disabling symptoms without structural heart disease.</p> <p><b>IV:</b> Arrhythmias (treatment or short-term prevention): For rapid control or short-term prophylaxis of arrhythmias including paroxysmal atrial fibrillation/flutter, paroxysmal supraventricular tachycardias (PSVT), and symptomatic arrhythmias associated with the Wolff-Parkinson-White syndrome, in patients without severe structural heart disease.</p>
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b>  <b>Note:</b> Patients who exhibit significant widening of QRS complex or second- or third-degree AV block may need dose reduction.  <b>Arrhythmias (treatment or short-term prevention):</b>                      IV: 1.5 to 2 mg/kg over 10 minutes. If a repeat dose is necessary, do not administer sooner than 90 minutes after initial dose.  <b>Atrial fibrillation, Paroxysmal supraventricular tachycardia (to prevent recurrence) or Ventricular arrhythmia:</b> Oral:                      Initial: 150 mg every 8 hours; dosage increase may be made at minimum of 3- to 4-day intervals, if further increase is necessary, may increase to 300 mg every 8 hours.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b>                      There are no dosage adjustments needed. Use caution  <b>Dosing: Hepatic Impairment: Adult</b>                      Give approximately 20—30% of the normal oral dosage for immediate-release tablets. No available dose adjustments for IV, use caution.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Acute bronchospasm</li> <li>• Asthma</li> <li>• AV block</li> <li>• Bradycardia</li> <li>• Brugada syndrome</li> <li>• Cardiogenic shock</li> <li>• Electrolyte imbalance</li> <li>• Heart failure</li> <li>• Hypotension</li> <li>• Sick sinus syndrome</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b>                      Gastrointestinal: Nausea (<math>\leq 11\%</math>), vomiting (<math>\leq 11\%</math>)                      Nervous system: Unusual taste (14%; dysgeusia: <math>\geq 2\%</math>)</p> <p><b>1% to 10%:</b></p>

	<p>Cardiovascular: Angina pectoris (<math>\geq 2\%</math>), bradycardia (2%), bundle branch block (1%; including right bundle branch block and left bundle branch block), cardiac conduction disorder (<math>\geq 2\%</math>; including atrioventricular conduction disturbance [slow]; cardiac conduction delay [1%]), chest pain (<math>\geq 1\%</math>), edema (<math>\geq 2\%</math>), heart block (including complete atrioventricular block [<math>&lt; 1\%</math>]), first-degree atrioventricular block [3%], second-degree atrioventricular block [<math>&lt; 1\%</math>]), heart failure (<math>\leq 2\%</math>; including worsening of heart failure), heart murmur (<math>\geq 2\%</math>), hypotension (<math>\geq 2\%</math>), palpitations (2%), sinus bradycardia (<math>\geq 2\%</math>), ventricular arrhythmia (new or worsened: <math>\leq 5\%</math>)</p> <p>Dermatologic: Ecchymosis (<math>\geq 2\%</math>)</p> <p>Gastrointestinal: Anorexia (2%), constipation (8%), diarrhea (2%), flatulence (<math>\geq 2\%</math>), xerostomia (<math>\geq 2\%</math>)</p> <p>Genitourinary: Hematuria (<math>\geq 2\%</math>)</p> <p>Hepatic: Increased serum alkaline phosphatase (<math>&gt; 1\%</math>)</p> <p>Nervous system: Anxiety (<math>\geq 2\%</math>), asthenia (3%), ataxia (2%), depression, dizziness (9%), drowsiness (<math>\geq 2\%</math>), fatigue (6%), headache (6%), myasthenia (including exacerbation of myasthenia gravis), tremor (2%)</p> <p>Ophthalmic: Blurred vision (3%)</p> <p>Respiratory: Dyspnea (2%), upper respiratory tract infection (<math>\geq 2\%</math>), wheezing (<math>\geq 2\%</math>)</p>
<b>Monitoring Parameters</b>	ECG, blood pressure, pulse (particularly at initiation of therapy)
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Adagrasib, Amiodarone, Asunaprevir, Bilastine, Doxorubicin, Fexinidazole, Fezolinetant, Fosamprenavir, Lefamulin, Levoketoconazole, Pazopanib, Posaconazole, Pimozide, Quinidine, Rimegepant, Ritonavir, Sertindole, Tipranavir, Topotecan, Vincristine (Liposomal)</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Afatinib, Berostralstat, Betrixaban, Cardiac Glycosides, Colchicine, Domperidone, Fingolimod, Methadone, Ponesimod, QT-Prolonging Class IA Antiarrhythmics (Highest Risk), QT-Prolonging Class III Antiarrhythmics (Highest Risk), QT-Prolonging Kinase Inhibitors (Highest Risk), QT-Prolonging Miscellaneous Agents (Highest Risk), Relugolix, Rimegepant, Siponimod, Sirolimus, Tizanidine, Ubrogepant, Venetoclax</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> The lowest effective dose is recommended; avoid use during the first trimester if possible. Propafenone may be used for the ongoing management of pregnant women with highly symptomatic supraventricular tachycardia (SVT). Use is also recommended for the prevention of SVT in patients with Wolff-Parkinson-White (WPW) syndrome. Until more information is available, when prevention of SVT in patients without WPW syndrome, atrial tachycardia, or atrial fibrillation is needed in pregnant women, propafenone is generally reserved for use when other agents are not effective.</p> <p><b>Lactation:</b> Propafenone and its active metabolite are present in human milk, but concentrations are likely to be low. There are no enough data. Other agents may be used during breast-feeding.</p>
<b>Administration</b>	<p><b>Administration: IV</b></p> <p>IV: Administer bolus dose undiluted over 10 minutes.</p> <p><b>Administration: Oral</b></p> <p>Tablet should be swallowed whole with liquid. To be administered without regards to food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

**Warnings/  
Precautions**
**Concerns related to adverse effects:**

- **Agranulocytosis:** Agranulocytosis has been reported; generally occurring within the first 2 months of therapy. Upon therapy discontinuation, WBC usually normalized by 14 days.
- **CNS effects:** May cause dizziness, fatigue, blurred vision; caution patients about performing dangerous tasks (eg, driving, operating machinery).
- **Conduction disturbances:** Slows atrioventricular conduction, potentially leading to first degree AV block; degree of PR interval prolongation and increased QRS duration are dose and concentration related. Avoid in patients with conduction disturbances (unless functioning pacemaker present).
- **Elevated antinuclear antibody titers:** Positive antinuclear antibody (ANA) titers have been reported with use. Titers have decreased with and without therapy discontinuation. Positive titers have not usually been associated with clinical symptoms, although at least one case of drug-induced lupus erythematosus has been reported. Consider therapy discontinuation in symptomatic patients with positive ANA titers.
- **Hepatotoxicity:** Hepatic abnormalities (including fulminant hepatitis and fatalities) have been reported; toxicity appeared due to hepatocellular injury and/or cholestasis.
- **Proarrhythmic effects:** Can cause life-threatening drug-induced arrhythmias. Monitor for proarrhythmic effects, and when necessary, adjust dose to prevent QT<sub>c</sub> prolongation.

**Disease-related concerns:**

- **Brugada syndrome:** Initiation of propafenone may unmask Brugada syndrome; obtain ECG after treatment initiation and discontinue if ECG indicative of Brugada syndrome.
- **Electrolyte imbalance:** Use is contraindicated in patients with uncorrected electrolyte abnormalities. Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy.
- **Heart failure (HF):** Avoid use in patients with HF; similar agents have been shown to increase mortality in this population; may precipitate or exacerbate condition.
- **Hepatic impairment:** Use with caution in patients with hepatic impairment.
- **Myasthenia gravis:** Use with caution; may exacerbate condition.
- **Pulmonary disease:** Use in patients with bronchospastic disease or severe obstructive lung disease is contraindicated.
- **Renal impairment:** Use with caution in patients with renal impairment.

**Other warnings/precautions:**

- **Pacemakers:** May alter pacing and sensing thresholds of artificial pacemakers.

**Storage**

Store between 15°C to 30°C.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Antihypertensive, Centrally Acting Agents



## Clonidine hydrochloride

<b>Generic name</b>	<b>Clonidine</b>
<b>Dosage form/strengths</b>	Tablets: 25 mcg, 150 mcg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha2-Adrenergic Agonist; Antihypertensive ATC: C02AC01
<b>Indications</b>	Management of hypertension
<b>Dosage Regimen</b>	<p><b>-Adult:</b>  <b>Hypertension</b>                      Oral: Initially 50–100 micrograms 3 times a day, increase dose every 2-3 days, usual maximum dose 1.2mg daily  <b>Prevention of recurrent migraine, Prevention of vascular, headache, Menopausal symptoms, particularly flushing, and vasomotor conditions</b>                      Oral: Initially 50 micrograms twice daily for 2 weeks, then increased if necessary to 75 micrograms twice daily.</p>
<b>Dosage adjustment</b>	<p><b>-Renal Impairment:</b>                      Clonidine is excreted primarily through the kidneys as unchanged drug (40% to 60%). For this reason, dose initiation and titration should be done cautiously with monitoring of response in patients with significant kidney impairment                      -Clcr <math>\geq</math>10 mL/minute: Dosage adjustment does not appear necessary.                      -Clcr &lt;10 mL/minute: Give 50–75% of the usual dosage.                      -Supplemental doses after hemodialysis are not necessary.</p> <p><b>-Hepatic Impairment:</b>                      No quantitative recommendations are available. Because clonidine is substantially metabolized by the liver, monitor patients for sedation and hypotension and adjust the dose if necessary.</p>
<b>Contra-indications</b>	<p>-Hypersensitivity to drug or any component of the formulation.                      -Severe bradyarrhythmia from second- or third-degree atrioventricular block or sick sinus syndrome; sinus node dysfunction</p>
<b>Adverse Drug Reactions</b>	<p><b>-&gt;10%:</b>                      -Gastrointestinal: Upper abdominal pain (15%), xerostomia (5% to 40%)                      -Nervous system: Dizziness (2% to 16%), drowsiness (12% to 38%), fatigue (6% to 16%), headache (1% to 20%)</p> <p><b>-1% to 10%:</b>                      -Cardiovascular: Bradycardia (4%), localized blanching (transdermal: 1%)                      -Gastrointestinal: Constipation (1% to 10%), dysgeusia (transdermal: 1%), nausea (1% to 5%), viral gastrointestinal infection (5%)                      -Genitourinary: Impotence (transdermal: <math>\leq</math>2%), sexual disorder (transdermal: <math>\leq</math>2%), urinary incontinence (4%)                      -Nervous system: Aggressive behavior (1% to 3%), emotional disturbance (4%), insomnia (5% to 6%), irritability (5% to 9%), lethargy (3%), nervousness (1%), night terrors (3%), nightmares (4% to 9%), restless sleep (3%), sedated state (3% to 10%),</p>

	<p>sleep disorder (1% to 3%), throbbing (transdermal: 1%)</p> <ul style="list-style-type: none"> <li>-Neuromuscular and skeletal: Tremor (1% to 4%)</li> <li>-Otic: Otitis media (3%; acute)</li> <li>-Respiratory: Dry throat (transdermal: 2%)</li> <li>-Miscellaneous: Crying (1% to 3%)</li> </ul>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>-Blood pressure, standing and sitting/supine</li> <li>-Mental status</li> <li>-Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b><u>- Risk X: Avoid combination:</u></b> Azelastine (Nasal), Bromperidol, Blonanserin, Fexinidazole, Flunarizine, Kratom, Macimorelin, Olopatadine (Nasal), Orphenadrine, Oxomemazine, Paraldehyde, Thalidomide</p> <p><b><u>-Risk D: Consider therapy modification:</u></b> Amifostine, Beta-Blockers, Blonanserin, Buprenorphine, Ceritinib, Chlormethiazole, Daridorexant, Dexmedetomidine, Droperidol, Fingolimod, Flunitrazepam, Hydroxyzine, Lemborexant, Methotrimeprazine, Mirtazapine, Obinutuzumab, Opioid Agonists, Oxybate Salt Products, Ponesimod, Ropeginterferon Alfa-2b, Siponimod, Suvorexant, Tricyclic Antidepressants, Zolpidem, Zuranolone</p>
<b>Pregnancy and Lactation</b>	<p><b><u>-Pregnancy:</u></b> Adequate and well-controlled studies of oral clonidine have not been performed during pregnancy in humans. Avoid use unless potential benefit outweighs risk.</p> <p><b><u>-Lactation:</u></b> Use is not recommended due to adverse events observed in breastfeeding infants.</p>
<b>Administration</b>	<p><b><u>-Oral:</u></b> May be taken with or without food. Swallow whole with water. Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>-May cause CNS depression (including sedation and somnolence), which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving).</li> <li>-Use with caution in patients with:                         <ul style="list-style-type: none"> <li>-Severe coronary insufficiency, including recent MI</li> <li>-Cerebrovascular disease</li> <li>-Chronic renal impairment. The hemodynamic effects may be prolonged in those with renal impairment; elimination half-life significantly prolonged (up to 41 hours) in patients with severe renal impairment.</li> <li>-Gradual withdrawal is needed (discontinue over 6 to 10 days to avoid rebound hypertension) if drug needs to be stopped. Patients should be instructed about abrupt discontinuation (causes rapid increase in BP and symptoms of sympathetic overactivity). In patients on both a beta-blocker and clonidine where withdrawal of clonidine is necessary, withdraw the beta-blocker first and several days before clonidine withdrawal, then slowly decrease clonidine.</li> </ul> </li> </ul>
<b>Storage</b>	<ul style="list-style-type: none"> <li>-Store between 15°C and 30 °C. Keep in dry place.</li> <li>Refer to manufacturer PIL if there are specific considerations.</li> </ul>



## Methyldopa

<b>Generic Name</b>	Methyldopa
<b>Dosage form/strengths</b>	Tablets: 250 mg, 500mg Capsules: 250mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Alpha2-Adrenergic Agonist; Antihypertensive ATC: C02AB01
<b>Indications</b>	Hypertension
<b>Dosage Regimen</b>	<p><b>-Adult:</b> Oral: Initial: 250 mg 2 to 3 times daily; titrate daily dose at least every 2 days based on response; usual dose range: 250 mg to 1 g daily in 2 to 4 divided doses; maximum dose: 3 g/day in divided doses</p> <p><b>-Pediatric:</b> Note: use has been replaced by other agents; methyldopa not suggested as a treatment option for hypertension Children and Adolescents: Oral: Initial: 10 mg/kg/day in 2 to 4 divided doses; titrate no more frequently than every 2 days until adequate response to maximum daily dose: 65 mg/kg/day or 3,000 mg/day whichever is less</p>
<b>Dosage adjustment</b>	<p><b>-Renal Impairment:</b> -CrCl &gt; 50 ml/min: No dosage adjustment is needed. -CrCl 10—50 ml/min: Administer the indicated dosage every 8—12 hours. -CrCl &lt; 10 ml/min: Administer the indicated dosage every 12—24 hours.</p> <p><b>-Hepatic Impairment:</b> No dosage adjustments available; use is contraindicated in patients with active hepatic disease such as acute hepatitis and decompensated cirrhosis.</p>
<b>Contra-indications</b>	<p>-Hypersensitivity to methyldopa or any component of the formulation. -Active hepatic disease (eg, acute hepatitis, active cirrhosis). -Hepatic disorders previously associated with use of methyldopa. -Concurrent use of MAO inhibitors.</p>
<b>Adverse Drug Reactions</b>	<p>-Frequency not defined.</p> <p><b>-Cardiovascular:</b> Bradycardia, cardiac failure, exacerbation of angina pectoris, myocarditis, orthostatic hypotension, pericarditis, peripheral edema, prolonged carotid sinus syncope, vasculitis</p> <p><b>-Central nervous system:</b> Bell's palsy, cerebrovascular insufficiency (symptoms), choreoathetosis, decreased mental acuity, depression, dizziness, drug fever, headache, nightmares, paresthesia, Parkinson's disease, sedation</p> <p><b>-Dermatologic:</b> Skin rash, toxic epidermal necrolysis</p> <p><b>-Endocrine and metabolic:</b> Amenorrhea, decreased libido, gynecomastia, hyperprolactinemia, weight gain</p> <p><b>-Gastrointestinal:</b> Abdominal distention, colitis, constipation, diarrhea, flatulence, glossalgia, melanoglossia, nausea, pancreatitis, sialadenitis, vomiting, xerostomia</p> <p><b>-Genitourinary:</b> Breast hypertrophy, impotence, lactation</p> <p><b>-Hematologic and oncologic:</b> Bone marrow depression, eosinophilia, granulocytopenia, hemolytic anemia, leukopenia, positive ANA titer, positive direct Coombs test, thrombocytopenia</p> <p><b>-Hepatic:</b> Abnormal hepatic function tests, hepatic disease (hepatitis), jaundice</p>

	<p><b>-Neuromuscular and skeletal:</b> Arthralgia, lupus-like syndrome, myalgia, positive rheumatoid factor, weakness</p> <p><b>-Renal:</b> Increased blood urea nitrogen</p> <p><b>-Respiratory:</b> Nasal congestion</p> <p><b>-Miscellaneous:</b> Positive Lupus Erythematosus cell preparation</p>
<b>Monitoring Parameters</b>	<p>- Blood pressure (standing and sitting/lying down).</p> <p>-CBC, liver enzymes (periodically during the first 6 to 12 weeks or when unexplained fever occurs).</p> <p>- Coombs test (direct) (may obtain prior to initiation and at 6 and 12 months).</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Monoamine Oxidase Inhibitors, Triptorelin</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Beta-Blockers, Iron Preparations, Mirtazapine, Multivitamins/Minerals (with ADEK, Folate, Iron), Obinutuzumab, Riluzole, Tricyclic Antidepressants</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b></p> <p>-Methyldopa crosses the placenta.</p> <p>-Available data show use during pregnancy does not cause fetal harm and improves fetal outcomes.</p> <p>-Chronic maternal hypertension may increase the risk of birth defects, low birth weight, preterm delivery, stillbirth, and neonatal death.</p> <p>If treatment for chronic hypertension during pregnancy is needed, oral methyldopa is an option; however, other agents may be preferred due to adverse events and decreased effectiveness when compared to other medications. Females with preexisting hypertension may continue their medication during pregnancy unless contraindications exist.</p> <p><b>-Lactation:</b></p> <p>Methyldopa is present in breast milk. Methyldopa is compatible with breastfeeding. However, because maternal depression has been reported following methyldopa administration, use of methyldopa should be avoided in the postnatal period due to the underlying risk of depression already present in this patient population.</p>
<b>Administration</b>	<p><b>Oral:</b> Administer new dosage increases in the evening to minimize sedation.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>-Patients with severe bilateral cerebrovascular disease have exhibited involuntary choreoathetotic movements (rare); discontinue use if these symptoms develop.</p> <p>-Use with caution in patients with history of hepatic disease or impairment.</p> <p>-Renal impairment; may respond to smaller doses. The active metabolites of methyldopa accumulate in patients with renal impairment.</p> <p>-Not recommended in patients with pheochromocytoma.</p> <p>-Tolerance may occur usually between the second and third month of therapy; adding a diuretic or increasing the dosage of methyldopa frequently restores blood pressure control.</p> <p>- Methyldopa is not considered a drug of first choice in the elderly because of its CNS effects.</p> <p>-Surgical patients: Patients on methyldopa may need less anesthetic agents</p>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Antihypertensive, Vasodilators

## Ambrisentan

Generic Name	Ambrisentan
Dosage form/strengths	Tablets 5mg, 10mg
Route of administration	Oral
Pharmacologic category	Endothelin Receptor Antagonist; Vasodilator ATC: C02KX02
Indications	<b>Pulmonary arterial hypertension:</b>
Dosage Regimen	<b>Adult:</b> 5 mg once daily, increased if necessary to 10 mg once daily after 4 weeks of evaluation. Safety and efficacy in pediatrics has not been established.
Dosage adjustment	<b>Dosing: Altered Kidney Function: Adult</b> Use with caution if creatinine clearance less than 30 mL/minute. <b>Dosing: Hepatic Impairment: Adult</b> Mild or moderate impairment: Use with caution and monitor closely, monitor liver functions monthly. Severe impairment or if baseline serum transaminases exceed 3 times the upper limit of normal: Use is contraindicated.
Contra-indications	<ul style="list-style-type: none"> <li>• Idiopathic pulmonary fibrosis</li> <li>• Pregnancy</li> <li>• Severe hepatic impairment</li> </ul>
Adverse Drug Reactions	<b>Common or very common (&gt;1%):</b> Abdominal pain, Anaemia, constipation, diarrhea, dizziness, Epistaxis, flushing, headaches, hypersensitivity, increased risk of infection, nasal congestion, nausea, palpitations, skin reactions, tinnitus, vision disorders, vomiting, Peripheral edema <b>Uncommon (0.1%-1%):</b> Hepatic disorders, sudden hearing loss, Oligospermia
Monitoring Parameters	<ul style="list-style-type: none"> <li>• Hemoglobin/hematocrit prior to initiation therapy, at 1 month, and periodically thereafter. Not to be initiated in patients with significant anemia.</li> <li>• Liver function test</li> <li>• Pregnancy testing.</li> </ul>
Drug Interactions	<b>Risk X: Avoid combination</b> Leniolisib, Sparsentan <b>Risk D: Consider therapy modification</b> Cyclosporine (Systemic), Trofinetide
Pregnancy and Lactation	<b>Pregnancy:</b> Do not administer Ambrisentan to a pregnant female or females liable to pregnancy without contraception, because it may cause fetal harm. <b>Lactation:</b> Potential Toxicity. Discontinue either treatment or breastfeeding.
Administration	Oral: Administer with or without food. Do not split, crush, or chew tablets. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
Warnings/ Precautions	<ul style="list-style-type: none"> <li>• Hazardous agent (NIOSH 2016 [group 3]): Warning on adverse reproductive effects; reduced sperm counts in patients.</li> <li>• Fluid retention or peripheral edema has occurred, determine cause and</li> </ul>

	<p>appropriate treatment or discontinue therapy.</p> <ul style="list-style-type: none"> <li>• Hematologic changes: Significant decreases in hemoglobin in the absence of other causes may necessitate discontinuation of therapy. Use not recommended in patients with clinically significant anemia.</li> <li>• Hepatic effects have been reported: Discontinue therapy if signs of hepatic toxicity appear, if serum liver aminotransferases &gt;3 times upper normal level.</li> <li>• Pulmonary veno-occlusive disease: Discontinue in any patient with pulmonary edema suggestive of PVOD.</li> <li>• Pregnancy: Ambrisentan is very likely to produce serious birth defects if used by pregnant females. Exclude pregnancy before the initiation of treatment. Obtain monthly pregnancy tests during treatment and 1 month after discontinuation of treatment.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Bosentan

Generic Name	Bosentan
Dosage form/strengths	Tablets: 62.5 mg, 125 mg
Route of administration	Oral
Pharmacologic category	Endothelin Receptor Antagonist; Vasodilator ATC: C02KX01
Indications	<b>Pulmonary arterial hypertension</b>
Dosage Regimen	<p><b>Adult dosing:</b>  <b>Pulmonary arterial hypertension:</b>                      Adult: Initially 62.5 mg twice daily for 4 weeks, Then in patients of body-weight 40 kg and above: increase to 125 mg twice daily (max. per dose 250 mg); maximum 500 mg per day</p> <p><b>Pediatric dosing:</b>  <b>Pulmonary arterial hypertension:</b>                      Children (body-weight 10–20 kg): Initially 31.25 mg once daily for 4 weeks, then increase to 31.25 mg twice daily.                      Children and adolescents (body-weight 20–40 kg): Initially 31.25 mg twice daily for 4 weeks, then increase to 62.5 mg twice daily.                      Adolescents (body-weight more than 40 kg): refer to adult dosing.</p>
Dosage Adjustment	<p><b>Dosing: Altered Kidney Function:</b>                      No dose adjustments necessary.</p> <p><b>Dosing: Hepatic Impairment:</b>                      Mild impairment: No dose adjustments necessary for initial dose.                      Moderate to severe impairment (Child-Pugh class B and C) and/or baseline transaminase &gt;3 times normal level: Avoid use.</p>
Contra-Indications	<ul style="list-style-type: none"> <li>• Hypersensitivity to bosentan or any component of the formulation</li> <li>• Concurrent use of cyclosporine or glyburide</li> <li>• Pregnancy.</li> <li>• Moderate to severe hepatic impairment (eg, ALT or AST &gt;3 times ULN)</li> <li>• Acute porphyrias</li> </ul>
Adverse Drug Reactions	<p><b>&gt;10%:</b>                      Cardiovascular: Edema (≤11%)                      Central nervous system: Headache (15%)                      Hepatic: Increased serum ALT (≥3 times ULN: ≤12%; 8 times ULN: ≤2%; dose-related), increased serum AST (≥3 times ULN: ≤12%; 8 times ULN: ≤2%; dose-related)                      Respiratory: Respiratory tract infection (22%)</p> <p><b>1% to 10%:</b>                      Cardiovascular: Chest pain (5%), syncope (5%), flushing (4%), hypotension (4%), palpitations (4%)                      Endocrine and metabolic: Fluid retention (≤2%)                      Hematologic and oncologic: Anemia (3%)                      Neuromuscular and skeletal: Arthralgia (4%)                      Respiratory: Sinusitis (4%)</p>

Monitoring Parameters	<ul style="list-style-type: none"> <li>• Haemoglobin before and during treatment (monthly for first 3-months).</li> <li>• Liver functions before and monthly during administration</li> <li>• Pregnancy test</li> </ul>
Drug Interactions	<p><b>Risk X: Avoid combination</b>                  Abemaciclib, Antihepaciviral Combination Products, Asunaprevir, Avacopan, Avanafil, Avapritinib, Axitinib, Bedaquiline, Capmatinib, Cariprazine, Cobimetinib, Cyclosporine (Systemic), Daridorexant, Dasabuvir, Deflazacort, Doxorubicin, Elacestrant, Elbasvir And Grazoprevir, Encorafenib, Entrectinib, Fedratinib, Fexinidazole, Finerenone, Flibanserin, Fluconazole, Glyburide, Ibrexafungerp, Infigratinib, Ivabradine, Lemborexant, Lenacapavir, Leniolisib, Letemovir, Lonafarnib, Lumateperone, Lurbinectedin, Mavacamten, Mifepristone, Mobocertinib, Nisoldipine, Olaparib, Olutasidenib, Omaveloxolone, Orelabrutinib, Pacritinib, Pemigatinib, Pimavanserin, Pretomanid, Quizartinib, Ranolazine, Rimegepant, Selpercatinib, Selumetinib, Simeprevir, Sonidegib, Sparsentan, Tazemetostat, Ulipristal, Velpatasvir, Venetoclax, Voclosporin, Vonoprazan, Vorapaxar, Voxilaprevir</p> <p><b>Risk D: Consider therapy modification</b>                  Alfentanil, Atazanavir, Atogepant, Brigatinib, Clarithromycin, Cobicistat, Daclatasvir, Duvelisib, Erdafitinib, Ganaxolone, Glasdegib, Guanfacine, Hormonal Contraceptives, Larotrectinib, Lefamulin, Lortatinib, Lurasidone, Maraviroc, Mitapivat, Nirmatrelvir And Ritonavir, Peramppanel, Pirtobrutinib, Praziquantel, Protease Inhibitors, Ripretinib, Sildenafil, Trofinetide, Ubrogepant, Voxelotor, Zanubrutinib</p>
Pregnancy and Lactation	<p><b>Pregnancy:</b> Contraindicated. Avoid</p> <p><b>Lactation:</b> Not recommended. potential for serious adverse reactions</p>
Administration	<p>Oral: Administer with or without food.</p> <p>N.B. Refer to manufacturer PIL for specific considerations.</p>
Warnings/ Precautions	<ul style="list-style-type: none"> <li>• Hazardous agent (NIOSH 2016 [group 3]): Warning on adverse reproductive effects.</li> <li>• Avoid abrupt withdrawal, withdraw treatment gradually.</li> <li>• Fluid retention/peripheral edema may occur.</li> <li>• Hematologic effects: Dose-related decreases in hematocrit/hemoglobin may be observed, Monitor hemoglobin prior to treatment initiation, and periodically.</li> <li>• Hepatotoxicity</li> <li>• Hypersensitivity: Hypersensitivity reactions have been observed.</li> <li>• Pulmonary veno-occlusive disease: Include signs of pulmonary edema occur; may require discontinuation of Bosentan.</li> <li>• Risks of hepatotoxicity and birth defects, close supervision is required.</li> </ul>
Storage	<p>Store between 15°C and 30°C</p> <p>N.B. Refer to manufacturer PIL for specific considerations.</p>



## Hydralazine

<b>Generic Name</b>	Hydralazine
<b>Dosage form/strengths</b>	Tablets: 25mg, 50mg, 100mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antihypertensive; Vasodilator ATC: C02DB02
<b>Indications</b>	<b>Hypertension, chronic:</b> Management of moderate to severe hypertension. <b>Note:</b> Not recommended for the initial treatment of hypertension
<b>Dosage Regimen</b>	<b>Dosing: Adult</b> <b>Oral:</b> Initial: 25 mg 2 times daily followed by titration based on response to 50 mg 4 times daily. Usual dosage range: 100 to 200 mg/day in divided doses. Maximum dose: 300 mg/day in divided doses; however, doses >200 mg/day are generally avoided due to increased risk of lupus-like reaction <b>Dosing: Pediatric</b> <b>Hypertension, chronic:</b> Children and Adolescents: Oral: Initial: 0.75 mg/kg/day in 2 to 4 divided doses; maximum initial adult dose: 10 mg/dose; may increase gradually over 3 to 4 weeks; maximum daily dose: 7.5 mg/kg/day not to exceed 200 mg/day
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function:</b> GFR <30 mL/minute: reduce dose or administer usual dose at extended time intervals. use with caution. More likely to develop hydralazine toxicity. <b>Dosing: Hepatic Impairment:</b> Risk of accumulation. Adjust dose or intervals according to clinical response.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to hydralazine or any component of the formulation</li> <li>• Coronary artery disease</li> <li>• Mitral valve rheumatic heart disease</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> Hydralazine-induced lupus-like syndrome (HILS) has occurred in up to 10% of patients on doses $\geq 200$ mg for $\geq 3$ months and is reversible upon discontinuation. <b>Frequency not defined:</b> Cardiovascular: Acute myocardial infarction, angina pectoris, edema, flushing, hypotension, myocardial stimulation, palpitations, paradoxical response to antihypertensive, tachycardia Dermatologic: Pruritus, skin rash (including eczema), urticaria Gastrointestinal: Anorexia, constipation, diarrhea, nausea, paralytic ileus, vomiting Genitourinary: Difficulty in micturition Hematologic and oncologic: Agranulocytosis, eosinophilia, leukopenia, lymphadenopathy, purpuric disease, splenomegaly Hepatic: Hepatitis Nervous system: Chills, dizziness, headache, peripheral neuropathy, psychotic reaction (including anxiety, depression, disorientation, euphoria, hypomania, nervousness) Neuromuscular and skeletal: Arthralgia, muscle cramps, tremor Ophthalmic: Conjunctivitis, lacrimation



	Respiratory: Dyspnea, nasal congestion Miscellaneous: Fever
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Antinuclear antibody (ANA) titer</li> <li>• Blood pressure</li> <li>• Heart rate</li> <li>• Kidney functions</li> <li>• Complete blood cell count (CBC)</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Agents other than oral hydralazine are more recommended. Females with preexisting hypertension may continue their medication during pregnancy unless contraindications exist.</p> <p><b>Lactation:</b> Caution should be used if administered to a breastfeeding woman. Hydralazine is considered compatible with breastfeeding; however, sufficient information is not available following long-term use</p>
<b>Administration</b>	<p><b>Administration: Oral</b> Administer without regard to meals. However, food enhances bioavailability; administer consistently with regard to meals. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Cardiovascular disease: Use is contraindicated in patients with coronary artery disease (CAD). Use with caution in patients with cerebral vascular accidents and suspected CAD; myocardial stimulation produced by hydralazine can cause anginal attacks and electrocardiogram (ECG) changes of myocardial ischemia; has been implicated in the production of myocardial infarction.</li> <li>• Kidney impairment: Use with caution in patients with advanced kidney impairment; dosage adjustment recommended.</li> <li>• Mitral valvular disease: Use with caution in patients with mitral valvular disease; may increase pulmonary artery pressure in these patients. Use is contraindicated in patients with mitral valve rheumatic heart disease.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Macitentan

<b>Generic name</b>	<b>Macitentan</b>
<b>Dosage form/strengths</b>	Tablet 10mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Endothelin Receptor Antagonist; Vasodilator ATC: C02KX04
<b>Indications</b>	<b>Pulmonary arterial hypertension for adults</b>
<b>Dosage Regimen</b>	<b>Pulmonary arterial hypertension:</b> Adult: 10 mg daily. maximum 10 mg/day
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> There are no dosage adjustments necessary. Caution. avoid in patients undergoing dialysis (no information available). Consider monitoring blood pressure (risk of hypotension).</p> <p><b>Dosing: Hepatic Impairment: Adult</b> Mild impairment: Dose adjustments not necessary. Moderate to severe impairment: Use is not recommended. Baseline ALT or AST &gt;3x ULN: Initiation of therapy is not recommended.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Severe anaemia</li> <li>Pregnancy, breastfeeding</li> <li>Hypersensetivity</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Hematologic and oncologic: Anemia (13%) Nervous system: Headache (14%) Respiratory: Bronchitis (12%), nasopharyngitis (≤20%), pharyngitis (≤20%)</p> <p><b>1% to 10%:</b> Genitourinary: Urinary tract infection (9%) Hepatic: Increased serum transaminases (including increased serum alanine aminotransferase, increased serum aspartate aminotransferase; &gt;8 × ULN: 2%) Infection: Influenza (6%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Liver function before treatment, then monthly thereafter.</li> <li>Monitor haemoglobin concentration before treatment and then as indicated.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Strong CYP3A4 Inducers (eg. Barbiturates (phenobarbital), Carbamazepine, Phenytoin, Rifampicin), Strong CYP3A4 Inhibitors (eg. Clarithromycin, Itraconazole, Ketoconazole, Posaconazole), Fexinidazole, Fluconazole, Fusidic Acid (Systemic), Sparsentan</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid, because it may cause fetal harm. <b>Lactation:</b> No data. Avoid, Due to the potential for adverse reactions in breastfeeding infants.</p>
<b>Administration</b>	Oral: Swallow tablet whole. May be administered with or without food. N.B. Refer to manufacturer PIL for specific considerations.

<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hazardous agent (NIOSH 2016 [group 3]): Warning for embryofetal toxicity; special warnings on contraception for females while taking and 1-month post-treatment.</li> <li>• Fluid retention/peripheral edema: Use with caution in patients with severe chronic heart failure.</li> <li>• Hematologic effects: A reduction in hematocrit/hemoglobin has been observed and may occur early in therapy with subsequent stabilization. Decreases in hemoglobin rarely required transfusion. Measure hemoglobin prior to initiating therapy and repeat as clinically appropriate. Use is not recommended in patients with severe anemia.</li> <li>• Hepatic effects: Increases in serum liver aminotransferases, hepatotoxicity, and liver failure have been reported.</li> <li>• Pulmonary veno-occlusive disease: If signs of pulmonary edema occur, consider the possibility of PVOD; discontinue.</li> </ul>
<b>Storage</b>	<p>Store between 15<sup>o</sup>C to 30<sup>o</sup>C. N.B. Refer to manufacturer PIL for specific considerations.</p>

## Nitroprusside Sodium

<b>Generic Name</b>	<b>Nitroprusside Sodium</b>
<b>Dosage form/strengths</b>	Lyophilized powder for IM, IV injections: 50mg, 60mg
<b>Route of administration</b>	IM, IV
<b>Pharmacologic category</b>	Antihypertensive; Vasodilator ATC: C02DD01
<b>Indications</b>	<b>Acute decompensated heart failure Management.</b> <b>Hypertensive emergency:</b> Management of hypertensive crises; used for controlled hypotension to reduce bleeding during surgery.
<b>Dosage Regimen</b>	<b>Note: Safety:</b> Use may be limited due to risk for cyanide and thiocyanate toxicity, which is increased with higher doses (eg, >2 mcg/kg/minute) and/or prolonged duration of use, especially in patients with kidney or hepatic impairment. Invasive blood pressure monitoring, preferably via arterial line in a critical care unit, is recommended for appropriate dose titration. <b>Acute decompensated heart failure (adjunctive agent):</b> <b>Continuous infusion: IV:</b> Initial: 0.1 to 0.3 mcg/kg/minute; titrate as needed every 5 to 15 minutes to achieve desired hemodynamic effect; usual dosage range: 1 to 3 mcg/kg/minute; maximum dose: 5 mcg/kg/minute for an 80 kg patient <b>Hypertensive emergency:</b> <b>Note:</b> Consider for use when preferred agents with less toxicity are unavailable. <b>Continuous infusion: IV:</b> Initial: 0.25 to 0.5 mcg/kg/minute; titrate as needed by 0.5 mcg/kg/minute every 5 minutes to achieve the target blood pressure; to avoid toxicity, limit dose to $\leq 2$ mcg/kg/minute if possible; maximum dose: 10 mcg/kg/minute. Higher doses (eg, 8 to 10 mcg/kg/minute) should only be used for a maximum of 10 minutes; use for the shortest duration possible to avoid toxicity
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> Use in patients with kidney impairment may lead to the accumulation of thiocyanate and subsequent toxicity; limit use. eGFR <30 mL/minute/1.73 m <sup>2</sup> : Limit mean infusion rate to <3 mcg/kg/minute. Anuric patients: Limit mean infusion rate to 1 mcg/kg/minute. <b>Dosing: Hepatic Impairment: Adult</b> Risk of cyanide toxicity, use with caution. Avoid in hepatic failure.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Acute heart failure</li> <li>• Impaired cerebral circulation</li> <li>• Compensatory hypertension (aortic coarctation, arteriovenous shunting)</li> <li>• Hereditary optic nerve atrophy (leber's disease) or toxic amblyopia</li> <li>• Severe vitamin B<sub>12</sub> deficiency</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Frequency not defined.</b> Cardiovascular: Bradycardia, ECG changes, flushing, palpitations, severe hypotension, substernal pain, tachycardia Central nervous system: Apprehension, dizziness, headache, increased intracranial pressure, restlessness Dermatologic: Diaphoresis, localized erythematous streaking, skin rash

	<p>Endocrine and metabolic: Hypothyroidism</p> <p>Gastrointestinal: Abdominal pain, intestinal obstruction, nausea, retching</p> <p>Hematologic and oncologic: Decreased platelet aggregation, methemoglobinemia</p> <p>Local: Irritation at injection site</p> <p>Neuromuscular and skeletal: Muscle twitching</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure (including arterial line)</li> <li>• Heart rate</li> <li>• Venous oxygen saturation and acid-base status as acidosis can be the earliest sign of cyanide toxicity</li> <li>• Blood cyanide concentration</li> <li>• Blood thiocyanate levels if requiring prolonged infusion (&gt;3 days) or dose &gt;3 mcg/kg/minute or patient has kidney dysfunction</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Phosphodiesterase Inhibitors (e.g sildenafil, tadalafil, vardenafil, and avanafil), Riociguat</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid prolonged use. Accumulation of Cyanide in fetus may occur.</p> <p><b>Lactation:</b> Due to the potential for serious adverse reactions in the breastfed infant, discontinue either drug administration or breastfeeding.</p>
<b>Administration</b>	<p><b>Usual Infusion Concentrations: Pediatric</b> <b>IV infusion:</b> 100 mcg/mL or 200 mcg/mL.</p> <p><b>Usual Infusion Concentrations: Adult</b> <b>IV infusion:</b> 50 mg in 250 mL (concentration: 200 mcg/mL) or 100 mg in 250 mL (concentration: 400 mcg/mL) of D<sub>5</sub>W</p> <p><b>Administration: IV</b> IV infusion only; infusion pump required. Due to potential for excessive hypotension, continuously monitor patient's blood pressure during therapy. Product should always be protected from light.</p> <p><b>Preparation for Administration: Adult</b> Prior to administration, nitroprusside sodium should be further diluted by diluting 50 mg in 250 to 1,000 mL of D<sub>5</sub>W (preferred) Use only clear solutions; solutions of nitroprusside exhibit a color described as brownish, brown, brownish-pink, light orange, and straw. Solutions are highly sensitive to light. Exposure to light causes decomposition, resulting in a highly colored solution of orange, dark brown or blue. <b>A blue color indicates almost complete decomposition.</b> Do not use discolored solutions (eg, blue, green, red) or solutions in which particulate matter is visible. <b>N.B.</b> Prepared solutions should be wrapped as soon as possible with aluminum foil or other opaque material to protect from light. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Cyanide toxicity: Occurs in prolonged use or at rate of infusion more than (2 mcg/kg/minute), nitroprusside gives rise to large cyanide quantities. Do not use the maximum dose for more than 10 minutes. Monitor for cyanide toxicity via acid-base balance and venous oxygen concentration; however, they are not always reliable indicators.</li> </ul>

	<ul style="list-style-type: none"> <li>• Hypotension: Can cause excessive hypotension leading to hypoperfusion of vital organs. Hypotension generally resolves within 1 to 10 minutes after discontinuation of the nitroprusside infusion; continuous blood pressure monitoring by experienced personnel is required.</li> <li>• Increased intracranial pressure: Use may elevate intracranial pressure.</li> <li>• Methemoglobinemia: Nitroprusside can cause a dose-dependent conversion of hemoglobin to methemoglobin. Methemoglobinemia should be suspected in any patient receiving &gt;10 mg/kg of nitroprusside and exhibiting signs of impaired oxygen delivery despite adequate cardiac output and arterial pO<sub>2</sub>. Symptomatic patients, regardless of methemoglobin level should be treated with methylene blue (first-line).</li> <li>• Thiocyanate toxicity: Can occur in patients with kidney impairment or those on prolonged infusions (ie, &gt;3 mcg/kg/minute for &gt;72 hours).</li> </ul> <p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Anemia: When nitroprusside is used for controlled hypotension during surgery, correct pre-existing anemia prior to use when possible.</li> <li>• Hepatic impairment: Use with extreme caution in patients with hepatic and Kidney impairment.</li> <li>• Hypovolemia: When nitroprusside is used for controlled hypotension during surgery, correct pre-existing hypovolemia prior to use when possible.</li> <li>• Myocardial infarction: Use caution in patients with acute myocardial infarction because of hemodynamic effects and possible coronary steal.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Appropriate administration: Solution must be further diluted with 5% dextrose in water. Do not administer by direct injection</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C. Protect from light; recommended to store in carton until used.</p> <p>Stability of parenteral admixture in Dextrose 5% at room temperature (25°C) and at refrigeration temperature (4°C) is 24 hours.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Antiplatelet Drugs

## Acetylsalicylic acid

<b>Generic Name</b>	<b>Acetylsalicylic acid</b>
<b>Dosage form/strengths</b>	<p><b>Tablet:</b> 75 mg, 100 mg, 250 mg single or in combination, 300 mg single or in combination, 320 mg, 500 mg</p> <p><b>Chewable tablet:</b> 75 mg, 81 mg, 150 mg</p> <p><b>Film coated tablet:</b> 250 mg in combination, 75 mg in combination, 770 mg in combination</p> <p><b>Enteric coated tablet:</b> 75 mg, 81 mg, 100 mg, 325 mg</p> <p><b>Effervescent tablet:</b> 325 mg, 400 mg in combination, 500 mg in combination,</p> <p><b>Capsule:</b> 250 mg in combination</p> <p><b>Hard gelatin capsule:</b> 75 mg in combination</p> <p><b>Rectal suppository:</b> 200 mg in combination</p>
<b>Route of administration</b>	Oral, rectal
<b>Pharmacologic category</b>	<p><b>Pharmacological category:</b> Analgesic, Nonopioid; Antipyretic; Antiplatelet Agent; Nonsteroidal Anti-inflammatory Drug (NSAID)</p> <p><b>ATC:</b> Tablet as NSAID: N02BA01 Acetylsalicylic acid preparations specifically intended for use as antithrombotic agents: B01AC06</p>
<b>Indications</b>	<p><b>Analgesic, antipyretic, and anti-inflammatory:</b> For the temporary relief of headache, pain, and fever caused by colds, muscle aches and pains, menstrual pain, toothache pain, migraine and minor aches and pains of arthritis.</p> <p><b>Vascular indications:</b> including ischemic stroke, transient ischemic attack, acute coronary syndromes, secondary prevention after acute coronary syndromes, and management of stable ischemic heart disease, and after coronary artery bypass graft.</p> <p><b>Use: Off-Label: Adult</b> Preeclampsia prevention; Surgical prosthetic heart valve replacement, thromboprophylaxis; Venous thromboembolism prevention, pulmonary embolism prevention.</p>
<b>Dosage Regimen</b>	<p><b>Check dosage regimen in product labelling in case of combination products.</b></p> <p><b>Adult and Geriatric:</b> <b>Analgesic and antipyretic:</b> Oral: 300 mg to 900 mg every 4 to 6 hours as needed; usual maximum daily dose: 4 g/day Rectal suppository: 450–900 mg every 4 hours; maximum 3.6 g per day.</p> <p><b>Migraine, acute treatment:</b> (For mild to moderate attacks not associated with vomiting or severe nausea) IR Oral tablet: 900 mg or 1 g once.</p> <p><b>Management of cardiovascular diseases:</b> 75mg-150mg once daily. Higher doses up to 300mg may be needed in acute cases for short time.</p> <p><b>Following coronary by-pass surgery</b> Oral: Adult: 75–300 mg daily</p> <p><b>Pediatric doses:</b></p> <ul style="list-style-type: none"> <li>(Do not use aspirin in pediatric patients &lt;18 years who have or who are</li> </ul>



	<p>recovering from chickenpox or flu symptoms (eg, viral illness) due to the association with Reye's)</p> <ul style="list-style-type: none"> <li>Aspirin should only be given to children under 16 on the advice of a doctor when the potential benefits outweigh the risks.</li> </ul> <p><b>Antiplatelet, Prevention of thrombus formation after cardiac surgery</b></p> <p>Oral:</p> <ul style="list-style-type: none"> <li>Neonate: 1–5 mg/kg once daily.</li> <li>Child 1 month–11 years: 1–5 mg/kg once daily (max. per dose 75 mg)</li> <li>Child 12–17 years: 75 mg once daily</li> </ul> <p><b>Kawasaki disease</b></p> <p>Oral</p> <ul style="list-style-type: none"> <li>Neonate: Initially 8 mg/kg 4 times a day for 2 weeks or until afebrile, followed by 5 mg/kg once daily for 6–8 weeks, if no evidence of coronary lesions after 8 weeks, discontinue treatment or seek expert advice.</li> <li>Child 1 month–11 years: Initially 7.5–12.5 mg/kg 4 times a day for 2 weeks or until afebrile, then 2–5 mg/kg once daily for 6–8 weeks, if no evidence of coronary lesions after 8 weeks, discontinue treatment or seek expert advice</li> </ul> <p><b>Mild to moderate pain, Pyrexia</b></p> <p>Oral: Child 12–17 years: 300–600 mg every 4–6 hours as required, maximum 2.4 g per day.</p> <p><b>Anti-inflammatory (juvenile idiopathic arthritis): Limited data available:</b></p> <p><u>Infants, Children, and Adolescents:</u> Oral: Initial: 60 to 90 mg/kg/day in divided doses; Maintenance: 80 to 100 mg/kg/day divided every 6 to 8 hours; monitor serum concentrations.</p>
<p><b>Dosage adjustment</b></p>	<p><b><u>Dosing: Renal Impairment: Adult</u></b></p> <p><b>Antiplatelet uses:</b> No dosage adjustment necessary</p> <p><b>Analgesia or anti-inflammatory uses:</b> CrCl &gt;10 mL/minute: Caution. High doses have been associated with acute kidney injury (AKI) Use lowest effective dosage and limit duration of therapy. CrCl &lt;10 mL/minute: Avoid use. May exacerbate uremic gastrointestinal and hematologic symptoms.</p> <p><b><u>Dosing: Renal Impairment: pediatrics</u></b> GFR ≥10 mL/minute/1.73 m<sup>2</sup>: Caution. GFR &lt;10 mL/minute/1.73 m<sup>2</sup>: Avoid use.</p> <p><b><u>Dosing: Hepatic Impairment: Adult, pediatrics</u></b> Caution in mild to moderate cases. Avoid use in severe liver disease.</p>
<p><b>Contra-indications</b></p>	<ul style="list-style-type: none"> <li>Hypersensitivity to NSAIDs</li> <li>Patients with asthma, rhinitis, and nasal polyps</li> <li>Active peptic ulceration</li> <li>Use in children or teenagers for viral infections, with or without fever.</li> </ul>
<p><b>Adverse Drug Reactions</b></p>	<p>Many adverse reactions with aspirin are dose related and are rare at low dosages plus presence of other risk factors.</p> <p><b><u>GI effects:</u></b></p>

	<p>Symptomatic or complicated gastrointestinal ulcers (upper, or lower) and GI mucosal damage. Symptoms can range from mild (dyspepsia) to severe (peptic ulcer disease, gastrointestinal hemorrhage). Enteric-coated preparations of aspirin do not decrease the risk of upper gastrointestinal events.</p> <p><b><u>Hypersensitivity reactions (immediate and delayed)</u></b>                  Involving the skin (eg, angioedema, urticaria), airways (eg, dyspnea, rhinorrhea), and/or other organs have been reported. Delayed hypersensitivity reactions, including drug rash with eosinophilia and systemic symptoms, have also been rarely associated with aspirin.</p> <p>- <b><u>Other adverse effects but frequency not defined:</u></b>  <b>Cardiovascular:</b> Cardiac arrhythmia, hypotension, tachycardia  <b>Endocrine and metabolic:</b> Dehydration, hyperglycemia, hyperkalemia, hypoglycemia (children), increased thirst, metabolic acidosis  <b>Gastrointestinal:</b> Abdominal pain, dyspepsia, gastrointestinal perforation, gastrointestinal ulcer, heartburn, nausea, vomiting  <b>Genitourinary:</b> Postpartum hemorrhage, post-term pregnancy, prolonged labor, proteinuria, stillborn infant  <b>Hematologic and oncologic:</b> Disorder of hemostatic components of blood, disseminated intravascular coagulation, hemorrhage, prolonged bleeding time, prolonged prothrombin time, thrombocytopenia  <b>Hepatic:</b> Hepatitis, increased liver enzymes  <b>Nervous system:</b> Agitation, brain edema, coma, confusion, dizziness, headache, hypothermia, lethargy, seizure  <b>Renal:</b> Increased blood urea nitrogen, increased serum creatinine, interstitial nephritis, renal failure syndrome, renal insufficiency, renal papillary necrosis  <b>Respiratory:</b> Hyperventilation, laryngeal edema, pulmonary edema, respiratory alkalosis, tachypnea  <b>Miscellaneous:</b> Fever, low birth weight</p>
<p><b>Monitoring Parameters</b></p>	<p>In prolonged therapy:</p> <ul style="list-style-type: none"> <li>• CBC, iron studies, ferritin</li> <li>• Stools for occult blood</li> <li>• Liver function tests, and renal function tests.</li> <li>• Monitor for signs and symptoms of bleeding and drug reaction with eosinophilia and systemic symptoms (eg, fever, rash, lymphadenopathy, eosinophilia in association with other organ system involvement such as hepatitis, nephritis, hematological abnormalities, myocarditis, myositis; early symptoms of hypersensitivity reaction may occur without rash).</li> </ul>
<p><b>Drug Interactions</b></p>	<p><b><i>Risk X: Avoid combination</i></b>                  Dexibuprofen, Dexketoprofen, Influenza Virus Vaccine (Live/Attenuated), Ketorolac (Nasal, systemic), Macimorelin, Omacetaxine, Probenecid, Sulfapyrazone, Urokinase, Varicella Virus-Containing Vaccines.</p> <p><b><i>Risk D: Consider therapy modification</i></b>                  Abrocitinib, Apixaban, Bemiparin, Caplacizumab, Carbonic Anhydrase Inhibitors, Dabigatran Etxilate, Edoxaban, Enoxaparin, Ginkgo Biloba, Heparin, Methotrexate, Nonsteroidal Anti-Inflammatory Agents (COX-2 Selective, nonselective, topical), Pralatrexate, Rivaroxaban, Sincalide, Sucroferric Oxyhydroxide, Talniflumate, Ticagrelor, Vitamin K Antagonists (eg, warfarin).</p>

<b>Pregnancy and Lactation</b>	<p><b><u>Pregnancy consideration:</u></b></p> <ul style="list-style-type: none"> <li>• Avoid aspirin use during the third trimester of pregnancy (starting at 30 weeks of gestation).</li> <li>• If NSAID treatment is deemed necessary between 20 to 30 weeks of pregnancy, limit use to the lowest effective dose and shortest duration possible.</li> <li>• These recommendations do not apply to low-dose 81 mg aspirin prescribed for certain conditions in pregnancy.</li> <li>• When needed as analgesic. Other agents are preferred and use in the third trimester is not recommended.</li> </ul> <p><b><u>Lactation consideration:</u></b></p> <p>- Occasional doses or low-dose aspirin are considered to be compatible with breastfeeding - Long-term therapy and high doses of aspirin while breastfeeding is not recommended due to the possible risk of Reye syndrome. Consider monitoring the infant for adverse effects (hemolysis, prolonged bleeding, metabolic acidosis).</p>
<b>Administration</b>	<p><b><u>Administration: Adult</u></b></p> <p><b><u>Oral:</u></b></p> <p><b>Tablets, capsule:</b> Swallow whole; do not cut, crush, or chew. Administer with food or a full glass of water or milk to minimize GI distress.</p> <p>But in situations for which a rapid onset of action is required (eg, acute treatment of myocardial infarction), patients chew tablet.</p> <p>Preeclampsia (prevention): Administration as an evening dose may be more beneficial than administration in the morning.</p> <p><b>Enteric coated tablet:</b> Do not cut, crush, or chew. Administer with a full glass of water at the same time each day.</p> <p><b>Rectal:</b> Remove suppository from plastic packet and insert into rectum as far as possible.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b><u>Disease-related concerns:</u></b></p> <ul style="list-style-type: none"> <li>• <b><u>Bariatric surgery:</u></b> <ul style="list-style-type: none"> <li>– Altered absorption and efficacy may occur.</li> <li>– Increase Gastric ulceration: Evaluate the risk vs benefit of aspirin after surgery; if aspirin therapy is continued (eg, cardiovascular indications), use the lowest possible dose with concurrent administration of proton pump inhibitor (PPI).</li> </ul> </li> <li>• <b><u>Bleeding disorders:</u></b> Use with caution in patients with platelet and bleeding disorders.</li> <li>• <b><u>Dehydration:</u></b> Use with caution in patients with dehydration.</li> <li>• <b><u>Ethanol use:</u></b> Increased bleeding risks.</li> <li>• <b><u>Gastrointestinal disease:</u></b> Use with caution in patients with erosive gastritis. Avoid use in patients with active peptic ulcer disease.</li> <li>• <b><u>Hepatic impairment:</u></b> Avoid use in severe hepatic failure.</li> <li>• <b><u>Renal impairment:</u></b> Use high dosages (eg, analgesic or anti-inflammatory uses) with caution. Low-dose aspirin (eg, 75 to 162 mg daily) may be safely used in patients with any degree of renal impairment.</li> </ul> <p><b><u>Concurrent drug therapy issues:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Thrombolytics:</b> In the treatment of acute ischemic stroke, avoid aspirin for 24 hours following administration of a thrombolytic; administration within 24 hours</li> </ul>

increases the risk of hemorrhagic transformation.

**Special populations:**

- **GI bleed patients:** Aspirin for primary prevention of cardiovascular events should be avoided in most patients with GI bleed who do not have high risk factors for cardiovascular events. However, aspirin for secondary cardiovascular prevention should not be discontinued in patients with established cardiovascular disease, even in the setting of a GI bleed. If held in the setting of a GI bleed, aspirin for secondary cardiovascular prevention should be resumed on the day hemostasis is confirmed by endoscopy.
- **Pediatric:** Do not use aspirin in pediatric patients <18 years of age who have or who are recovering from chickenpox or flu symptoms.
- **Geriatric:** are at high risk for adverse effects from NSAIDs, Using the lowest effective dose for shortest period possible is recommended.

**Other warnings/precautions:**

- **Resistance:** Aspirin resistance is defined as measurable, persistent platelet activation that occurs in patients prescribed a therapeutic dose of aspirin. Aspirin resistance is likely dose-related but may be influenced by dynamic factors yet to be identified; further research is required.

**Storage**

- Store oral dosage forms (tablets, capsules, effervescent tablet) between 15°C to 30°C; protect from moisture;
- Keep suppositories in refrigerator; do not freeze.
- Hydrolysis of aspirin occurs upon exposure to water or moist air, resulting in salicylate and acetate, which possess a vinegar-like odor. Do not use if a strong odor is present.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Cilostazol

<b>Generic name</b>	<b>Cilostazol</b>
<b>Dosage form/strengths</b>	Cilostazol 50, 100 mg tablets
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antiplatelet Agent; Phosphodiesterase-3 Enzyme Inhibitor; Vasodilator ATC: B01AC23
<b>Indications</b>	<b><u>Intermittent claudication:</u></b> Reduction of symptoms of intermittent claudication due to peripheral vascular disease, and increase walking distance.
<b>Dosage Regimen</b>	<b><u>-Adults:</u></b> <b><u>-Intermittent claudication: Oral:</u></b> -Immediate-release: 100 mg twice daily -A dosage of 50 mg twice daily should be considered for patients concomitantly receiving inhibitors of CYP3A4 or CYP2C19.
<b>Dosage adjustment</b>	<b><u>-Renal Impairment:</u></b> -Mild to moderate renal impairment: No dosage adjustment necessary -Severe renal impairment: use with caution as increases metabolite concentrations occur.  <b><u>-Hepatic Impairment:</u></b> -Mild impairment: No dose adjustment necessary. - Moderate to severe impairment: There are no dosage adjustments available. It has not been studied.
<b>Contra-indications</b>	-Hypersensitivity to Cilostazol or any component of the formulation. -Heart failure of any severity.
<b>Adverse Drug Reactions</b>	<b><u>&gt;10%:</u></b> -Central nervous system: Headache (27% to 34%) -Gastrointestinal: Diarrhea (12% to 19%), abnormal stools (12% to 15%) -Infection: Infection (10% to 14%) -Respiratory: Rhinitis (7% to 12%)  <b><u>-1% to 10%:</u></b> -Cardiovascular: Palpitations (5% to 10%), peripheral edema (7% to 9%), tachycardia (4%), atrial fibrillation (<2%), atrial flutter (<2%), cardiac arrest (<2%), cardiac failure (<2%), cerebral infarction (<2%), edema (<2%), facial edema (<2%), hypotension (<2%), myocardial infarction (<2%), nodal arrhythmia (<2%), orthostatic hypotension (<2%), supraventricular tachycardia (<2%), syncope (<2%), varicose veins (<2%), ventricular premature contractions (<2%), ventricular tachycardia (<2%) -Central nervous system: Dizziness (9% to 10%), vertigo (3%), anxiety (<2%), chills (<2%), insomnia (<2%), malaise (<2%), neuralgia (<2%) -Dermatologic: Ecchymoses (<2%), furunculosis (eye: <2%), skin hypertrophy (<2%), urticaria (<2%), xeroderma (<2%) -Endocrine and metabolic: Albuminuria (<2%), diabetes mellitus (<2%), gout (<2%), hyperlipidemia (<2%), hyperuricemia (<2%), increased gamma-glutamyl transferase (<2%) -Gastrointestinal: Nausea (7%), dyspepsia (6%), abdominal pain (4% to 5%),

	<p>flatulence (3%), anorexia (&lt;2%), cholelithiasis (&lt;2%), colitis (&lt;2%), duodenal ulcer (&lt;2%), duodenitis (&lt;2%), esophageal hemorrhage (&lt;2%), esophagitis (&lt;2%), gastric ulcer (&lt;2%), gastritis (&lt;2%), gastroenteritis (&lt;2%), gingival hemorrhage (&lt;2%), hematemesis (&lt;2%), melena (&lt;2%), peptic ulcer (&lt;2%), periodontal abscess (&lt;2%)</p> <p>-Genitourinary: Cystitis (&lt;2%), pelvic pain (&lt;2%), urinary frequency (&lt;2%), vaginal hemorrhage (&lt;2%), vaginitis (&lt;2%)</p> <p>-Hematologic and oncologic: Anemia (&lt;2%), hemorrhage (&lt;2%), hemorrhage (eye, &lt;2%), iron deficiency anemia (&lt;2%), polycythemia (&lt;2%), purpura (&lt;2%), rectal hemorrhage (&lt;2%), retroperitoneal hemorrhage (&lt;2%)</p> <p>-Hypersensitivity: Tongue edema (&lt;2%)</p> <p>-Neuromuscular and skeletal: Back pain (7%), myalgia (3%), arthralgia (&lt;2%), bursitis (&lt;2%), neck stiffness (&lt;2%), ostealgia (&lt;2%)</p> <p>-Ophthalmic: Amblyopia (&lt;2%), blindness (&lt;2%), conjunctivitis (&lt;2%), diplopia (&lt;2%), retinal hemorrhage (&lt;2%)</p> <p>-Otic: Otagia (&lt;2%), tinnitus (&lt;2%)</p> <p>-Renal: Increased serum creatinine (&lt;2%)</p> <p>-Respiratory: Pharyngitis (10%), cough (3% to 4%), asthma (&lt;2%), epistaxis (&lt;2%), hemoptysis (&lt;2%), pneumonia (&lt;2%), sinusitis (&lt;2%)</p> <p>-Miscellaneous: Fever (&lt;2%)</p>
<b>Monitoring Parameters</b>	<p>-Platelets and WBC counts periodically.</p> <p>- Monitoring for the development of a new systolic murmur or cardiac symptoms.</p>
<b>Drug Interactions</b>	<p><b><u>-Risk X: Avoid combination</u></b> Anagrelide, Fexinidazole, Fusidic Acid (Systemic), Pimozide, Urokinase</p> <p><b><u>-Risk D: Consider therapy modification</u></b> Cladribine, CYP2C19 Inhibitors (Moderate), CYP3A4 Inhibitors (Amiodarone, Aprepitant, Cimetidine, Ciprofloxacin, Clarithromycin, Diltiazem, Erythromycin, Fluconazole, Grapefruit juice, Itraconazole, Ketoconazole, Posaconazole, Voriconazole, Verapamil), Enoxaparin, Heparin, Lemborexant, Lomitapide, Lonafarnib, Omeprazole, Sirolimus (Protein Bound), Ubrogepant</p>
<b>Pregnancy and Lactation</b>	<p><b><u>-Pregnancy:</u></b> There are no well-controlled, adequate clinical studies in pregnant women. Adverse events have been observed in animal reproduction studies.</p> <p><b><u>-Lactation:</u></b> No human data. Due to potential for serious adverse events in breast-feeding infants, discontinue cilostazol or discontinue breast-feeding.</p>
<b>Administration</b>	<p>Oral: Administer on empty stomach (30 minutes before or 2 hours after meals). Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>-Avoid use in patients with active pathological bleeding or hemostatic disorders.</p> <p>-Patients with history of ischemic heart disease may be at increased risk for exacerbation of angina pectoris or myocardial infarction.</p> <p>-Use with caution in patients with moderate to severe hepatic impairment and severe renal impairment.</p> <p>-If a patient is to undergo elective surgery, Cilostazol should be discontinued at least 2 days prior to the surgery to recover adequate platelet function.</p>
<b>Storage</b>	<p>-Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.</p>



## Clopidogrel

<b>Generic Name</b>	Clopidogrel
<b>Dosage form/strengths</b>	Tablet 75mg, 300mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antiplatelet Agent; Antiplatelet Agent, Thienopyridine; P2Y12 Antagonist ATC: B01AC04
<b>Indications</b>	<b>Acute coronary syndrome:</b> ST-segment elevation myocardial infarction Non-ST-segment elevation acute coronary syndromes <b>Myocardial infarction, ischemic stroke, or peripheral atherosclerotic disease</b>
<b>Dosage Regimen</b>	<b>Dosing: adult</b> <b>Acute coronary syndrome:</b> <b>ST-segment elevation myocardial infarction:</b> - Age ≤75 years: <b>Oral:</b> Initial loading dose: 300 mg once at the time of diagnosis; followed by 75 mg once daily. - Age >75 years: <b>Oral:</b> 75 mg once daily. <b>Non-ST-segment elevation acute coronary syndromes:</b> <b>Oral:</b> Initial: 600 mg once at the time of diagnosis; followed by 75 mg once daily. <b>Myocardial infarction, ischemic stroke, or peripheral atherosclerotic disease</b> <b>Peripheral atherosclerotic disease:</b> 75 mg once daily
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function:</b> No dosage adjustment necessary. use with caution. <b>Dosing: Hepatic Impairment:</b> Caution in moderate impairment in patients with an increased risk of bleeding—limited information available; avoid in severe impairment.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity (eg, anaphylaxis) to clopidogrel or any component of the formulation</li> <li>• Active pathological bleeding (eg, peptic ulcer, intracranial hemorrhage).</li> <li>• Significant liver impairment or cholestatic jaundice</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> Bleeding Hypersensitivity reactions (immediate and delayed) Thrombotic thrombocytopenic purpura <b>1% to 10%:</b> Hematologic and oncologic: Major hemorrhage (≤4%; major hemorrhage, life-threatening: ≤2%), minor hemorrhage (4% to 5%) <b>&lt;1%:</b> Cardiovascular: Hemorrhagic stroke Nervous system: Intracranial hemorrhage
<b>Monitoring Parameters</b>	Signs of bleeding; hemoglobin and hematocrit periodically.
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Abrocitinib, Amodiaquine, Esomeprazole, Omeprazole, Pazopanib, Rimegepant,

	<p>Topotecan, Urokinase</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Alpelisib, Apixaban, Bemiparin, Berotralstat, Cangrelor, Caplacizumab, Cladribine, Cobicistat, CYP2C19 Inducers (Strong), CYP2C19 Inhibitors (Strong), Dabigatran Etexilate, Daprodustat, Enoxaparin, Etravirine, Grapefruit Juice, Heparin, Morphine (Systemic), Repaglinide, Ritonavir, Rivaroxaban, Selexipag, Sodium Zirconium Cyclosilicate, Ubrogepant</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Not recommended due to limited data. Available guidelines recommend using clopidogrel only when strictly needed and for the shortest duration possible until additional fetal safety data are available.</p> <p><b>Lactation:</b> Adverse events have not been reported in breastfed infants (limited data). Not recommended.</p>
<b>Administration</b>	<p>Administer without regard to meals. Avoid or minimize the consumption of grapefruit juice.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Lacunar stroke: In patients with recent lacunar stroke (within 180 days), the use of clopidogrel in addition to aspirin did not significantly reduce the incidence of the primary outcome of stroke recurrence compared to aspirin alone; the use of clopidogrel in addition to aspirin did, however, increase the risk of major hemorrhage and the rate of all-cause mortality.</li> <li>• Caution in patients with risk or history of non-traumatic bleeding.</li> <li>• Consider use of another platelet P2Y<sub>12</sub> inhibitor in patients identified as CYP2C19 poor metabolizers due to reduced antiplatelet effect.</li> <li>• Renal impairment: Use with caution in patients with kidney impairment.</li> <li>• Surgical patients: In patients undergoing cardiac surgery (eg, coronary artery bypass graft surgery), discontinue clopidogrel at least 24 hours and up to 5 days before surgery in consultation with a cardiologist, interventional cardiologist, and cardiac surgeon.</li> <li>• Coronary artery stents: Premature interruption of therapy may result in stent thrombosis with subsequent myocardial infarction.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>



## Ticagrelor

<b>Generic Name</b>	<b>Ticagrelor</b>
<b>Dosage form/strengths</b>	Tablets: 60mg, 90mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antiplatelet Agent, Non-thienopyridine; P2Y <sub>12</sub> Antagonist
<b>Indications</b>	<b>Prevention of atherothrombotic events</b> in patients with acute coronary syndrome and in Patients with a history of myocardial infarction and a high risk of an atherothrombotic event.
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b>  <b>Prevention of atherothrombotic events in patients with</b></p> <p>a) Acute coronary syndrome:                      Oral: Initially 180 mg for 1 dose, then 90 mg twice daily for up to a year (in combination with aspirin).</p> <p>b) History of myocardial infarction and a high risk of an atherothrombotic event:                      Oral: 60 mg twice daily (in combination with aspirin).</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b>                      No dose adjustment necessary.</p> <p><b>Dosing: Hepatic Impairment: Adult</b>                      Mild impairment: No dosage adjustment necessary.                      Moderate impairment: limited experience. Use caution as it undergoes hepatic metabolism                      Severe impairment: Avoid use.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity (eg, angioedema) to ticagrelor or any component of the formulation</li> <li>• Active pathological bleeding (eg, peptic ulcer)</li> <li>• History of intracranial hemorrhage</li> <li>• Severe hepatic impairment</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions:</b>  <b>Significant Considerations:</b></p> <p><u>Bleeding</u>: Ticagrelor may cause hemorrhage, including major hemorrhage. risk factors: recent trauma, surgery, gastrointestinal bleeding, or coagulation disorders and in cases of concurrent use of other medications that increase bleeding risk</p> <p><u>Brady arrhythmias</u>:                      Risk factors include Concurrent use of AV nodal blocking agents or Underlying conduction disorder unless pacemaker fitted.</p> <p><u>Respiratory effects</u>, including dyspnea and sleep apnea. Risk factor is chronic obstructive pulmonary disease</p> <p><b>&gt;10%:</b> Respiratory: Dyspnea (14% to 21%)</p> <p><b>1% to 10%:</b>                      Cardiovascular: ECG abnormality (ventricular pause: 2% to 6%)                      Gastrointestinal: Nausea (4%)                      Hematologic and oncologic: Hemorrhage (4%; major hemorrhage: 4%)                      Nervous system: Dizziness (5%)</p>

	<p>Neuromuscular and skeletal: Gout (<math>\leq 2\%</math>)                  Renal: Increased serum creatinine (4% to 7%; transient)  <b>Frequency not defined:</b> Endocrine and metabolic: Increased uric acid.</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• CBC</li> <li>• Sign/symptoms of bradycardia, dyspnea, bleeding</li> <li>• Renal function</li> <li>• Uric acid levels (patients with gout or at risk of hyperuricemia)</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Abrocitinib, Strong CYP3A4 Inducers (e.g. Barbiturates (phenobarbital) Carbamazepine Phenytoin Rifampicin), Strong CYP3A4 Inhibitors (e.g Clarithromycin Itraconazole Ketoconazole Posaconazole), Fexinidazole, Fusidic Acid (Systemic), Urokinase</p> <p><b>Risk D: Consider therapy modification</b>                  Apixaban, Aspirin, Bemiparin, Caplacizumab, Dabigatran Etxilate, Edoxaban, Enoxaparin, Heparin, Lomitapide, Lovastatin, Morphine (Systemic), Rivaroxaban, Simvastatin</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Limited Human Data, Animal Data Suggest Risk. Not recommended.  <b>Lactation:</b> No Human Data, Potential Toxicity. Not recommended</p>
<b>Administration</b>	<p>Oral: Administer with or without food.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hyperuricemia: Risk of hyperuricemia may be increased. Caution in history of hyperuricemia.</li> <li>• Bleeding disorders: Use with caution in patients with platelet disorders, bleeding disorders, performance of percutaneous invasive procedures, and/or at increased risk for bleeding. In order to decrease the risk of bleeding, discontinue ticagrelor at least 5 days prior to any surgery, particularly in those with a high risk of bleeding, when possible; ticagrelor may be resumed once hemostasis achieved.</li> <li>• Antifibrinolytic therapy (aminocaproic acid or tranexamic acid) and/or recombinant factor VII may enhance hemostasis. Ticagrelor may be resumed after the cause of bleeding have been identified and controlled.</li> <li>• False-negative results may occur for platelet activation functional assays, which are used to diagnose heparin-induced thrombocytopenia.</li> <li>• Renal impairment: Creatinine levels may rise during therapy; monitor renal function.</li> <li>• Maintenance doses of aspirin <math>&gt;100</math> mg daily reduce the effectiveness of ticagrelor and should be avoided.</li> <li>• Do not start ticagrelor in patients undergoing urgent coronary artery bypass graft surgery.</li> <li>• In patients with moderate hepatic impairment, consider the risks and benefits of treatment, noting the probable increase in exposure to ticagrelor. Avoid in severe impairment.</li> </ul>
<b>Storage</b>	<p>Store between <math>15^{\circ}\text{C}</math> to <math>30^{\circ}\text{C}</math>.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Beta- Blockers

## Atenolol

<b>Generic name</b>	<b>Atenolol</b>
<b>Dosage form/strengths</b>	Tablets: 25 mg, 50 mg and 100 mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Beta1-selective adrenergic blocking agent ATC: C07AB03
<b>Indications</b>	<ul style="list-style-type: none"> <li>• <b>Hypertension</b> management</li> <li>• <b>Angina:</b> Long-term management of patients with angina pectoris.</li> <li>• <b>Myocardial infarction:</b> Early treatment and secondary prevention</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Hypertension:</b> 25 mg once or twice daily; increase gradually as needed based on response and tolerability by more than a week interval up to 100 mg/day in 1 or 2 divided doses</p> <p><b>Angina:</b> 50 mg once daily; may increase dose gradually at weekly intervals according to frequency and severity of anginal symptoms and tolerability; usual dosage range: 50 to 100 mg once daily.</p> <p><b>Myocardial infarction, early treatment and secondary prevention:</b> Initial: 25 to 50 mg twice daily; titrate as tolerated based on heart rate and BP up to a usual maximum dose of 100 mg/day administered in 1 or 2 divided doses</p> <p><b>Pediatrics dosing:</b></p> <p><b>Hypertension:</b> Initial: Usual range: 0.5 to 1.5 mg/kg/day once daily or divided in doses twice daily; maximum daily dose: 2 mg/kg/day not to exceed 100 mg/day</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> CrCl &gt;30 mL/minute: No dosage adjustment necessary. CrCl 10 to 30 mL/minute: Maximum dose: 50 mg daily. CrCl &lt;10 mL/minute: Maximum dose: 25 mg daily.</p> <p><b>Hemodialysis, intermittent:</b> 25 to 50 mg daily; administer post dialysis in dialysis days</p> <p><b>Dosing: Altered Kidney Function: Pediatric: Infants, Children, and Adolescents:</b> Oral: GFR &gt;50 mL/minute/1.73 m<sup>2</sup>: No dosage adjustment necessary. GFR 30 to 50 mL/minute/1.73 m<sup>2</sup>: Maximum dose: 1 mg/kg/dose every 24 hours. GFR 10 to &lt;30 mL/minute/1.73 m<sup>2</sup>: Maximum dose: 1 mg/kg/dose every 48 hours. GFR &lt;10 mL/minute/1.73 m<sup>2</sup>: Maximum dose: 1 mg/kg/dose every 48 hours. based on adult information, maximum dose should not exceed 25 mg/dose.</p> <p><b>Dosing: Hepatic Impairment:</b> There are no dose adjustments needed.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Atenolol or any component of the formulation</li> <li>• Bradycardia</li> <li>• Heart block greater than first-degree (except in patients with a functioning artificial pacemaker)</li> <li>• Cardiogenic shock</li> <li>• Uncompensated cardiac failure</li> </ul>

	<ul style="list-style-type: none"> <li>• Severe peripheral arterial disorders</li> <li>• Anesthesia with agents that produce myocardial depression</li> <li>• Pheochromocytoma (in the absence of alpha-blockade)</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions (Significant): Considerations</b></p> <ul style="list-style-type: none"> <li>– Bradyarrhythmias</li> <li>– Bronchospasm: Lower risk of bronchospasm compared to non-cardioselective beta-blockers</li> <li>– CNS effects: as fatigue, insomnia, memory disorders, and sexual disorder</li> <li>– Hypoglycemia may worsen, prolong, or cause hypoglycemia. Also, beta-blockers may mask symptoms of hypoglycemia (eg. palpitations),</li> <li>– Beta-blocker therapy should not be withdrawn abruptly.</li> </ul> <p><b>&gt;10%:</b>                  Cardiovascular: Bradycardia (3%; acute myocardial infarction: 18%), heart failure (acute myocardial infarction: 19%), hypotension (acute myocardial infarction: 25%), supraventricular tachycardia (acute myocardial infarction: 12%), ventricular tachycardia (acute myocardial infarction: 16%)</p> <p><b>1% to 10%:</b>                  Cardiovascular: Atrial fibrillation (acute myocardial infarction: 5%), atrial flutter (acute myocardial infarction: 2%), bundle branch block (acute myocardial infarction: 7%), heart block (acute myocardial infarction: 5%), orthostatic hypotension (2%), pulmonary embolism (acute myocardial infarction: 1%)                  Gastrointestinal: Diarrhea (2%), nausea (4%)                  Nervous system: Dizziness (1% to 4%), fatigue (<math>\leq 3\%</math>), lethargy (1%), vertigo (2%)                  Respiratory: Bronchospasm (acute myocardial infarction: 1%)</p>
<b>Monitoring Parameters</b>	Signs of bronchospasm (in patients with preexisting bronchospastic disease). <b>Acute cardiac treatment:</b> Monitor ECG and BP. <b>Hypertension:</b> BP, heart rate, serum glucose regularly (in patients with diabetes).
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Etofylline, Fexinidazole, Rivastigmine, White Birch Allergen Extract</p> <p><b>Risk D: Consider therapy modification</b>                  Alpha2-Agonists, Amifostine, Ceritinib, Dronedarone, Fingolimod, Grass Pollen Allergen Extract, Obinutuzumab, Ponesimod, Siponimod, Tasimelteon</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Atenolol is not recommended due to adverse events in fetus.</p> <p><b>Lactation:</b> Bradycardia and hypoglycemia has been observed in some breastfeeding infants and neonates particularly in premature or impaired renal function infants. Use of a beta-blocker other than atenolol may be preferred in a breastfeeding female</p>
<b>Administration</b>	Oral: May be administered without regard to meals. Refer to manufacturer PIL if there are specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Beta-blocker therapy should not be withdrawn abruptly to avoid exacerbation of angina, the occurrence of myocardial infarction or ventricular arrhythmias</li> <li>• Heart failure: Stabilize patients on heart failure regimen prior to initiation or titration of beta-blocker. Beta-blocker therapy should be initiated at very low doses with gradual and very careful titration.</li> <li>• Myasthenia gravis: Use with caution in patients with myasthenia gravis.</li> <li>• Peripheral vascular disease (PVD) and Raynaud disease: Use with caution and monitor for progression of arterial obstruction.</li> <li>• Pheochromocytoma (untreated): Adequate alpha-blockade is required prior to use</li> </ul>

	<p>of any beta-blocker.</p> <ul style="list-style-type: none"> <li>• Psoriasis: Beta-blocker use has been associated with induction or exacerbation of psoriasis.</li> <li>• Renal impairment: Use with caution in patients with renal impairment; dosage adjustment required.</li> <li>• Thyroid disease: May mask signs of hyperthyroidism (eg, tachycardia).</li> <li>• Vasospastic angina: Unopposed alpha1-adrenergic receptors mediate coronary vasoconstriction and can worsen anginal symptoms.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Major surgery: Chronic beta-blocker therapy should not be routinely withdrawn prior to major surgery.</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.</p>

## Bisoprolol

<b>Generic Name</b>	Bisoprolol
<b>Dosage form/strengths</b>	Tablet: 2.5mg, 5mg, 10mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antihypertensive; Beta-Blocker, Beta-1 Selective ATC: C07AB07
<b>Indications</b>	<b>Hypertension</b> management. <b>Note:</b> Beta-blockers are not recommended as first-line therapy
<b>Dosage Regimen</b>	<b>Hypertension:</b> <b>Oral:</b> Initial: 2.5 to 5 mg once daily; increase at more than a week intervals as needed based on patient response. Usual dosage range: 2.5 to 10 mg once daily Maximum dose: 20 mg/day
<b>Dosage adjustment</b>	<b>Renal Impairment:</b> CrCl $\geq$ 40 mL/minute: No dose adjustments needed. CrCl <40 mL/minute: Initial: 2.5 mg daily; increase cautiously. Cl <sub>cr</sub> <20 mL/minute: maximum 10 mg once daily. Hemodialysis: Not dialyzable <b>Hepatic Impairment:</b> Hepatitis or cirrhosis: Initial: 2.5 mg once daily; increase cautiously.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Cardiogenic shock</li> <li>• Overt cardiac failure</li> <li>• Marked sinus bradycardia or heart block greater than first-degree (except in patients with a functioning artificial pacemaker).</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> <ul style="list-style-type: none"> <li>– Bradyarrhythmias</li> <li>– Bronchospasm: Lower risk of bronchospasm compared to noncardioselective beta-blockers</li> <li>– CNS effects: as fatigue, insomnia, memory disorders, and sexual disorder</li> <li>– Hypoglycemia may worsen, prolong, or cause hypoglycemia. Also, beta-blockers may mask symptoms of hypoglycemia (eg. palpitations),</li> <li>– Beta-blocker therapy should not be withdrawn abruptly</li> </ul> <b>1% to 10%:</b> Cardiovascular: Chest pain (1%) Gastrointestinal: Diarrhea (3%), vomiting (1%) Nervous system: Fatigue (7%), hypoesthesia (1%) Respiratory: Dyspnea (1%), upper respiratory tract infection (5%)
<b>Monitoring Parameters</b>	-Blood pressure -Heart rate - ECG - Serum glucose in diabetic patients - Signs and symptoms of bronchospasm (in patients with preexisting bronchospastic disease)



<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Etofylline, Rivastigmine, White Birch Allergen Extract</p> <p><b>Risk D: Consider therapy modification</b> Alpha2-Agonists (Clonidine, Tizanidine, Dexmedetomidine), Amifostine, Ceritinib, Dronedarone, Fingolimod, Grass Pollen Allergen Extract, Obinutuzumab, Patiromer, Ponesimod, Siponimod, Tasimelteon</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Beta-blockers use during pregnancy may increase the risk of adverse events in neonates. For chronic hypertension in pregnancy, agents other than Bisoprolol are preferred</p> <p><b>Lactation:</b> No human data. Caution. When beta-blocker therapy is indicated in a patient who is breast-feeding, Labetalol and Propranolol are generally recommended as the preferred beta-blockers.</p>
<b>Administration</b>	<p><b>Administration: Oral</b></p> <p>May be administered without regard to meals. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Heart failure with reduced ejection fraction: Stabilize patients on heart failure regimen prior to initiation or titration of beta-blocker.</li> <li>• Hepatic impairment: Use with caution; dosage adjustment may be required.</li> <li>• Kidney impairment: Use with caution; dosage adjustment may be required.</li> <li>• Myasthenia gravis: Use with caution in patients with myasthenia gravis.</li> <li>• Peripheral vascular disease (PVD) and Raynaud disease: Use with caution and monitor for progression of arterial obstruction in patients with PVD and Raynaud disease.</li> <li>• Pheochromocytoma (untreated): Adequate alpha-blockade is required prior to use of any beta-blocker.</li> <li>• Psoriasis: Beta-blocker use has been associated with induction or exacerbation of psoriasis, but cause and effect have not been firmly established.</li> <li>• Thyroid disease: May mask signs of hyperthyroidism (eg, tachycardia). If hyperthyroidism is suspected, manage and monitor. Withdrawal should be gradually to avoid thyroid storm.</li> <li>• Vasospastic angina: Beta-blockers without alpha1-adrenergic receptor blocking activity should be avoided in patients with vasospastic angina.</li> </ul> <p><b>Special populations:</b></p> <ul style="list-style-type: none"> <li>• Elderly: Dosage reductions may be necessary.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Abrupt withdrawal: Beta-blocker therapy should not be withdrawn abruptly particularly in patients with coronary artery disease, but gradually tapered to avoid acute tachycardia, hypertension, and/or ischemia.</li> <li>• Major surgery: Chronic beta-blocker therapy should not be routinely withdrawn prior to major surgery.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from moisture.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>



## Metoprolol

<b>Generic Name</b>	<b>Metoprolol</b>
<b>Dosage form/strengths</b>	Metoprolol Succinate: Modified release tablets: 25mg, 50mg, 100mg, 200mg Metoprolol Tartrate: Solution for intravenous injection: 5mg/ml
<b>Route of administration</b>	<i>Oral, IV</i>
<b>Pharmacologic category</b>	Selective Beta-1 blocker; Antianginal Agent; Antihypertensive ATC: C07AB02
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Angina pectoris.</li> <li>• Hypertension.</li> <li>• Heart failure</li> <li>• Myocardial infarction</li> <li>• Arrhythmias</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Angina:</b> <u>Metoprolol Succinate</u> <b>Oral:</b> 100 mg-200 mg daily; may increase dose till 400 mg according to response at weekly intervals.</p> <p><b>Hypertension:</b> <u>Metoprolol Succinate:</u> <b>Oral:</b> 25 to 100 mg once daily; may increase dose till 400 mg according to response at weekly intervals.</p> <p><b>Heart failure</b> <u>Metoprolol succinate:</u> <b>Oral:</b> Initial: 12.5 to 25 mg once daily; may increase dose till 200 mg according to response at intervals of 2 weeks.</p> <p><b>Migraine prophylaxis</b> <u>Metoprolol succinate:</u> Oral: 50 - 200 mg daily</p> <p><b>Myocardial infarction, early treatment and secondary prevention:</b> <u>Metoprolol tartrate:</u> <b>IV:</b> Initial: 5 mg; repeat dose every 2minutes for up to 3 doses (15mg) according to response. Start oral therapy 15 minutes after the last IV dose 50 mg every 6 hours for 48 hours; Maintenance dose 200 mg daily.</p> <p><b>Arrhythmias</b> <u>Metoprolol tartrate:</u> <b>IV:</b> Up to 5 mg, dose to be given at a rate of 1–2 mg/minute, may repeat every 5 minutes may administer up to 5 mg if required, total dose of 10–15 mg.</p> <p><b>In surgery</b> <u>Metoprolol tartrate:</u> by slow <b>IV:</b> Initially 2–4 mg, given to control arrhythmias during anaesthesia, then 2 mg, repeated if necessary; maximum 10 mg.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b> No dosage adjustment necessary</p> <p><b>Dosing: Hepatic Impairment:</b> Metoprolol should be initiated at a low dose and titrated slowly according to</p>

	clinical response. Caution in severe impairment and liver cirrhosis.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• AV block</li> <li>• Hypersensitivity to Metoprolol or any ingredient of the formulation</li> <li>• Bradycardia (<i>heart rate less than 45 beats/minute</i>)</li> <li>• Cardiogenic shock</li> <li>• Hypotension</li> <li>• Sick sinus syndrome</li> <li>• Untreated Pheochromocytoma (suitable alpha-blocker is required prior to use)</li> <li>• Severe peripheral arterial circulatory disturbances.</li> <li>• <i>During myocardial infarction</i>: second or third-degree AV block unless a functioning pacemaker is present</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <ul style="list-style-type: none"> <li>– Bradyarrhythmias</li> <li>– Bronchospasm: Lower risk of bronchospasm compared to noncardioselective beta-blockers</li> <li>– CNS effects: as fatigue, insomnia, memory disorders, and sexual disorder</li> <li>– Hypoglycemia may worsen, prolong, or cause hypoglycemia. Also, beta-blockers may mask symptoms of hypoglycemia (eg. palpitations),</li> <li>– Beta-blocker therapy should not be withdrawn abruptly</li> </ul> <p><b>&gt;10%:</b> Cardiovascular: Bradycardia (2% to 16%), hypotension (1% to 27%)</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Arterial insufficiency</p> <p>Dermatologic: Gangrene (1%), pruritus (5%), skin rash (&gt;2% to 5%)</p> <p>Gastrointestinal: Constipation (1%), diarrhea (&gt;2% to 5%), flatulence (1%), heartburn (1%), nausea (<math>\leq 1\%</math>), stomach pain (1%), xerostomia (1%)</p> <p>Nervous system: Cerebrovascular accident (1%), depression (&gt;2% to 5%), dizziness (2% to 10%), fatigue (1% to 10%), vertigo (<math>\leq 2\%</math>)</p> <p>Respiratory: Bronchospasm (1%), dyspnea (<math>\leq 3\%</math>), wheezing (1%)</p> <p>Miscellaneous: Accidental injury (1%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> <li>• Serum glucose (in patients with diabetes);</li> <li>• Mental alertness</li> <li>• In treatment myocardial infarction patients before 2<sup>nd</sup> dose : Heart rate should be less than 45 beats/min, systolic blood pressure less than 100 mmHg, P-Q time (PR interval) more than 0.24 sec.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Bromperidol, Etofylline, Fexinidazole, Rivastigmine</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Alpha2-Agonists, Amifostine, Ceritinib, Dronedarone, Fingolimod, Grass Pollen Allergen Extract, Obinutuzumab, Ponesimod, Siponimod, Tasimelteon</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Use of beta-blockers during pregnancy may affect fetus by reducing placental perfusion. Benefit risk should be considered.</p> <p><b>Lactation:</b> limited human data. Not recommended due to potential toxicity.</p>
<b>Administration</b>	<p><b>Oral:</b></p> <ul style="list-style-type: none"> <li>• Tablets are scored and may be halved; however, swallow whole or half</li> </ul>

	<p>tablet without chewing or crushing.</p> <ul style="list-style-type: none"> <li>Administer consistently in relation to meals, preferably with a meal.</li> </ul> <p><b>Intravenous</b></p> <ul style="list-style-type: none"> <li>No dilution necessary. Given as IV push over 1 minute for acute treatment. May also be administered by slow infusion (ie, 5 to 10 mg of metoprolol in 50 mL of fluid) over half or an hour.</li> </ul> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<p><b>Warnings/ Precautions</b></p>	<ul style="list-style-type: none"> <li><b>Bradyarrhythmias:</b> Dose-related, <i>Onset:</i> Varied, <i>Risk factors:</i> elderly, Impaired AV node conduction or sinus node dysfunction or Concurrent use of other agents that impair AV nodal conduction (eg, non-dihydropyridine calcium channel blockers, Digoxin, Ivabradine)</li> <li><b>Bronchospasm:</b> Bronchospasm is reversible upon discontinuation or use of bronchodilators</li> <li><b>CNS effects:</b> Dose-related, reversible symptoms include: memory impairment, fatigue, insomnia. Often occur within the first few weeks of treatment particularly in <i>elderly</i>. Taking the medicine can lead to deterioration in reactions; dizziness and tiredness. Caution in driving and using machines.</li> <li><b>Withdrawal:</b> gradually tapered to avoid acute tachycardia, hypertension, and/or ischemia.</li> <li>Caution with patients with history of severe anaphylaxis incidences; may increase seriousness of anaphylactic reactions. Treatment of anaphylaxis (eg, epinephrine) in patients taking beta-blockers may be ineffective or promote undesirable effects.</li> <li><b>Caution in patients</b> with Diabetes, Hepatic impairment, Myasthenia gravis, Peripheral vascular disease and Thyroid disease as may mask or worsen symptoms.</li> <li>May increase incidences and duration of Prinzmetal's angina.</li> <li>Heart failure with reduced ejection fraction: Stabilize patients prior to initiation of beta-blocker. Initiate Beta-blockers gradually and with careful titration to avoid worsening heart failure or fluid retention.</li> <li>Chronic beta-blocker therapy should not be routinely withdrawn prior to major surgery.</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C. Protect from light, moisture and heat.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Nebivolol

<b>Generic Name</b>	<b>Nebivolol</b>
<b>Dosage form/strengths</b>	Tablets: 2.5 mg, 5mg, 10mg, 20mg And in combinations
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antihypertensive; Beta-Blocker, Beta-1 Selective ATC: C07AB12
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Management of <b>hypertension</b>.</li> <li>• Treatment of <b>stable mild and chronic heart failure</b> in addition to standard therapy in elderly over 70 years.</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Hypertension:</b> <b>Oral:</b> Initial: 5 mg once daily (preferred) or divided in 2 doses; titrate as needed at 2-week intervals based on patient response to a maximum dose of 40 mg once daily</p> <p><b>Adjunct in stable mild to moderate heart failure:</b> Adult 70 years and over: Initially 1.25 mg once daily for 1–2 weeks, then increased by doubling if tolerated every 1–2 weeks, up to 10 mg once daily</p> <p><b>Pediatrics:</b> Use in children is not recommended.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b> CrCl &lt;30 mL/minute: Initial: 2.5 mg once daily; if initial response is inadequate, may increase cautiously. Nebivolol has not been evaluated in dialysis-dependent patients.</p> <p><b>Dosing: Hepatic Impairment: Adult</b> Moderate impairment: Initial: 2.5 mg once daily; if initial response is inadequate, may increase cautiously. Severe impairment: Use is contraindicated.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Nebivolol or any component of the formulation</li> <li>• Acute heart failure, cardiogenic shock requiring IV inotropic therapy.</li> <li>• AV block 2<sup>nd</sup> or 3<sup>rd</sup> degree without pacemaker</li> <li>• Bradycardia</li> <li>• Sick sinus syndrome</li> <li>• Severe Hepatic disease</li> </ul>
<b>Adverse Drug Reactions</b>	<ul style="list-style-type: none"> <li>– Bradyarrhythmias</li> <li>– Bronchospasm</li> <li>– CNS effects: as fatigue, insomnia, memory disorders, and sexual disorder</li> <li>– Hypoglycemia may worsen, prolong, or cause hypoglycemia. Also, beta-blockers may mask symptoms of hypoglycemia (eg. palpitations),</li> <li>– Beta-blocker therapy should not be withdrawn abruptly</li> </ul> <p><b>1% to 10%:</b> Cardiovascular: Peripheral edema, bradycardia, chest pain Central nervous system: Headache, fatigue, dizziness, insomnia, paresthesia Dermatologic: Skin rash Endocrine and metabolic: Decreased HDL cholesterol, hypercholesterolemia, increased serum triglycerides, increased uric acid Gastrointestinal: Diarrhea, nausea, abdominal pain</p>

	<p>Hematologic and oncologic: Decreased platelet count                  Neuromuscular and skeletal: Weakness                  Renal: Increased blood urea nitrogen                  Respiratory: Dyspnea</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> <li>• Kidney and liver functions</li> <li>• Serum glucose (in diabetic patients); signs and symptoms of bronchospasm in patients with existing bronchospastic disease; mental alertness.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Bromperidol, Etofylline, Fexinidazole, Rivastigmine, White Birch Allergen Extract</p> <p><b>Risk D: Consider therapy modification</b>                  Alpha2-Agonists, Amifostine, Ceritinib, Dronedarone, Fingolimod, Grass Pollen Allergen Extract, Obinutuzumab, Patiromer, Ponesimod, Siponimod, Tasimelteon</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Not recommended, Human Data Suggest Risk in 2nd and 3rd Trimesters</p> <p><b>Lactation:</b> Not recommended, No Human Data, Potential Toxicity</p>
<b>Administration</b>	<p>Oral: May be administered without regard to food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Anaphylactic reactions: Use caution with history of severe anaphylaxis to a variety of allergens; patients taking beta-blockers may become more sensitive to repeated challenges.</li> <li>• Bronchospastic disease: Beta-1-selective beta-blockers, such as Nebivolol, are preferred over nonselective agents in patients with asthma or other pulmonary disease in which acute bronchospasm would put them at risk, all beta-blockers should nevertheless be used with caution in these patients, particularly with high-dose therapy. Ensure patient has an inhaled beta<sub>2</sub>-agonist immediately available.</li> <li>• Diabetes: Use with caution in patients with diabetes mellitus; may potentiate hypoglycemia and/or mask signs and symptoms.</li> <li>• Myasthenia gravis: Use with caution in patients with myasthenia gravis.</li> <li>• Peripheral vascular disease (PVD) and Raynaud disease: Nebivolol can exacerbate symptoms. Use with caution and monitor for progression of arterial obstruction.</li> <li>• Pheochromocytoma: Adequate alpha-blockade is required prior to use of any beta-blocker.</li> <li>• Thyroid disease: should be used with caution in patients with hyperthyroidism or thyrotoxicosis as it may mask signs of hyperthyroidism (eg, tachycardia). If hyperthyroidism is suspected, carefully manage and monitor; abrupt withdrawal may exacerbate symptoms of hyperthyroidism or precipitate thyroid storm.</li> <li>• Abrupt withdrawal: Can result in severe exacerbation of angina, myocardial infarction, or ventricular arrhythmias. During discontinuation, careful monitoring should occur and the patient should be advised to minimize physical activity. If possible, Nebivolol should be tapered over 1—2 weeks. If coronary insufficiency or angina develops during discontinuation, Nebivolol therapy should be reinitiated, at least temporarily.</li> <li>• Surgery: The necessity or desirability of withdrawing beta-blockers, prior to major surgery is controversial; the risks versus benefits should be evaluated in individual patients.</li> </ul>

### Storage

Store between 15°C to 30°C. Protect from light.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Propranolol

<b>Generic Name</b>	<b>Propranolol</b>
<b>Dosage form/strengths</b>	Tablet 10mg, 40mg Ampoule 1mg/ml
<b>Route of administration</b>	Oral, IV
<b>Pharmacologic category</b>	Beta Adrenergic Nonselective Blocking Agents, Antianginal Agent; Antiarrhythmic Agent, Class II; Antihypertensive ATC code: C07AA05
<b>Indications</b>	Arrhythmias Adjunctive management of Thyrotoxicosis and Thyrotoxic crisis Hypertension, portal hypertension and variceal hemorrhage prophylaxis Pheochromocytoma Chronic Stable angina Hypertrophic cardiomyopathy Anxiety tachycardia Prophylaxis after myocardial infarction Essential tremor Migraine prophylaxis
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b></p> <p><b>Arrhythmias</b>                      Prevention: Oral: 10–40 mg 3–4 times a day                      Acute case: IV: 1 mg, to be given over 1 minute, dose may be repeated if necessary at intervals of 2 minutes, maximum 10 mg per course (5 mg in anaesthesia)</p> <p><b>Thyrotoxicosis (adjunct)</b>                      Oral: 10–40 mg 3–4 times a day</p> <p><b>Thyrotoxic crisis</b>                      IV: 1 mg, over 1 minute, repeat dose after 2-minute interval if necessary. Maximum dose is 10 mg per course (5 mg in anaesthesia).</p> <p><b>Hypertension, portal hypertension:</b>                      Oral: Initially 40 mg twice daily, dose may be increased at weekly intervals as required up to 320 mg daily</p> <p><b>Pheochromocytoma</b> (only with an alpha-blocker)                      Oral: in preparation for surgery 60 mg daily for 3 days before surgery                      Oral: 30mg daily in non-surgery cases.</p> <p><b>Angina</b>                      Oral: Initially 40 mg 2–3 times a day; usual maintenance dose: 120–240 mg daily</p> <p><b>Hypertrophic cardiomyopathy, Anxiety tachycardia</b>                      Oral: 10–40 mg 3–4 times a day</p> <p><b>Prophylaxis after myocardial infarction</b>                      Oral: Initially 40 mg 4 times a day then titrate dose as tolerated to 180-240 mg daily in divided doses.</p> <p><b>Essential tremor</b>                      Oral: Initially 40 mg 2–3 times a day; usual maintenance dose 80–160 mg daily</p> <p><b>Migraine prophylaxis</b>                      Oral: 80–240 mg daily in divided doses, increased and withdrawn gradually.</p>



	<p><b>Dosing: Older Adult</b> Refer to the adult dosage. Consider lower initial doses.</p> <p><b>Dosing: Pediatric</b> <b>Cardiac Arrhythmias, Thyrotoxicosis, Thyrotoxic crisis:</b> Adjust according to response IV: an initial dose of 0.01–0.05 mg/kg infused over 10 minutes then every 6-8 hours if required. Oral: 0.25–0.5mg/kg 3–4 times a day (max. per dose 1 mg/kg 4 times a day),</p>
<b>Dosage adjustment</b>	<p><b>Dosing Altered Kidney Function</b> No dosage adjustment needed. Use with caution</p> <p><b>Dosing Hepatic impairment</b> Metabolized by liver. Initiate therapy at a lower dose for the specified indication; carefully titrate the dosage to attain the desired response.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Acute heart failure</li> <li>• Asthma</li> <li>• AV block greater than first degree</li> <li>• Severe bradycardia</li> <li>• Cardiogenic shock</li> <li>• Sick sinus syndrome</li> <li>• Hypersensitivity to propranolol or any component of the formulation</li> </ul>
<b>Major Adverse Drug Reactions</b>	<p>Adverse reactions are more frequent and may be more severe after IV administration than after oral administration.</p> <p><b>&gt;10%:</b> Nervous system: sleep disorder (infants: 16% to 18%) Respiratory: Bronchiolitis (infants), bronchitis (infants: 8% to 13%)</p> <p><b>1% to 10%:</b> Cardiovascular: Cold extremity (infants: 7% to 8%) Gastrointestinal: Abdominal pain (infants: 4%), constipation (1% to 3%), decreased appetite (infants: 3% to 4%), diarrhea (infants: 5% to 6%) Nervous system: Agitation (infants: 5% to 9%), dizziness (4% to 7%), drowsiness (infants: 5%), fatigue (5% to 7%), irritability (infants: 6%), nightmares (infants: 6%)</p>
<b>Monitoring Parameters</b>	<p>ECG, heart rate, and blood pressure. Serum glucose, symptoms of bronchospasm in risk patients.</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Beta2-Agonists, Bromperidol, Etofylline, Fexinidazole, Fezolinetant, Thioridazine, White Birch Allergen Extract.</p> <p><b>Risk D: Consider therapy modification</b> Alpha2-Agonists, Amifostine, Ceritinib, CYP1A2 Inhibitors (Strong), Fingolimod, Dronedarone, Grass Pollen Allergen Extract, Obinutuzumab, Ponesimod, Siponimod, Tasimelteon, Tizanidine</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Human data suggest risk in 2nd and 3rd Trimesters Use of beta-blockers during the third trimester of pregnancy may increase the risk for bradycardia, hypoglycemia, hypotension, and respiratory depression in the neonate.</p> <p><b>Lactation:</b></p>



	<p>Propranolol may be compatible with breastfeeding when used at usual doses, but with potential risk. Breastfeeding infants should be monitored for bradycardia, cyanosis, and hypoglycemia</p>
<b>Administration</b>	<p><b>Administration:</b>  <b>Administer oral tablets (immediate release)</b> in divided doses, before meals (empty stomach) and at bedtime.  <b>Administration: IV</b> by rapid infusion (IV push) at a rate of 1 mg/minute or by slow infusion in D5W or NS over ~30 minutes.</p> <p>Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Anaphylactic reactions: Use caution with history of severe anaphylaxis to allergens; patients taking beta-blockers may become more sensitive. Treatment of anaphylaxis (e.g., epinephrine) in patients taking beta-blockers may be ineffective or promote undesirable effects.</li> <li>• Heart failure: Use with caution, monitor for a worsening of the condition (efficacy of propranolol in heart failure has not been demonstrated).</li> <li>• Caution, monitor worsening of cases of Myasthenia gravis, Peripheral vascular disease and Raynaud disease, Psoriasis and Respiratory disease.</li> <li>• Adequate alpha-blockade is required prior to use of any beta-blocker in cases of Pheochromocytoma and Vasospastic angina.</li> <li>• Thyroid disease: May mask signs of hyperthyroidism (e.g., tachycardia). Monitor; gradual withdrawal when needed. Alterations in thyroid function tests may be observed.</li> <li>• Considerations when treating infantile hemangioma include close monitoring of cardiovascular events (blood pressure and heart rate), serum glucose (hypoglycemia) and respiratory conditions (bronchospasm).</li> <li>• Hypoglycemia: May potentiate hypoglycemia and/or mask signs and symptoms. Regular feeding habits are recommended</li> <li>• Smokers: Cigarette smoking may decrease plasma levels of propranolol by increasing metabolism. Patients should be advised to avoid smoking.</li> <li>• Major surgery: Chronic beta-blocker therapy should not be routinely withdrawn prior to major surgery.</li> </ul>
<b>Storage</b>	<p>Store between 15 to 30°C.                  After dilution, propranolol is stable for 24 hours at room temperature in D<sub>5</sub>W or NS. Protect from freezing, excessive heat, light and moisture.                  Refer to manufacturer PIL if there are specific considerations.</p>

## Calcium-Channel Blockers, Dihydropyridine

## Amlodipine

<b>Generic Name</b>	Amlodipine
<b>Dosage form/strengths</b>	Tablets or capsules: 2.5mg, 5mg, 10mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antianginal Agent; Antihypertensive; Calcium Channel Blocker; Dihydropyridine ATC: C08CA01
<b>Indications</b>	<b>Angina:</b> Treatment of symptomatic chronic stable angina; treatment of confirmed or suspected vasospastic angina (variant angina). <b>Hypertension, chronic:</b> Management of hypertension in adults and children $\geq 6$ years of age.
<b>Dosage Regimen</b>	<b>Angina pectoris:</b> <b>Chronic stable angina (alternative agent) or Vasospastic angina:</b> <b>Oral:</b> 5 to 10 mg once daily. <b>Hypertension, chronic:</b> <b>Oral:</b> Initial: 2.5 to 5 mg once daily; evaluate response after 2 to 4 weeks and titrate dose, as needed, up to a maximum of 10 mg once daily; if additional blood pressure control is needed, consider combination therapy. <b>Dosing: Pediatric Hypertension</b> Children $\geq 6$ years and Adolescents: Oral: Initial: 2.5 mg once daily; titrate based on clinical response; maximum dose: 10 mg/day.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function:</b> <b>Altered kidney function:</b> Mild to severe impairment: No dosage adjustment necessary <b>Dosing: Hepatic Impairment:</b> Angina: Initial: 5 mg once daily; titrate slowly in patients with severe hepatic impairment. Hypertension, chronic: Initial: 2.5 mg once daily; titrate slowly in patients with severe hepatic impairment.
<b>Contra-indications</b>	Hypersensitivity to amlodipine or any component of the formulation.
<b>Adverse Drug Reactions</b>	<b>Significant Adverse Reactions:</b> <b>Peripheral edema:</b> is the most common adverse reaction with amlodipine, characterized by ankle and leg swelling independent of fluid retention <b>&gt;10%:</b> Cardiovascular: Peripheral edema (2% to 11%, dose related; females: 15%; males: 6%) <b>1% to 10%:</b> Cardiovascular: Flushing, palpitations Dermatologic: Pruritus, skin rash Gastrointestinal: Abdominal pain, nausea Genitourinary: Male sexual disorder Nervous system: Asthenia, dizziness, drowsiness, fatigue Neuromuscular and skeletal: Muscle cramps

	Respiratory: Dyspnea
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Amifostine, Dantrolene, Fexinidazole, Fusidic Acid (Systemic), Pimozide</p> <p><b>Risk D: Consider therapy modification</b> Antifungal Agents (Azole Derivatives, Systemic), Amifostine, Lemborexant, Lomitapide, Obinutuzumab, Simvastatin, Sincalide, Sirolimus, Ubrogepant</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Human Data suggest low risk. Agents other than Amlodipine are more commonly used during pregnancy initially. Females with preexisting hypertension may continue their medication during pregnancy.</p> <p><b>Lactation:</b> Amlodipine is present in human breastmilk; however, no adverse effects of amlodipine on the breast-fed infant have been observed. Compatible.</p>
<b>Administration</b>	<p><b>Administration: Oral:</b> Administer without regard to meals.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Aortic stenosis: Amlodipine may reduce coronary perfusion resulting in ischemia in patients with severe aortic stenosis. Caution.</li> <li>• Hepatic impairment: Use with caution in patients with hepatic impairment; may require lower starting dose; titrate slowly in patients with severe hepatic impairment.</li> <li>• Hypertrophic cardiomyopathy with left ventricular outflow tract obstruction: Use with caution since reduction in afterload may worsen symptoms associated with this condition.</li> </ul> <p><b>Special populations:</b></p> <ul style="list-style-type: none"> <li>• Older adult: Initiate at a lower dose in the elderly.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Titration: Peak hypotensive effect is delayed; dosage titration should occur after 7 to 14 days on a given dose.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Felodipine

<b>Generic Name</b>	<b>Felodipine</b>
<b>Dosage form/strengths</b>	Modified Release Tablets: 2.5mg, 5mg, 10mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antihypertensive; Calcium Channel Blocker, Dihydropyridine ATC: C08CA02
<b>Indications</b>	Management of hypertension Prophylaxis of angina
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Hypertension</b> Initially 2.5 mg once daily; titrate every 1-2 weeks. Usual maintenance 2.5–10 mg once daily, to be taken in the morning.</p> <p><b>Prophylaxis of angina</b> Initially 5 mg once daily (2.5mg in elderly); titrate every 2-4 weeks up to 10 mg if needed. To be taken in the morning.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b> No dosage adjustment necessary.</p> <p><b>Dosing: Hepatic Impairment:</b> Initial: 2.5 mg once daily; caution.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to felodipine or any component of the formulation.</li> <li>• Pregnant or lactating women</li> <li>• Cardiac outflow obstruction.</li> <li>• Significant cardiac valvular obstruction (e.g. aortic stenosis)</li> <li>• Uncontrolled heart failure</li> <li>• Unstable angina within 1 month of myocardial infarction</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>10%:</b> Cardiovascular: Peripheral edema (2% to 17%) Central nervous system: Headache (11% to 15%)</p> <p><b>1% to 10%:</b> Cardiovascular: Flushing (4% to 7%), tachycardia (≤3%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Heart rate</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Bromperidol, Dantrolene, Fexinidazole, Fusidic Acid (Systemic), Itraconazole, Ketoconazole (Systemic)</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Strong CYP3A4 Inducers (eg. Barbiturates (phenobarbital), Carbamazepine, Phenytoin, Rifampicin), Strong CYP3A4 Inhibitors (eg. Clarithromycin, Posaconazole), Obinutuzumab, Sincalide, Thioridazine</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Avoid in pregnant women. Agents other than felodipine are more commonly used.</p> <p><b>Lactation:</b> Present in milk. Potential for serious adverse reactions in the</p>

	breastfeeding infant.
<b>Administration</b>	<p><b>Oral:</b> Swallow tablet whole; do not crush, or chew. Administer without food or with low in fat and carbohydrates meals.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Discontinue if ischemic pain occurs or existing pain worsens shortly after initiating treatment.</li> <li>• Peripheral edema: Common adverse effect, dose dependent; may occur in 2 to 3 weeks after starting therapy.</li> <li>• Heart failure: use is not recommended</li> <li>• <u>Caution in patients</u> with hepatic impairment, Hypertrophic cardiomyopathy, and in elderly.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Nifedipine

<b>Generic Name</b>	Nifedipine
<b>Dosage form/strengths</b>	Soft Gelatin Capsule: 10mg Retard Tablet (sustained release): 20mg Sustained Release Hard Gelatin Capsules: 30 mg, 60 mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antianginal Agent; Antihypertensive; Calcium Channel Blocker, Dihydropyridine ATC: C08CA05
<b>Indications</b>	-Angina: Management of chronic stable or vasospastic angina. -Hypertension, chronic: Management of hypertension (Extended Release products only).
<b>Dosage Regimen</b>	<p><b>-Adult:</b></p> <p><b>-Chronic stable angina, Vasospastic angina:</b> Oral: Extended release: Initial: 30 or 60 mg once daily; increase as needed to effective antianginal dose over 1 to 2 weeks. Doses &gt;90 mg/day are rarely needed; maximum: 120 mg/day.</p> <p><b>-Hypertension, chronic:</b> Oral: Extended release: Initial: 30 or 60 mg once daily; evaluate response after ~2 to 4 weeks and titrate dose as needed up to 90 mg once daily; if additional blood pressure control is needed, consider combination therapy.</p> <p><b>-Pediatric:</b></p> <p><b>-Hypertension, chronic:</b> Children and Adolescents (able to swallow whole tablet): Extended release: Oral: Initial: 0.2 to 0.5 mg/kg/day once daily or divided in 2 doses every 12 hours; do not exceed initial daily dose of 30 to 60 mg/day; titrate dose; maximum daily dose: 3 mg/kg/day up to 120 mg/day</p>
<b>Dosage adjustment</b>	<p><b>-Renal impairment:</b> -Mild to severe impairment: No dosage adjustment necessary. Lower initial doses and more frequent monitoring is recommended in severe impairment (eg, CrCl &lt;30 mL/minute).</p> <p><b>-Hepatic Impairment:</b> No dosage adjustments available (has not been studied); use with caution. Clearance of Nifedipine is reduced in cirrhotic patients, monitor closely for adverse effects and consider dose adjustments.</p>
<b>Contra-indications</b>	-Hypersensitivity to Nifedipine or any component of the formulation. -ST-elevation myocardial infarction (STEMI).
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b> Angina/Myocardial infarction Hypotension/syncope Peripheral edema</p> <p><b>-&gt;10%:</b> -Cardiovascular: Flushing (IR: 25%; ER: &lt;3%), peripheral edema (4% to 30%)</p>

	<p>Gastrointestinal: Heartburn (IR: <math>\leq 11\%</math>), nausea (IR: <math>\leq 11\%</math>; ER: 3%)                      -Nervous system: Dizziness (IR: 27%), headache (16% to 23%)                      -Neuromuscular and skeletal: Asthenia (IR: 12%; ER: <math>&lt; 3\%</math>)</p> <p><b>-1% to 10%:</b></p> <p>-Cardiovascular: Acute myocardial infarction (4%), cardiac failure (2%), palpitations (<math>\leq 7\%</math>), transient hypotension (5%)                      -Dermatologic: Dermatitis (IR), diaphoresis, pruritus, skin rash (ER), urticaria                      -Gastrointestinal: Abdominal cramps (IR), abdominal pain (ER), constipation (<math>\leq 3\%</math>), diarrhea, dyspepsia (ER), flatulence, xerostomia (ER)                      -Genitourinary: Impotence (ER), sexual difficulty (IR)                      -Nervous system: Balance impairment (IR), chills (IR), drowsiness (ER), fatigue (ER: 6%), insomnia (ER), jitteriness (IR), mood changes (IR: <math>\leq 7\%</math>), nervousness (<math>\leq 7\%</math>), pain (ER), paresthesia (ER), shakiness (IR), sleep disturbance (IR)                      -Neuromuscular and skeletal: Arthralgia (ER), joint stiffness (IR), lower limb cramp (ER), muscle cramps (IR: <math>\leq 8\%</math>), tremor (IR: <math>\leq 8\%</math>; ER: <math>&lt; 1\%</math>)                      -Ophthalmic: Blurred vision (IR)                      -Renal: Polyuria (ER: <math>&lt; 3\%</math>; IR: <math>&lt; 1\%</math>)                      -Respiratory: Chest congestion (IR), cough (IR: <math>\leq 6\%</math>; ER: <math>&lt; 1\%</math>), dyspnea, nasal congestion (IR), pleuritic chest pain (ER), pulmonary edema (2%), wheezing (IR: <math>\leq 6\%</math>)                      -Miscellaneous: Fever, inflammation (IR)</p>
<b>Monitoring Parameters</b>	<p>-Heart rate, Blood pressure                      -Signs and symptoms of heart failure                      -Peripheral edema.</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                      Bromperidol, Dantrolene, Fexinidazole, Fusidic Acid (Systemic), Grapefruit Juice  <b>Risk D: Consider therapy modification</b>                      Amifostine, Cladribine, Strong CYP3A4 Inducers (including; Barbiturates (phenobarbital), Carbamazepine, Phenytoin, Rifampicin), Obinutuzumab, Sinalide</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b>                      - Human Data suggest low risk -If treatment for chronic hypertension during pregnancy is needed, oral nifedipine is one of the preferred agents.</p> <p><b>-Lactation:</b>                      Nifedipine is present in breast milk. Nifedipine is considered compatible with breastfeeding, although data following long-term use is limited</p>
<b>Administration</b>	<p><b>-Immediate release:</b> May be administered with or without food.  <b>-Extended release:</b> Tablets should be swallowed whole; do not crush, split, or chew.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>- Use with caution in patients with:                      Severe aortic stenosis                      Hepatic impairment                      Hypertrophic cardiomyopathy (HCM) with outflow tract obstruction                      Before major surgery</p> <p>- Alterations in GI anatomy (eg, severe GI narrowing, history of GI cancer, obstruction, bowel resection, gastric bypass, vertical banded gastroplasty) and underlying hypomotility disorders have led to bezoar formation with extended release forms.</p>



	<ul style="list-style-type: none"> <li>- Immediate release formulations should not be used to manage primary hypertension; adequate studies to evaluate outcomes have not been conducted.</li> <li>- Abrupt withdrawal may cause rebound angina in patients with coronary artery disease.</li> </ul>
<b>Storage</b>	<p>-Store between 15°C to 30°C; protect from light and moisture.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Calcium-Channel Blockers, Non-dihydropyridine

## Diltiazem

<b>Generic Name</b>	<b>Diltiazem</b>
<b>Dosage form/strengths</b>	Tablets: 60mg Modified release tablets: 60mg Sustained Release Capsule: 90mg, 120mg, 180mg, 240mg Topical Cream 20mg/g Rectal Cream 20mg/g
<b>Route of administration</b>	<i>Oral, topical</i>
<b>Pharmacologic category</b>	Calcium Channel Blocker, Nondihydropyridine, Antianginal Agent; Antiarrhythmic Agent, Class IV; Antihypertensive Topical: C05AE03 Systemic: C08DB01
<b>Indications</b>	<b>Oral:</b> Hypertension Angina <b>Topical:</b> Chronic anal fissure
<b>Dosage Regimen</b>	<b>Adult dosing</b> <b>Oral:</b> Doses vary according to formulation release and to patient response. Refer to manufacturer label. Angina or hypertension: dose ranges 60mg 2-3 times daily, titrate until required response, up to 360mg daily. <b>Topical:</b> Chronic anal fissure: Adult: Apply to the anal canal twice daily until pain subsides. Maximum duration: 8 weeks.  <b>Pediatrics:</b> Safety and efficacy in children has not been proved.
<b>Dosage adjustment</b>	<b>Elderly:</b> lower initial doses. <b>Kidney impairment:</b> lower initial doses. Use with caution. <b>Hepatic impairment:</b> lower initial doses. Use with caution; extensively metabolized by the liver
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to diltiazem or any component of the formulation;</li> <li>• Sick sinus syndrome (unless pacemaker fitted).</li> <li>• Second- or third-degree AV block (unless pacemaker fitted).</li> <li>• Left ventricular failure with pulmonary congestion</li> <li>• Cardiogenic shock, heart failure (with reduced ejection fraction)</li> <li>• Hypotension (systolic &lt;90 mm Hg) or severe bradycardia.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Common or very common:</b> Cardiac conduction disorders, constipation, gastrointestinal discomfort, malaise <b>Uncommon:</b> Arrhythmias, diarrhea, insomnia, nervousness, postural hypotension <b>Rare or very rare</b> Dry mouth <b>Frequency not known</b> Cardiac arrest, congestive heart failure, extrapyramidal symptoms, fever, gynaecomastia, hepatitis, hyperglycaemia, hyperhidrosis, mood

	altered, photosensitivity reaction, severe cutaneous adverse reactions (SCARs), thrombocytopenia, vasculitis
<b>Monitoring Parameters</b>	Blood Pressure Heart rate Kidney and liver functions.
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Aprepitant, Asunaprevir, Bosutinib, Bromperidol, Budesonide (Topical), Dantrolene, Domperidone, Doxorubicin, Elacestrant, Eletriptan, Fexinidazole, Flibanserin, Fosaprepitant, Fusidic Acid (Systemic), Infigratinib, Ivabradine, Lemborexant, Lomitapide, Lonafarnib, Methysergide, Nisoldipine, Orelabrutinib, Pacritinib, Pimozide, Sertindole, Simeprevir</p> <p><b>Risk D: Consider therapy modification</b> Acalabrutinib, ALfentanil, Alprazolam, Amifostine, Astemizole, Avanafil, Avapritinib, Budesonide (Systemic), Carbamazepine, Ceritinib, Ciclosporin, Cilostazol, Cisapride, Cobimetinib, Colchicine, CYP3A4 Inducers (Strong, eg. Barbiturates (phenobarbital) Carbamazepine Phenytoin Rifampicin), Dapoxetine, Daridorexant, Deflazacort, Dronedarone, Eliglustat, Encorafenib, Entrectinib, Eplerenone, Esmolol, Fentanyl, Fingolimod, Guanfacine, Ibrutinib, Ivacaftor, Ivosidenib, Lovastatin, Lumateperone, Lurasidone, Lurbinectedin, Mavacamten, Methadone, Midazolam, Midostaurin, Mitapivat, Mobocertinib, Naloxegol, Obinutuzumab, Olaparib, Omaveloxolone, Pemigatinib, Pexidartinib, Phenytoin, Ponesimod, Ranolazine, Rimegepant, Selpercatinib, Selumetinib, Simvastatin, Sinalide, Siponimod, Sirolimus, Sonidegib, Suvorexant, Tazemetostat, Thioridazine, Tolvaptan, Triazolam, Ubrogepant, Vardenafil, Venetoclax, Voclosporin, Zanubrutinib</p>
<b>Pregnancy and Lactation</b>	<p>Systemic use: <b>Pregnancy:</b> Adverse events have been observed in animal reproduction studies. Avoid use. <b>Lactation:</b> Potential for serious adverse reactions in the breastfed infant. Discontinue either Diltiazem or breastfeeding</p>
<b>Administration</b>	<p><b>Administration: Oral,</b> Administer at the same time of day. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Cardiac conduction disorders: Diltiazem may cause first-degree atrioventricular (AV) block, second-degree atrioventricular block, complete atrioventricular block, or sinus bradycardia. May occur at clinical doses, at any time during therapy. <u>Risk factors:</u> elderly, renal impairment, concomitant use of beta blockers or AV conditions abnormalities.</li> <li>• Use with caution in left ventricular dysfunction; due to negative inotropic effects, may exacerbate condition.</li> <li>• Diltiazem may cause <u>cutaneous hypersensitivity reactions</u>. e.g Maculopapular rash, Stevens-Johnson syndrome. Non-dose-related; immunologic and may occur at any time during therapy.</li> <li>• Mild elevations of <u>hepatic enzymes</u> occurred and self-resolved. While significant elevations are reversible upon discontinuation.</li> <li>• Systemic absorption following <u>rectal use</u> is unknown; therefore, consider all the contra-indications and warnings.</li> <li>• <u>Caution</u> in diabetic patients, patients liable to intestinal obstruction.</li> </ul>

	<ul style="list-style-type: none"> <li>• <u>Monitor</u> signs of mood changes (including depression), respiratory impairment symptoms.</li> </ul>
<p><b>Storage</b></p>	<p>Capsule, tablet: Store below 30°C. Protect from light and humidity.            Topical cream: store between 2-8 °C  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Verapamil

<b>Generic Name</b>	Verapamil
<b>Dosage form/strengths</b>	Sustained or prolonged Release Capsule: 120mg, 240mg Tablets: 40mg, 80mg, Sustained release tablets: 240mg Solution for I.V injection \Infusion: 5mg/2ml, And in combinations
<b>Route of administration</b>	Oral, IV
<b>Pharmacologic category</b>	Antiarrhythmic /Antihypertensive (Calcium channel blocker Class IV) ATC: C08DA01
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Angina.</li> <li>• Atrial fibrillation or atrial flutter, rate control</li> <li>• Hypertension: Oral: immediate or extended release capsule and tablet</li> <li>• Supraventricular tachycardia</li> </ul>
<b>Dosage Regimen</b>	<p>Maximum dose: 480 mg/day in 1 to 3 divided doses.</p> <p><b>1-Angina pectoris</b> (Chronic stable angina or Vasospastic angina) Used in chronic stable angina as alternative therapy if there are contraindications to or unacceptable adverse effects with beta-blockade Oral: <b>A</b>-Immediate release: Initial: 80 to 120 mg 3 times daily May increase as needed at 1- to 2-day intervals to effective antianginal dose <b>B</b>-Extended release: Initial: 240 mg once daily; increase as needed at 7- to 14-day intervals to effective antianginal dose.</p> <p><b>2- Atrial fibrillation or atrial flutter, rate control:</b> -Do not use in patients with preexcitation associated with an accessory pathway, to avoid ventricular arrhythmias <b>A</b>-Acute ventricular rate control: IV Bolus: Initial: 5 to 10 mg; if there is inadequate response, dose may be repeated after 15 to 30 minutes; if there is adequate response after 1 to 2 bolus doses, then may begin a continuous infusion. Continuous infusion: Initial: 5 mg/hour; titrate to goal heart rate up to a maximum of 20 mg/hour. <b>B</b>- Chronic ventricular rate control: Oral: Immediate release: Initial: 40 mg 3 to 4 times daily; increase as needed to get desired rate control.</p> <p><b>3-Hypertension:</b> Oral: <b>A</b>-Immediate release: Initial: 40 to 80 mg 3 times daily; increase dose as needed at weekly intervals; usual dose: 120 to 360 mg/day in 3 divided doses. <b>B</b>-Extended release: Initial: 120 or 240 mg once daily; increase dose as needed at weekly intervals; usual dose: 120 to 360 mg/day in 1 to 2 divided doses.</p> <p><b>4-Supraventricular tachycardia:</b>(alternative agent) -Do not use in patients with pre-excitation associated with an accessory pathway, to avoid ventricular arrhythmias.</p>

	<p>Chronic maintenance: Oral: Immediate release: Initial: 40 mg 3 to 4 times daily; increase as needed for heart rate control.</p> <p><b>Conversion between oral formulations:</b> When switching from IR to ER formulations, the total daily dose remains nearly the same. Some high dose ER products are recommended to be given twice daily.</p>
<p><b>Dosage adjustment</b></p>	<p><b><u>Dosing: Altered Kidney Function</u></b>  <b>Oral:</b>                  - There are no dosage adjustments available, however, use with caution and consider additional ECG monitoring  <b>Injection:</b>                  There are no dosage adjustments available; however, repeated injections in patients with renal failure may lead to accumulation. If repeated injections are essential, monitor BP and PR interval closely and use smaller doses  <b>Dialysis:</b> Not removed by hemodialysis.  <b><u>Dosing: Altered Hepatic Function</u></b>  <b>Oral:</b> Administer 30% of the normal dose in severe hepatic impairment  <b>Injection:</b> use with caution and consider additional ECG monitoring in severe impairment. In cirrhosis, reduce dose and monitor ECG.                  If repeated injections are essential, monitor BP and PR interval closely and use smaller doses</p>
<p><b>Contra-indications</b></p>	<ul style="list-style-type: none"> <li>• Hypersensitivity</li> <li>• Acute porphyrias</li> <li>• Atrial flutter or fibrillation associated with accessory conducting pathways (e.g. Wolff-Parkinson-White-syndrome)</li> <li>• AV block</li> <li>• Cardiogenic shock</li> <li>• Heart failure</li> <li>• Hypotension</li> <li>• Lown-Ganong-Levine syndrome</li> <li>• Sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker)</li> <li>• Severe ventricular dysfunction</li> </ul>
<p><b>Adverse Drug Reactions</b></p>	<p><b>Significant Adverse Reactions:</b>                  Acute decompensated heart failure                  Bradyarrhythmias                  Hepatic effects  <b>&gt;10%:</b> Nervous system: Headache (IV, oral: 1% to 12%)  <b>1% to 10%:</b>                  Cardiovascular: Acute myocardial infarction (<math>\leq 1\%</math>), angina pectoris (<math>\leq 1\%</math>), ankle edema (1%), atrioventricular block (IV, oral: <math>\leq 1\%</math>), atrioventricular dissociation (<math>\leq 1\%</math>), bradycardia (IV, oral: <math>\leq 1\%</math>), cardiac failure (<math>\leq 2\%</math>), cerebrovascular accident (<math>\leq 1\%</math>), chest pain (<math>\leq 1\%</math>), claudication (<math>\leq 1\%</math>), ECG abnormality (<math>\leq 2\%</math>), edema (2%), hypotension (IV, oral: 2% to 3%, can be symptomatic), palpitations (<math>\leq 1\%</math>), peripheral edema (4%) (See Table 1), syncope (<math>\leq 1\%</math>), tachycardia (IV: 1%; severe)                  Dermatologic: Alopecia (<math>\leq 1\%</math>), diaphoresis (IV, oral: <math>\leq 1\%</math>), ecchymoses (<math>\leq 1\%</math>), erythema multiforme (<math>\leq 1\%</math>), hyperkeratosis (<math>\leq 1\%</math>), macular eruption (<math>\leq 1\%</math>), skin rash (<math>\leq 1\%</math>), Stevens-Johnson syndrome (<math>\leq 1\%</math>), urticaria (<math>\leq 1\%</math>)</p>

	<p>Endocrine and metabolic: Galactorrhea not associated with childbirth (<math>\leq 1\%</math>), gynecomastia (<math>\leq 1\%</math>), hyperprolactinemia (<math>\leq 1\%</math>), spotty menstruation (<math>\leq 1\%</math>)</p> <p>Gastrointestinal: Constipation (4% to 9%) (See Table 2), diarrhea (<math>\leq 1\%</math>), dyspepsia (3%), gastrointestinal distress (<math>\leq 1\%</math>), gingival hyperplasia (<math>\leq 1\%</math>), nausea (IV, oral: <math>\leq 3\%</math>), xerostomia (<math>\leq 1\%</math>)</p> <p>Genitourinary: Impotence (<math>\leq 1\%</math>)</p> <p>Hematologic and oncologic: Bruise (<math>\leq 1\%</math>), purpuric vasculitis (<math>\leq 1\%</math>)</p> <p>Hepatic: Increased serum transaminases (<math>\leq 2\%</math>)</p> <p>Nervous system: Balance impairment (<math>\leq 1\%</math>), confusion (<math>\leq 1\%</math>), dizziness (IV, oral: 1% to 4%), drowsiness (IV, oral: <math>\leq 1\%</math>), extrapyramidal reaction (<math>\leq 1\%</math>), fatigue (2%), insomnia (<math>\leq 1\%</math>), lethargy (3%), paresthesia (<math>\leq 1\%</math>), psychosis (<math>\leq 1\%</math>), shakiness (<math>\leq 1\%</math>), sleep disorder (1%)</p> <p>Neuromuscular and skeletal: Arthralgia (<math>\leq 1\%</math>), asthenia (<math>\leq 2\%</math>), muscle cramps (<math>\leq 1\%</math>), myalgia (1%)</p> <p>Ophthalmic: Blurred vision (<math>\leq 1\%</math>)</p> <p>Otic: Tinnitus (<math>\leq 1\%</math>)</p> <p>Renal: Polyuria (<math>\leq 1\%</math>)</p> <p>Respiratory: Dyspnea (<math>\leq 1\%</math>), flu-like symptoms (4%), pulmonary edema (<math>\leq 2\%</math>)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure and heart rate</li> <li>• Periodic liver function tests</li> <li>• ECG, especially with renal and/or hepatic impairment.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Aprepitant, Asunaprevir, Bilastine, Bosutinib, Budesonide (Topical), Bromperidol, Dantrolene, Disopyramide, Dofetilide, Domperidone, Doxorubicin, Fexinidazole, Flibanserin, Fosaprepitant, Fusidic Acid (Systemic), Ivabradine, Lemborexant, Lomitapide, Lonafarnib, Methysergide, Neratinib, Nisoldipine, Orelabrutinib, Pacritinib, Pazopanib, Pimozide, Sirolimus (Protein Bound), Simeprevir, Sertindole, Topotecan, Valbenazine, Vincristine (Liposomal)</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Acalabrutinib, Afatinib, Alfentanil, Alprazolam, Amifostine, Astemizole, Atorvastatin, Avanafil, Avapritinib, Berotralstat, Betrixaban, Brigatinib, Bromocriptine, Budesonide (Systemic), Carbamazepine, Celiprolol, Ceritinib, Cilostazol, Cisapride, Cobimetinib, Colchicine, Strong CYP3A4 Inducers, Dapoxetine, Daridorexant, Deflazacort, Dronedarone, Edoxaban, Eliglustat, Encorafenib, Entrectinib, Eplerenone, Esmolol, Everolimus, Fentanyl, Fingolimod, Fosphenytoin-Phenytoin, Guanfacine, Ibrutinib, Ivacaftor, Ivosidenib, Lefamulin, Lovastatin, Lumateperone, Lurasidone, Lurbinectedin, Mavacamten, Methadone, Midazolam, Mitapivat, Mobocertinib, Naloxegol, Obinutuzumab, Olaparib, Omaprelodolone, Palovarotene, Pemigatinib, Pexidartinib, Ponesimod, Pralsetinib, Ranolazine, Red Yeast Rice, Relugolix, Rimegepant, Rivaroxaban, Selpercatinib, Selumetinib, Simvastatin, Sinalcide, Siponimod, Sirolimus (Conventional), Sonidegib, Suvorexant, Talazoparib, Tazemetostat, Tezacaftor and Ivacaftor, Tizanidine, Tolvaptan, Triazolam, Vardenafil, Venetoclax, Voclosporin, Zanubrutinib</p>



<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Verapamil crosses the placenta. May reduce uterine blood flow with fetal hypoxia. Use verapamil during pregnancy only if clearly needed. The lowest effective dose is recommended; avoid use during the first trimester unless absolutely necessary.</p> <p><b>Breastfeeding:</b> Verapamil is considered compatible with breastfeeding.</p>
<b>Administration</b>	<p><b>Oral:</b> Immediate release: Can be administered with or without food.</p> <p><b>Parenteral:</b> IV: Administer undiluted dose over 2 to 3 minutes Avoid grapefruit juice before or after administration to avoid potential increases in verapamil bioavailability. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Accessory pathway</b> (eg, Wolff-Parkinson-White syndrome): During an episode of atrial fibrillation or flutter in patients with an accessory pathway or preexcitation syndrome.</p> <p><b>Arrhythmia:</b> Considered contraindicated in patients with wide complex tachycardia unless known to be supraventricular in origin</p> <p><b>Attenuated neuromuscular transmission:</b> use with caution in patients with attenuated neuromuscular transmission dosage reduction may be required</p> <p><b>Hepatic or Renal impairment:</b> Use with caution; dosage reduction may be required; in severe impairment monitoring hemodynamics and ECG may be needed.</p> <p><b>Increased intracranial pressure:</b> IV verapamil has increased intracranial pressure in patients with supratentorial tumors at the time of anesthesia induction</p> <p><b>Left ventricular dysfunction:</b> Avoid use in patients with heart failure.</p> <p><b>Special Populations Pediatric:</b> Avoid IV In neonates and young infants, due to severe apnea, bradycardia, hypotensive reactions, and cardiac arrest. <b>For older children,</b> use IV with caution as myocardial depression and hypotension may occur</p> <p><b>Bradyarrhythmias:</b> Verapamil may cause first-, second-, or third-degree atrioventricular (AV) block or sinus bradycardia. May be reversible after discontinuation, however, some patients continue to have symptoms.</p>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light and moisture. N.B. Refer to manufacturer PIL for specific considerations.</p>

## Cardiac Glycoside

## Digoxin

<b>Generic Name</b>	<b>Digoxin</b>																																				
<b>Dosage form/strengths</b>	Solution for I.V injection \Infusion: 0.5 mg/2ml Solution for I.M or slow I.V Injection: 0.5 mg/2ml Tablets: 0.25 mg Elixir: 0.05 mg/ml																																				
<b>Route of administration</b>	Oral, IM, IV																																				
<b>Pharmacologic category</b>	Antiarrhythmic Agent, Miscellaneous; Cardiac Glycoside ATC: C01AA05																																				
<b>Indications</b>	<ul style="list-style-type: none"> <li>- Rate control for Atrial fibrillation or atrial flutter</li> <li>- Heart failure with reduced ejection fraction</li> </ul>																																				
<b>Dosage Regimen</b>	<p><b>Adult Dosing:</b></p> <p><b>1- Atrial fibrillation or atrial flutter, rate control:</b>                      -Total digitalizing dose (TDD): Initial:                      -IV: 0.25 to 0.5 mg over several minutes, with repeat doses of 0.25 mg every 6 hours to a maximum of 1.5 mg over 24 hours  <b>or</b>                      -IV: A total of 8 to 12 mcg/kg (use lean body weight) (not to exceed 0.75 to 1.5 mg) administered by giving 50% of TDD over 5 minutes and the remaining 50% as 2 doses of 25% of TDD at 4- to 8-hour intervals after the initial dose.                      Note: follow either of these TDD regimens with an oral maintenance regimen.                      -Maintenance dose: Oral: 0.125 to 0.25 mg once daily</p> <p><b>2-Heart failure with reduced ejection fraction:</b>                      Maintenance dose (loading dose not recommended): Oral: 0.125 to 0.25 mg once daily</p> <p><b>Dosing: Pediatric</b></p> <p><b>Dosage Recommendations for Digitalizing Dose (Optional)</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Age</th> <th colspan="3">Total Digitalizing Dose Administer in 3 divided doses (mcg/kg)</th> </tr> <tr> <th>Oral solution</th> <th>Tablets</th> <th>IV</th> </tr> </thead> <tbody> <tr> <td>1 to 24 months</td> <td>35 to 60</td> <td>-</td> <td>30 to 50</td> </tr> <tr> <td>2 to 5 years</td> <td>30 to 45</td> <td>-</td> <td>25 to 35</td> </tr> <tr> <td>5 to 10 years</td> <td>20 to 35</td> <td>20 to 45</td> <td>15 to 30</td> </tr> <tr> <td>&gt;10 years</td> <td>10 to 15</td> <td>10 to 15</td> <td>8 to 12</td> </tr> </tbody> </table> <p><b>Maintenance Dosage Recommendations for Digoxin</b></p> <table border="1"> <thead> <tr> <th rowspan="2">Age</th> <th colspan="3">Daily Maintenance Dose If ≤10 years, administer in equal divided doses twice daily If &gt;10 years, administer once daily (mcg/kg/day)</th> </tr> <tr> <th>Oral solution</th> <th>Tablets</th> <th>IV</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>			Age	Total Digitalizing Dose Administer in 3 divided doses (mcg/kg)			Oral solution	Tablets	IV	1 to 24 months	35 to 60	-	30 to 50	2 to 5 years	30 to 45	-	25 to 35	5 to 10 years	20 to 35	20 to 45	15 to 30	>10 years	10 to 15	10 to 15	8 to 12	Age	Daily Maintenance Dose If ≤10 years, administer in equal divided doses twice daily If >10 years, administer once daily (mcg/kg/day)			Oral solution	Tablets	IV				
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<b>Dosage adjustment</b>	<p><b>Renal Impairment for adults:</b></p> <p>-Atrial fibrillation/flutter, supraventricular tachycardia:</p> <p>-IV, Oral:</p> <p>-Loading dose:</p> <p>CrCl &gt;15 mL/minute: No dosage adjustment necessary.</p> <p>CrCl ≤15 mL/minute: Administer 50% of usual dose</p> <p>-Maintenance dose</p> <p>CrCl ≥60 mL/minute: No dosage adjustment necessary.</p> <p>CrCl 45 to &lt;60 mL/minute: 0.0625 to 0.125 mg once daily.</p> <p>CrCl 30 to &lt;45 mL/minute: 0.0625 mg once daily.</p> <p>CrCl &lt;30 mL/minute: 0.0625 mg every 48 hours or consider alternative agent.</p> <p><b>-Heart failure:</b></p> <p><b>-Oral:</b></p> <table border="1"> <thead> <tr> <th>Ideal Body Weight</th> <th>CrCl (mL/minute)</th> <th>Digoxin dose</th> </tr> </thead> <tbody> <tr> <td rowspan="2">45 to 50</td> <td>&gt;60</td> <td>0.125 mg once daily</td> </tr> <tr> <td>15 to 60</td> <td>0.0625 mg once daily</td> </tr> <tr> <td rowspan="3">&gt;50 to 60</td> <td>&gt;110</td> <td>0.25 mg once daily</td> </tr> <tr> <td>&gt;45 to 110</td> <td>0.125 mg once daily</td> </tr> <tr> <td>15 to 45</td> <td>0.0625 mg once daily</td> </tr> <tr> <td rowspan="3">&gt;60 to 70</td> <td>&gt;110</td> <td>0.25 mg once daily</td> </tr> <tr> <td>&gt;35 to 110</td> <td>0.125 mg once daily</td> </tr> <tr> <td>15 to 35</td> <td>0.0625 mg once daily</td> </tr> <tr> <td rowspan="3">&gt;70 to 80</td> <td>&gt;80 to 110</td> <td>0.25 mg once daily</td> </tr> <tr> <td>&gt;20 to 80</td> <td>0.125 mg once daily</td> </tr> <tr> <td>15 to 20</td> <td>0.0625 mg once daily</td> </tr> <tr> <td rowspan="2">&gt;80</td> <td>&gt;70</td> <td>0.25 mg once daily</td> </tr> <tr> <td>15 to 70</td> <td>0.125 mg once daily</td> </tr> </tbody> </table> <p><b>-Hepatic Impairment:</b></p> <p>No dosage adjustment necessary.</p>	Ideal Body Weight	CrCl (mL/minute)	Digoxin dose	45 to 50	>60	0.125 mg once daily	15 to 60	0.0625 mg once daily	>50 to 60	>110	0.25 mg once daily	>45 to 110	0.125 mg once daily	15 to 45	0.0625 mg once daily	>60 to 70	>110	0.25 mg once daily	>35 to 110	0.125 mg once daily	15 to 35	0.0625 mg once daily	>70 to 80	>80 to 110	0.25 mg once daily	>20 to 80	0.125 mg once daily	15 to 20	0.0625 mg once daily	>80	>70	0.25 mg once daily	15 to 70	0.125 mg once daily
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<b>Contra-indications</b>	<p>-Hypersensitivity to digoxin, other forms of digitalis, or any component of the formulation</p> <p>-Ventricular fibrillation</p>																																		
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><b>Digoxin toxicity:</b> Associated with levels &gt;2 ng/mL; however, due to its narrow therapeutic window, digoxin toxicity is possible at therapeutic levels. Symptoms of toxicity may include nausea, vomiting, visual disturbances, lethargy, and/or life-threatening arrhythmias.</p>																																		

	<p><b>1-10%:</b> Nervous system disorder, dizziness Visual impairment (blurred vision or xanthopsia) Arrhythmia, conduction disorder, bigeminy, trigeminy, PR prolongation, sinus bradycardia Nausea, vomiting, diarrhoea Rash</p> <p><b>0.1-1%:</b> Depression</p>
<b>Monitoring Parameters</b>	<p>-Heart rate, periodic ECGs -Baseline and periodic serum creatinine -Serum electrolytes; potassium, magnesium, and calcium -Noncardiac signs of toxicity, confusion, and depression</p> <p><b>Digoxin therapeutic serum concentrations:</b> N.B. Blood should be taken six hours or more after the last dose of digoxin. Heart failure: 0.5 to 1 ng/mL (SI: 0.64 to 1.28 nmol/L) Toxicity: Risk (including mortality) &gt;2 ng/mL (SI: &gt;2.56 nmol/L) However, serum digoxin concentration should be interpreted in the clinical context. Toxicity may occur with lower digoxin serum concentrations. Atrial fibrillation: 0.8 to 2 ng/mL (SI: 1 to 2.6 nmol/L) Underdigitalization: &lt;0.5 ng/mL (SI: &lt;0.6 nmol/L) unless there are special circumstances.</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Disulfiram, Fexinidazole, Lasmiditan, Methotrimeprazine, Metronidazole, Milnacipran, Ornidazole, Pacritinib, Secnidazole</p> <p><b>Risk D: Consider therapy modification</b> Adagrasib, Amiodarone, Bretylium, Ceritinib, Dronedarone, Erdafitinib, Fingolimod, Flibanserin, Itraconazole, Lapatinib, Mirabegron, P-glycoprotein/ABCB1 Inhibitors, Polyethylene Glycol-Electrolyte Solution, Ponesimod, Propafenone, Quinidine, Ranolazine, Ritonavir, Siponimod, Sotorasib, Sucralfate, Vemurafenib, Venetoclax</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Compatible. Digoxin is recommended as a first-line agent for the chronic treatment of highly symptomatic supraventricular tachycardia (SVT) in pregnancy; the lowest effective dose is recommended. Digoxin may be considered for long-term rate control of maternal atrial tachycardia or atrial fibrillation when preferred agents fail. Monitor for an increased risk of maternal arrhythmias during labor and delivery.</p> <p><b>Lactation:</b> The amount of digoxin available to the infant via breast milk is not likely to be clinically significant. Compatible with breastfeeding.</p>
<b>Administration</b>	<p><b>Oral:</b> Administer consistently with relationship to meals; avoid concurrent administration (ie, administer digoxin 1 hour before or 2 hours after) with meals high in fiber or pectin and with drugs that decrease oral absorption of digoxin.</p> <p><b>Oral solution:</b> only a calibrated oral syringe should be used to measure the dose. Maintain adequate amounts of potassium in diet to decrease risk of hypokalemia (hypokalemia may increase risk of digoxin toxicity).</p> <p><b>N.B.</b> If patients are switched from oral to the I.V. formulation the dosage should be reduced by approximately 33%.</p> <p><b>Parenteral:</b></p> <p><b>Preparation for administration:</b> IV: May be administered undiluted or diluted fourfold in D<sub>5</sub>W, NS, or SWFI for direct injection. (i.e. add 2 ml ampoule of digoxin to 6 ml of injection solution). Less than fourfold dilution may lead to drug precipitation.</p>

	<p>Dilution for infusion 1:250ml solution is stable for 48 hours in room temperature if prepared in aseptic conditions.                      IM: No dilution required.</p> <p><b>Administration: IV</b>                      May be administered undiluted or diluted. Inject slowly over <math>\geq 5</math> minutes up to 20 minutes                      Vesicant; avoid extravasation.</p> <p><b>Administration: IM</b>                      This route cannot be recommended. May be administered by deep injection followed by massage at the injection site. Inject no more than 2 mL per injection site. The I.M. route is painful and is associated with muscle necrosis.</p> <p><b>Extravasation management:</b> If extravasation occurs, stop IV administration immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<p><b>Warnings/ Precautions</b></p>	<ul style="list-style-type: none"> <li>-Avoid use in patients with Accessory bypass tract.</li> <li>-Use with caution in patients with an acute MI.</li> <li>- Monitor serum concentrations closely in patients with Atrial Fibrillation</li> <li>-Patients with beri beri heart disease may fail to adequately respond to digoxin therapy; treat underlying thiamine deficiency concomitantly.</li> <li>- Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy; toxicity may occur despite therapeutic digoxin concentrations, maintain normocalcemia.</li> <li>-Withdrawal of digoxin in clinically stable patients with HF may lead to recurrence of HF symptoms. Monitor serum concentrations closely; may be associated with an increased risk of mortality especially when serum concentrations are not properly controlled</li> <li>-Avoid use in patients with Hypertrophic cardiomyopathy unless used to control ventricular response with atrial fibrillation</li> <li>-Avoid use of in patients with myocarditis.</li> <li>-Avoid use in patients with second- or third-degree heart block</li> <li>- Use with caution in patients with hypothyroidism</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C. Protect from light.                      Dilution for infusion 1:250ml solution is stable for 48 hours in room temperature.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Diuretics, Loop

## Bumetanide

<b>Generic Name</b>	<b>Bumetanide</b>
<b>Dosage form/strengths</b>	Tablets: 1mg Solution for I.M or slow I.V Injection: 0.25 mg/ml
<b>Route of administration</b>	<i>Oral, IM, IV</i>
<b>Pharmacologic category</b>	Loop Diuretic ATC: C03CA02
<b>Indications</b>	Edema in heart failure, kidney disease, and hepatic disease and Pulmonary edema
<b>Dosage Regimen</b>	<p><b>Adult and adolescents 12-17 years dosing:</b></p> <p><b>Edema:</b> Oral: 1 mg (for elderly: 0.5mg is sufficient), in the morning, if needed may take another tablet 1 mg after 6–8 hours.</p> <p><b>Severe edema:</b> Oral: Initially 5 mg daily, adjust according to response by adding 5mg every 12–24 hours. Maximum daily dose is 10 mg</p> <p><b>N.B.</b> Oral bioavailability is high, IV and oral dose may be nearly the same. <b>N.B.</b> Bumetanide may be administered parenterally (IV or IM) to patients who can't administer orally. Parenteral treatment should be terminated and oral treatment started as soon as possible.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b> eGFR &lt;30 mL/minute/1.73 m<sup>2</sup>: Higher doses may be required to achieve desired diuretic response due to decreased secretion into the tubular fluid</p> <p><b>Dosing: Hepatic Impairment:</b> Initiate with conservative doses and monitoring. Use is contraindicated in hepatic coma. Use with caution in cirrhosis and ascites.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to bumetanide or any component of the formulation</li> <li>• Anuria</li> <li>• Hepatic coma</li> <li>• Severe electrolyte depletion until the condition improves or is corrected.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Major Adverse Reactions:</b> May lead to <u>acute kidney injury</u>, <u>Fluid/electrolyte loss</u> eg, hypocalcemia, hypokalemia, hypomagnesemia which may predispose a patient to serious cardiac arrhythmias. <u>Ototoxicity</u>: hearing loss and tinnitus, which is generally reversible - <i>Risk factors</i>: elderly, high doses, Concurrent administration of diuretic, nephrotoxic agents or other ototoxic agents (eg, aminoglycosides), volume depletion, bolus IV administration or Very high or very restricted dietary sodium or electrolytes.</p> <p><b>&gt;10%:</b> Endocrine and metabolic: Hyperuricemia (18%), hypochloremia (15%), hypokalemia (15%) Genitourinary: Azotemia (11%)</p> <p><b>1% to 10%:</b> Endocrine and metabolic: Abnormal lactate dehydrogenase (1%), abnormal serum calcium or carbonate (2%), hyperglycemia (7%), hyponatremia (9%) Hematologic and oncologic: Abnormal serum phosphorus level (5%)</p>



	<p>Nervous system: Dizziness (1%)                  Neuromuscular and skeletal: Muscle cramps (1%)                  Renal: Increased serum creatinine (7%)                  Respiratory: Variations in CO<sub>2</sub> concentration (4%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Serum electrolytes</li> <li>• Serum uric acid</li> <li>• Kidney function</li> <li>• Fluid intake and output.</li> <li>• Glucose level in diabetic patients.</li> <li>• Audiometry with high doses, long treatment or when suspected</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Aminolevulinic Acid (Systemic), Bromperidol, Cephaloridine, Desmopressin, Levosulpiride, Mecamylamine, Netilmicin (Ophthalmic), Promazine, Taurursodiol</p> <p><b>Risk D: Consider therapy modification</b>                  Amifostine, Arsenic Trioxide, Dofetilide, Fexinidazole, Foscarnet, Nonsteroidal Anti-Inflammatory Agents, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Not recommended. Given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.</p> <p><b>Lactation:</b> Breastfeeding is not recommended. Diuretics have the potential to decrease milk volume and suppress lactation.</p>
<b>Administration</b>	<p><b>Administration: IV</b>                  Administer undiluted injections at a rate of 0.5 to 1 mg over 1 to 2 minutes, or further diluted in D5W or NS and administered over 5 minutes</p> <p><b>Administration: Oral</b>                  May administer with or without food. If multiple daily dosing, administer early in day to avoid nocturia.                  May cause potassium loss; potassium supplement may be required.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Careful medical supervision is needed because Bumetanide is a potent diuretic which, if given in excessive amounts, can lead to water and electrolyte depletion.</li> <li>• Hypersensitivity (immediate and delayed) may occur. Patients allergic to sulfonamides may show hypersensitivity.</li> <li>• Hyperuricemia: Asymptomatic hyperuricemia has been reported with use.</li> <li>• Hepatic impairment: Use caution in patients with cirrhosis; close monitoring of electrolytes; avoid sudden changes in fluid and electrolyte balance and acid/base status which may lead to hepatic encephalopathy.</li> <li>• Surgical patients: If given the morning of surgery, Bumetanide may render the patient volume depleted and blood pressure may be labile during general anesthesia.</li> </ul>
<b>Storage</b>	<ul style="list-style-type: none"> <li>• IV, Tablet: Store vials between 15<sup>o</sup>C to 30<sup>o</sup>C. protect from light.</li> <li>• Infusion solutions should be used within 24 hours after preparation. Light sensitive; discoloration may occur when exposed to light.</li> </ul> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Furosemide

<b>Generic Name</b>	Furosemide
<b>Dosage form/strengths</b>	Solution for IM, slow IV injection or IV infusion: 40mg/4ml, 20mg/2ml Ampoule: 20mg/2ml Tablets: 20mg, 40mg, 80mg, 500mg Oral solution: 20mg/5ml, 50mg/5ml And in combinations.
<b>Route of administration</b>	IV, IM, Oral
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Loop ATC: C03CA01
<b>Indications</b>	<b>Edema or volume overload:</b> Management of edema associated with heart failure, cirrhosis of the liver (ie, ascites), or kidney disease (including nephrotic syndrome); acute pulmonary edema.
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b></p> <p><b>Edema or volume overload:</b> <b>Naive to loop diuretics:</b> <b>Oral:</b> Initial: 20-50 mg once then titrate as needed to achieve targeted effect. <b>IV, IM:</b> Initial: 20 to 50 mg once then titrate as needed to targeted effect. Increment of 20mg increased after 2 hours if required, doses greater than 50mg given by intravenous infusion only; maximum 1.5 g per day</p> <p><b>Refractory edema or acute decompensation in patients taking oral loop diuretics:</b> Bolos/intermittent dosing: <b>IV:</b> Initial: Administer 1 to 2.5 times the total daily oral maintenance dose once then titrate as needed to an effective dose; maximum effective single dose: 80 to 200 mg depending on kidney function, maximum recommended total daily dose: 600 mg/day</p> <p><b>Note:</b> Oral bioavailability varies widely but on average is 50% of the IV dose.</p> <p><b>Transitioning from IV to oral:</b> There is substantial variability in oral bioavailability; typically administer 1 to 2 times the IV dose orally (eg, total daily IV dose of 80 mg/day should be converted to an oral dose of 80 to 160 mg/day in 1 to 2 divided doses); monitor urine output and adjust oral dose as needed.</p> <p><b>Dosing: Pediatric</b></p> <p><b>Edema (diuresis):</b> <b>Infants, Children, and Adolescents:</b> <b>Oral:</b> <b>Acute:</b> Initial: 2 mg/kg as a single dose; if ineffective, may increase in 6 to 8 hours in increments of 1 to 2 mg/kg/dose; maximum dose: 6 mg/kg/dose. <b>Maintenance dosing (chronic):</b> Limited data available: Initial: 0.5 to 2 mg/kg/dose every 6 to 24 hours; <b>IM, intermittent IV:</b> Limited data available: Initial: 0.5 to 2 mg/kg/dose every 6 to 12 hours; if initial dose ineffective after 2 hours, may increase dose by 1 mg/kg/dose; maximum dose: 6 mg/kg/dose not to exceed maximum adult dose: 200 mg/dose mg/kg/hour; usual adult dosing range: 10 to 40 mg/hour.</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Older Adult</b> Oral, IV: Initial: 20 mg/day; increase slowly to desired response.</p> <p><b>Dosing: Altered Kidney Function: Adult</b> <b>Altered kidney function: IV, Oral:</b> eGFR &gt;30 mL/minute/1.73 m<sup>2</sup>: No dosage adjustment necessary.</p>

	<p>eGFR <math>\leq</math>30 mL/minute/1.73 m<sup>2</sup>: Higher doses is needed. However, single doses &gt;160 to 200 mg IV (or oral equivalent) are unlikely to result in additional diuretic effect</p> <p><b>Dosing: Hepatic Impairment: Adult</b></p> <p>No specific dosage adjustment is needed. Diuretics should be used with caution in patients with hepatic disease. Monitor effects. Changes of fluid and electrolyte balance may precipitate hepatic coma.</p>
<p><b>Contra-indications</b></p>	<ul style="list-style-type: none"> <li>• Hypersensitivity to sulfonamide-derived drugs</li> <li>• Anuria</li> <li>• Hepatic disease</li> <li>• Severe electrolyte depletion until the condition improves or is corrected.</li> </ul>
<p><b>Adverse Drug Reactions</b></p>	<p><b>Significant Adverse Reactions:</b></p> <p>Acute kidney injury              Fluid/electrolyte loss              Hypersensitivity reactions (immediate and delayed)              Ototoxicity</p> <p><b>Frequency not defined:</b></p> <p>Cardiovascular: Necrotizing angitis, orthostatic hypotension, thrombophlebitis              Dermatologic: Acute generalized exanthematous pustulosis, bullous pemphigoid, erythema multiforme, exfoliative dermatitis, lichenoid eruption, pruritus, skin photosensitivity, skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria              Endocrine and metabolic: Glycosuria, hyperglycemia, hyperuricemia, hypocalcemia, hypochloremic alkalosis, hypokalemia, hypomagnesemia, hypovolemia, increased serum cholesterol, increased serum triglycerides              Gastrointestinal: Abdominal cramps, anorexia, constipation, diarrhea, gastric irritation, nausea, oral irritation, pancreatitis, vomiting              Genitourinary: Bladder spasm              Hematologic and oncologic: Agranulocytosis, anemia, aplastic anemia, hemolytic anemia, leukopenia, purpuric disease, thrombocytopenia              Hepatic: Hepatic encephalopathy, increased liver enzymes, intrahepatic cholestatic jaundice              Hypersensitivity: Anaphylactic shock, anaphylaxis, angioedema, nonimmune anaphylaxis              Immunologic: Drug reaction with eosinophilia and systemic symptoms              Nervous system: Dizziness, headache, paresthesia, restlessness, vertigo              Neuromuscular and skeletal: Asthenia, muscle spasm              Ophthalmic: Blurred vision, xanthopsia              Otic: Deafness, tinnitus              Renal: Acute kidney injury, calcium nephrolithiasis (pediatric patients), interstitial nephritis (allergic), nephrolithiasis (pediatric patients)              Miscellaneous: Fever</p>
<p><b>Monitoring Parameters</b></p>	<ul style="list-style-type: none"> <li>• Audiometry with high doses or rapid IV administration</li> <li>• Glucose level in diabetic patients.</li> <li>• Blood pressure</li> <li>• Kidney function</li> <li>• Monitor fluid intake and output (inpatient setting)</li> <li>• Serum electrolytes</li> <li>• Serum uric acid</li> </ul>

<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Aminolevulinic Acid (Systemic), Bromperidol, Cefaloridine, Chloral Hydrate, Desmopressin, Ethacrynic Acid, Levosulpiride, Mecamylamine, Netilmicin (Ophthalmic), Promazine, Taurursodiol</p> <p><b>Risk D: Consider therapy modification</b>                  Amifostine, Arsenic Trioxide, Chloral Betaine, Dofetilide, Fexinidazole, Foscarnet, Nonsteroidal Anti-Inflammatory Agents, Obinutuzumab, Sucralfate</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy</b> Monitor fetal growth if used during pregnancy.</p> <p><b>Lactation</b> Contraindicated. Large doses of loop diuretics have the potential to decrease milk volume and suppress lactation; use should be avoided when possible</p>
<b>Administration</b>	<p><b>Administration: Oral</b>                  May administer with or without food. May administer with food or milk to decrease GI distress.                  If multiple daily dosing, administer early in day to avoid nocturia unless instructed otherwise.</p> <p><b>Administration: IV</b>  <b>Usual Infusion Concentrations: Adult, Pediatric</b>                  IV infusion: 1 mg/mL or 2 mg/mL may be mixed in NS or D5W solution. May also be undiluted as 10 mg/mL</p> <p><b>Rate of administration:</b>                  Undiluted direct IV injections: 20 to 40 mg over 1 to 2 minutes.                  For high doses (eg, ≥160 mg), consider a short-term infusion at a maximum rate of administration of 4 mg/minute; rapid administration increases the risk of ototoxicity due to the high concentrations achieved in a short period of time.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Hyperuricemia: Asymptomatic hyperuricemia occurred and rarely, may precipitate gout.</li> <li>• Sulfonamide allergy: Potential cross-reactivity between members of a specific class.</li> <li>• Thyroid effects: Doses &gt;80 mg may result in transient increase in free thyroid hormones, followed by an overall decrease in total thyroid hormone levels.</li> <li>• Adrenal insufficiency: Avoid use of diuretics for treatment of elevated blood pressure in patients with primary adrenal insufficiency (Addison disease).</li> <li>• Cirrhosis: Correct electrolyte and acid/base imbalances prior to initiation. Supplemental potassium or an aldosterone antagonist, when appropriate, may reduce risk of hypokalemia and metabolic alkalosis. Close monitoring needed with initiation of therapy.</li> <li>• Diabetes: Use with caution in patients with diabetes mellitus or prediabetes; changes in glucose levels may occur.</li> <li>• Prostatic hyperplasia or urinary stricture: May cause urinary retention due to increased urine production, especially upon initiation of therapy.</li> <li>• Systemic lupus erythematosus: May cause systemic lupus erythematosus exacerbation or activation.</li> <li>• Pediatric: May lead to nephrocalcinosis or nephrolithiasis in premature infants</li> </ul>

and in infants and children <4 years of age with chronic use. May prevent closure of patent ductus arteriosus in premature infants.

- Surgical patients: avoid at the morning of surgery due to risk of volume depletion

***Dosage form specific issues:***

- Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression; use caution

***Other warnings and precautions:***

- Diuretic resistance: For some patients, despite high doses of loop diuretic, an adequate diuretic response cannot be attained. Diuretic resistance may be overcome by IV rather than oral administration or the use of two diuretics together (eg, a loop diuretic in combination with a thiazide diuretic). When multiple diuretics are used, serum electrolytes need to be monitored even more closely.

**Storage**

**Tablet, solution:** Store between 15°C to 30°C. Protect from light. Discard opened bottle of solution after 90 days.

**Injection:** Store intact vial/syringe between 15°C to 30°C. Protect from light.

Exposure to light may cause discoloration; do not use furosemide solutions if they have a yellow color. Furosemide solutions are unstable in acidic media, but very stable in basic media. Refrigeration may cause precipitation or crystallization; however, resolubilized by warming at room temperature without affecting the drug's stability.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Torsemide (Torasemide)

<b>Generic Name</b>	Torsemide (Torasemide)
<b>Dosage form/strengths</b>	Modified release tablet: 5mg, 10mg Tablets: 5mg, 10mg, 20g, 100mg Solution for intravenous injection: 10 mg/ml, 20 mg/2ml, 50mg
<b>Route of administration</b>	<i>IV, Oral</i>
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Loop ATC: C03CA04
<b>Indications</b>	Edema or volume overload: Treatment of edema.
<b>Dosage Regimen</b>	<b>Edema:</b> Oral: Adult: 5 mg once daily, to be taken preferably in the morning, then increased (by doubling) if necessary to 20 mg once daily. Patients with nephrotic syndrome or kidney failure need higher doses. Maximum effective single dose: 50 to 100 mg; maximum recommended total daily dose: 200 mg in 2 divided doses to minimize risk of ototoxicity. <b>Hypertension:</b> 5mg once daily may be increased to 10mg. Torsemide can be administered safely with beta blockers, ACE inhibitors and Ca channel blockers.
<b>Dosage Adjustment</b>	<b>Altered kidney function:</b> <b>IV, Oral:</b> eGFR >30 mL/minute/1.73 m <sup>2</sup> : No dosage adjustment necessary. eGFR ≤30 mL/minute/1.73 m <sup>2</sup> : Higher doses may be required to achieve desired diuretic response due to decreased secretion into the tubular fluid. However, single doses >50 to 100 mg are unlikely to result in additional diuretic effect <b>Hemodialysis, intermittent (thrice weekly):</b> Not dialyzable <b>Anuric patients:</b> There is no expected clinical benefit; use not recommended. <b>Dosing: Hepatic Impairment: Adult</b> There are no specific dosage adjustments available; use with caution. Use is contraindicated in hepatic coma.
<b>Contra-Indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Torsemide or any component of the formulation</li> <li>• Anuria</li> <li>• Hepatic coma.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Common or very common</b> Asthenia, gastrointestinal disorder, Polyuria <b>Uncommon</b> Bladder dilation, urinary retention <b>Rare or very rare</b> Allergic dermatitis <b>Frequency not known</b> Anaemia, cerebral ischaemia, confusion, dry mouth, embolism, ischaemic heart disease, myocardial infarction, pancreatitis, syncope, visual impairment
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Fluid intake and output</li> <li>• Kidney function</li> <li>• Serum electrolytes</li> <li>• Serum glucose in diabetic patients</li> <li>• Audiometry with high doses or rapid IV administration</li> </ul>



<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Aminolevulinic Acid (Systemic), Bromperidol, Cephaloridine, Desmopressin, Levosulpiride, Mecamylamine, Netilmicin (Ophthalmic), Promazine, Taurursodiol</p> <p><b>Risk D: Consider therapy modification</b>                  Amifostine, Arsenic Trioxide, Dofetilide, Fexinidazole, Foscarnet, Nonsteroidal Anti-Inflammatory Agents, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy</b>                  Avoid. Adverse events occurred in animal reproduction studies.</p> <p><b>Breastfeeding</b>                  Avoid. It is not known if tosemide is present in breast milk. Diuretics can suppress lactation.</p>
<b>Administration</b>	<p>Oral: Administer without regard to meals. If multiple daily dosing, administer early in day to avoid nocturia unless instructed otherwise.</p> <p>N.B. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Hyperuricemia: Asymptomatic hyperuricemia may occur; gout may be precipitated (rarely).</li> <li>• Sulfonamide (“sulfa”) allergy: There is a potential for cross-reactivity among all compounds containing the sulfonamide structure (SO<sub>2</sub>NH<sub>2</sub>).</li> <li>• Hypotension: extensive diuresis causes dehydration, hypotension. Monitor symptoms.</li> <li>• worsening renal function: particularly in salt depleted patients and in case of concomitantly use with nephrotoxic drugs. Monitor kidney functions.</li> <li>• Electrolyte and metabolic disorders. Electrolyte disturbances (eg, Hypocalcemia, hypokalemia, hypomagnesemia) may occur. Monitor serum electrolytes.</li> <li>• Ototoxicity: reversible tinnitus and hearing loss has been observed with loop diuretics. Higher doses, severe renal disease and hypoproteinemia are risk factors. It lasts from 30 minutes to 24 hours after administration.</li> <li>• Diabetes: Use with caution in patients with diabetes; increased blood glucose levels and hyperglycemia may occur. Monitor blood glucose periodically.</li> <li>• Hepatic impairment: Use with caution in patients with hepatic impairment; in patients with cirrhosis, avoid electrolyte and acid/base imbalances that may lead to hepatic encephalopathy.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.                  N.B. Refer to manufacturer PIL for specific considerations.</p>

## Diuretics, Osmotic



## Mannitol

<b>Generic Name</b>	<b>Mannitol</b>
<b>Dosage form/strengths</b>	Solution for I.V infusion: 10%, 15%, 20% (10,15 or 20 gm / 100 ml)
<b>Route of administration</b>	I.V
<b>Pharmacologic category</b>	Diuretic, Osmotic; Genitourinary Irrigant ATC: Osmotic: B05BC01 Irrigant: B05CX04
<b>Indications</b>	-Reduction of increased intracranial pressure (associated with cerebral edema and/or brain mass). -Reduction of increased intraocular pressure.
<b>Dosage Regimen</b>	<p><b>-Adult:</b></p> <p><b><u>1-Intracranial pressure reduction:</u></b> (eg, due to cerebral edema, trauma, intracerebral hemorrhage, acute ischemic stroke, hepatic encephalopathy, transtentorial herniation syndrome): -IV (using 20% solution): 0.5 to 2 g/kg once; may repeat 0.25 to 1 g/kg per dose every 4 to 6 hours based on response and clinical status.</p> <p><b><u>2-Intraocular pressure reduction:</u></b> -Presurgical dosing: IV: 1.5 to 2 g/kg administered over 30 to 60 minutes 1 to 1.5 hours prior to surgery. -Traumatic hyphema: IV: 1.5 g/kg administered over 45 minutes twice daily for IOP &gt;35 mm Hg; may administer every 8 hours in patients with extremely high pressure.</p> <p><b>-Pediatric:</b></p> <p><b><u>1-Intracranial pressure (ICP), reduction:</u></b> - Infants, Children, and Adolescents: IV: Usual range: 0.25 to 1 g/kg/dose infused over 20 to 30 minutes; repeat as needed to maintain serum osmolality &lt;320 mOsm/kg</p> <p><b><u>-Intraocular pressure (IOP), reduction:</u></b> Infants, Children, and Adolescents: IV: 1.5 to 2 g/kg/dose infused over ≥30 minutes. Note: When used preoperatively, administer 60 to 90 minutes prior to surgery.</p>
<b>Dosage adjustment</b>	<p><b><u>-Renal Impairment:</u></b> -Contraindicated in severe kidney impairment. - Use caution in patients with underlying kidney disease. May be used to reduce the incidence of acute kidney injury when administered prior to revascularization during kidney transplantation.</p> <p><b><u>-Hepatic impairment:</u></b> No dose adjustment necessary.</p>
<b>Contra-indications</b>	<p>-Hypersensitivity to mannitol or any component of the formulation.</p> <p>-Anuria</p> <p>-Severe hypovolemia</p> <p>-Active intracranial bleeding except during craniotomy</p> <p>-Preexisting severe pulmonary vascular congestion or pulmonary edema.</p>

<b>Adverse Drug Reactions</b>	<p><b>Frequency not defined:</b></p> <ul style="list-style-type: none"> <li>-Cardiovascular: Cardiac failure, chest pain, edema, hypertension, localized phlebitis, palpitations, peripheral edema, tachycardia, thrombophlebitis</li> <li>-Central nervous system: Chills, coma, confusion, dizziness, headache, increased intracranial pressure (rebound), lethargy, malaise, pain, seizure</li> <li>-Dermatologic: Diaphoresis, localized erythema, localized rash, pruritus, skin necrosis, skin rash, urticaria</li> <li>-Endocrine and metabolic: Dehydration, fluid and electrolyte disturbance, hyperkalemia, hyponatremia, hypervolemia, hypokalemia, hyponatremia, hypovolemia, increased thirst, metabolic acidosis, metabolic alkalosis</li> <li>-Gastrointestinal: Nausea, vomiting, xerostomia</li> <li>-Genitourinary: Anuria, azotemia, diuresis, hematuria, oliguria, osmotic nephrosis, urinary retention</li> <li>-Hematologic and oncologic: Hemoconcentration</li> <li>-Local: Local inflammation, local pain, local pruritus</li> <li>-Neuromuscular and skeletal: Arm and/or wrist pain, asthenia, muscle rigidity, myalgia</li> <li>-Ophthalmic: Blurred vision</li> <li>-Renal: Polyuria</li> <li>-Respiratory: Cough, pulmonary congestion, pulmonary edema, rhinitis</li> <li>-Miscellaneous: Fever</li> </ul>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>-Kidney function and urine output</li> <li>-Cardiac and pulmonary function</li> <li>-Intravascular volume status</li> <li>-Serum electrolytes, serum osmolality (measured)</li> <li>-Osmolar gap</li> <li>-Acid-base status</li> <li>-Serum glucose</li> <li>-Intracranial pressure (if applicable).</li> <li>-Monitoring infusion site.</li> </ul>
<b>Drug Interactions</b>	<p><b><u>Risk X: Avoid combination</u></b> Amikacin, Liposome (Oral Inhalation), Aminoglycosides, Tobramycin (Oral Inhalation)</p> <p><b><u>Risk D: Consider therapy modification</u></b> Arsenic Trioxide</p>
<b>Pregnancy and Lactation</b>	<p><b><u>-Pregnancy:</u></b></p> <ul style="list-style-type: none"> <li>-Mannitol crosses the placenta.</li> <li>-Outcome information following surgical use in pregnancy is limited; amniotic fluid volume may be decreased.</li> </ul> <p><b><u>-Lactation:</u></b></p> <ul style="list-style-type: none"> <li>-No human data. Considered compatible with breastfeeding.</li> </ul>
<b>Administration</b>	<p><b><u>-IV:</u></b></p> <p>Concentration and rate of administration depends on indication/severity. Use of an administration set with a final in-line filter (eg, ≤5 micron) is recommended. For cerebral edema or elevated intracranial pressure, administer over 10 to 30 minutes; for patients with high risk for cerebral herniation, use faster administration rates (over ~10 minutes). Inspect for crystals prior to administration. If crystals are present, redissolve by warming solution.</p> <ul style="list-style-type: none"> <li>-Do not administer simultaneously with blood due to the possibility of</li> </ul>

	<p>pseudoagglutination or hemolysis. If coadministration with blood is essential, at least 20 mEq sodium chloride should be added to each liter of mannitol.</p> <p>-Vesicant (at concentrations &gt;5%); ensure proper catheter or needle position prior to and during IV infusion. Avoid extravasation of IV infusions. Administration into a large central vein is recommended.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<p><b>Warnings/ Precautions</b></p>	<p>-May cause hypervolemia and electrolyte disturbances; monitor for new onset or worsening cardiac or pulmonary congestion. Also may cause profound diuresis with fluid and electrolyte loss; close medical supervision and dose evaluation are required. Correct electrolyte disturbances; adjust dose to avoid dehydration.</p> <p>-May cause kidney dysfunction, especially with high doses; use caution in patients taking other nephrotoxic agents, with sepsis, or preexisting kidney disease. To minimize adverse kidney effects, monitor serum osmolality or osmolar gap. Discontinue mannitol if acute kidney injury develops.</p> <p>-Mannitol may initially worsen pulmonary edema or heart failure by causing hypervolemia before diuresis ensues. Do not administer large volumes of mannitol to patients with preexisting severe pulmonary edema or heart failure. Discontinue mannitol if cardiac or pulmonary status worsens.</p> <p>-In patients being treated for cerebral edema, mannitol may accumulate in the brain (causing rebound increases in intracranial pressure) if circulating for long periods of time as with continuous infusion; intermittent boluses preferred. If hypotension occurs, monitor cerebral perfusion pressure; reassess dose and mannitol therapy if there is a decrease in cerebral perfusion pressure.</p> <p>-CNS toxicity (eg, coma, confusion, lethargy) may occur; risk may be increased in patients with impaired kidney function or with concomitant use of neurotoxic drugs. Discontinue mannitol if CNS toxicity develops.</p> <p>-Use with caution. In patients with severe impairment; do not use until adequacy of kidney function and urine flow is established.</p>
<p><b>Storage</b></p>	<p>-Store between 15°C to 30°C. Crystallization of solution may occur at low temperatures; do not use solutions that contain crystals.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Diuretics, Potassium-sparing

## Eplerenone

<b>Generic Name</b>	<b>Eplerenone</b>
<b>Dosage form/strengths</b>	Tablets: 25mg, 50mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Potassium Sparing; Mineralocorticoid (Aldosterone) Receptor Antagonist
<b>Indications</b>	<ul style="list-style-type: none"> <li>Improve survival of stable patients with left ventricular ejection fraction (LVEF <math>\leq 40\%</math>) and congestive heart failure after an acute myocardial infarction.</li> <li>Adjunct in chronic mild heart failure with left ventricular ejection fraction 30%</li> <li>Treatment of hypertension, to reduce risk of fatal and nonfatal cardiovascular events.</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b>  <b>Oral:</b> initial 25 mg increased to 50mg in 4 weeks if necessary with respect to potassium levels.                      In hypertension, dose may be increased up to maximum 50 mg twice daily if necessary.</p>
<b>Dosage Adjustment</b>	<p><b>Renal impairment dosing:</b>                      Mild to moderate impairment: caution, initial dose may be taken every other day.                      If CrCl <math>\leq</math> than 30 mL/minute: Avoid use  <b>Hepatic impairment dosing:</b>                      Moderate hepatic impairment: Caution as systemic exposure is increased.                      Severe impairment: Avoid use. (not studied)</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hyperkalemia (Serum potassium <math>&gt;5.5</math> mEq/L at initiation)</li> <li>CrCl <math>\leq 30</math> mL/minute</li> <li>Concomitant use of strong CYP3A4 inhibitors (eg, Ketoconazole, Itraconazole, Clarithromycin, Ritonavir, Nelfinavir) or potassium sparing diuretics.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Common <math>\geq 1\%</math>:</b> Arrhythmias, asthenia, constipation, cough, diarrhea, dizziness, dyslipidaemia, electrolyte imbalance, headache, insomnia, muscle spasms, nausea, pain, renal impairment, skin reactions, syncope, vomiting.</p> <p><b>Uncommon <math>\leq 1\%</math>:</b> Angioedema, arterial thrombosis, cholecystitis, eosinophilia, flatulence, gynaecomastia, hyperhidrosis, hypothyroidism, increased risk of infection, malaise, numbness, postural hypotension</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>Potassium serum level: before initiating therapy, within the first week, and at one month after the start of treatment or dose adjustment and periodically.</li> <li>Check serum potassium and serum creatinine within a week of a initiating a moderate CYP3A inhibitor ACE inhibitors, angiotensin-II blockers or non-steroidal-anti-inflammatories.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                      Bromperidol, Cyclosporine (Systemic), Strong CYP3A4 Inhibitors (e.g Clarithromycin Itraconazole, high amount of Grapefruit juice, Ketoconazole, Posaconazole), Fexinidazole, Fusidic Acid (Systemic), Potassium-Sparing Diuretics</p> <p><b>Risk D: Consider therapy modification</b></p>

	Amifostine, Moderate CYP3A4 Inhibitors (e.g., erythromycin, saquinavir, verapamil, and fluconazole), Obinutuzumab, Potassium Salts
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Caution, no information available. Use only if the potential benefit justifies the potential risk to the fetus.</p> <p><b>Lactation:</b> No information available. Decision to discontinue drug or breastfeeding must be made.</p>
<b>Administration</b>	<p><b>Oral:</b> Administer with or without food.</p> <p>If multiple daily dosing, administer early in day to avoid nocturia unless instructed otherwise.</p> <p>Do not take supplements of potassium during treatment.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>- Avoid use of concurrent potassium-conserving drugs or supplements without monitoring of serum potassium.</li> <li>- Risk of hyperkalaemia: Periodic monitoring is recommended especially in patients at risk for the development of hyperkalaemia, such as elderly patients, patients with renal insufficiency and patients with diabetes.</li> <li>- Caution in renal and hepatic impairment.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Spironolactone

<b>Generic Name</b>	<b>Spironolactone</b>
<b>Dosage form/strengths</b>	Tablets: 25 mg; 50 mg; 100 mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Potassium Sparing; Mineralocorticoid (Aldosterone) Receptor Antagonist ATC: C03DA01
<b>Indications</b>	-Ascites due to cirrhosis. -Heart failure with reduced ejection fraction. -Hypertension: Management of hypertension unresponsive to other therapies. -Primary hyperaldosteronism.
<b>Dosage Regimen</b>	<p><b>-Adult:</b></p> <p><b>1-Ascites due to cirrhosis:</b> Initial: 100 mg once daily; adjust every 3 to 5 days based on response. Maximum dose: 400 mg once daily.</p> <p><b>2-Heart failure with reduced ejection fraction:</b> - Initial: 12.5 to 25 mg once daily; adjust dose every 4 weeks if serum potassium and kidney function are stable, Maximum dose of 50 mg/day in 1 to 2 divided doses.</p> <p><b>3-Hypertension, chronic (alternative agent):</b> -Initial: 25 mg once daily; titrate as needed after ~2 to 4 weeks based on response and tolerability up to 100 mg once daily.</p> <p><b>4-Primary aldosteronism:</b> -Initial: 12.5 to 25 mg once daily; gradually adjust to the lowest effective dose; usual dose: 100-400 mg/day</p> <p><b>-Pediatric:</b></p> <p><b>1-Edema (diuresis):</b> - Infants, Children, and Adolescents: - Initial: 1 to 3 mg/kg/day divided every 6 to 24 hours; titrate as needed; reported maximum daily dose range: 4 to 6 mg/kg/day in divided doses every 6 to 12 hours or 400 mg/day, whichever is less.</p> <p><b>2-Hypertension:</b> -Infants, Children, and Adolescents: - Initial: 1 mg/kg/day divided every 12 to 24 hours; titrate as needed up to a maximum daily dose: 3.3 mg/kg/day or 100 mg/day, whichever is less.</p> <p><b>3-Primary aldosteronism (caused by adrenal hyperplasia), treatment:</b> -Infants, Children, and Adolescents: Oral: 1 to 3 mg/kg/day; maximum daily dose: 100 mg/day</p>
<b>Dosage adjustment</b>	<p><b>-Renal Impairment:</b></p> <p><b>1-Ascites due to cirrhosis; hypertension; primary aldosteronism:</b> -No specific dosage adjustments available (has not been studied); use with caution.</p>

	<p><b>2-Heart failure:</b></p> <ul style="list-style-type: none"> <li>-eGFR &gt;50 mL/minute/1.73 m<sup>2</sup>: No initial dosage adjustment necessary.</li> <li>-eGFR 30 to 50 mL/minute/1.73 m<sup>2</sup>: Initial: 12.5 mg once daily or every other day; may adjust the dose up to 25mg/day after 4 weeks if serum potassium remains &lt;5 mEq/L and kidney function is stable.</li> <li>-eGFR &lt;30 mL/minute/1.73 m<sup>2</sup>: Use not recommended.</li> </ul> <p><b>-Hepatic impairment:</b></p> <ul style="list-style-type: none"> <li>-No specific dosage adjustments available; initiate with low dose and titrate slowly (cirrhosis). Use with caution; minor alterations of fluid and electrolyte balance may precipitate hepatic coma.</li> </ul>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>-Hyperkalemia.</li> <li>-Addison disease.</li> <li>-Concomitant use with eplerenone.</li> <li>-Anuria</li> <li>-Any renal disease associated with severe renal impairment (CrCl less than 10 mL/minute) or acute renal failure</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions: Considerations</b></p> <p><b>Gynecomastia:</b> is usually reversible following discontinuation of therapy, <i>Onset:</i> Delayed; may occur after 1 to 2 months to over a year of therapy <i>Risk factors:</i> Higher doses (eg, ≥150 mg/day) and longer duration of therapy.</p> <p><b>Hyperkalemia:</b> reversible, may be fatal. <i>Onset:</i> Intermediate; usually occurs within 4 weeks of initiation or dose titration. <i>Risk factors:</i> Old age, Kidney impairment, Excessive potassium intake, Concomitant use of certain drugs (eg, ACE inhibitors, angiotensin-receptor blockers, drospirenone, nonsteroidal anti-inflammatory drugs). Heart failure.</p> <p>≥10%: Hyperkalaemia 1-10%: Confusional state, Dizziness, Headache, Drowsiness, Lethargy, Ataxia, Nausea, Vomiting, Abdominal pain, Diarrhoea, Hepatotoxicity, Pruritus, Rash, Muscle spasms, Acute kidney injury, Gynaecomastia, Breast pain (male), Malaise</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood Pressure</li> <li>• Serum electrolytes (potassium [within 1 week of initiation or dose titration and regularly thereafter], sodium)</li> <li>• Uric acid</li> <li>• Serum Glucose</li> <li>• Kidney function</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Amiloride, Bromperidol, Cyclosporine (Systemic), Potassium Salts, Potassium-Sparing Diuretics (Eplerenone, Triamterene)</p> <p><b>Risk D: Consider therapy modification</b> Abiraterone Acetate, Amifostine, Cosyntropin, Obinutuzumab,</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b> Limited Human Data—Animal Data Suggest Risk. may cause feminization of a male fetus. High doses late in pregnancy may be associated with intrauterine growth restriction.</p> <p>-Use not recommended in pregnancy if used for hypertension, Heart failure or</p>



	<p>Primary aldosteronism.</p> <p><b>-Lactation:</b> The active metabolite of spironolactone is present in breast milk. Spironolactone is considered compatible with breastfeeding. Consider risk benefit ratio.</p>
<b>Administration</b>	<p>-Oral: Administer with or without food; however, administer consistently with respect to food. If multiple daily dosing, administer early in day to avoid nocturia unless instructed otherwise. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>-Fluid and electrolyte imbalance (eg, hypomagnesemia, hyponatremia, hypocalcemia, hyperglycemia, hyperkalemia) may occur. Patients with heart failure, kidney disease, or cirrhosis may be particularly susceptible. Monitor and correct electrolyte disturbances; adjust dose to avoid dehydration.</p> <p>-Tumorigenic: Shown to be a tumorigen in chronic toxicity animal studies. Recent retrospective and observational studies do not suggest an increased risk of prostate or breast cancer.</p> <p>-When evaluating a heart failure patient for spironolactone treatment, eGFR should be <math>&gt;30</math> mL/minute/1.73 m<sup>2</sup> or creatinine should be <math>\leq 2.5</math> mg/dL (men) or <math>\leq 2</math> mg/dL (women) with no recent worsening and potassium <math>&lt;5</math> mEq/L with no history of severe hyperkalemia. Discontinue therapy if serum potassium cannot be maintained <math>&lt;5.5</math> mEq/L or if kidney function worsens. Consider the entire medical regimen and other potential causes of hyperkalemia.</p> <p>-Discontinue use prior to adrenal vein catheterization.</p> <p>-When used in combination with ACE inhibitors or ARBs, monitor patient for increased risk of hyperkalemia in older patients.</p>
<b>Storage</b>	<p>Tablet: Store between 15°C to 30°C. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Diuretics, Thiazides

## Chlorthalidone

<b>Generic Name</b>	<b>Chlorthalidone</b>
<b>Dosage form/strengths</b>	Tablets: 12.5 or 25mg in combinations with Atenolol or Metoprolol or Azilsartan.
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antihypertensive; Thiazide-Related Diuretic ATC: C03BA04
<b>Indications</b>	Management of chronic hypertension.
<b>Dosage Regimen</b>	<b>Adult dosing:</b> <b>Hypertension</b> Oral: 12.5mg to 25 mg once daily, dose to be taken in the morning, evaluate and increase up to 25 mg (in combination therapy) after 2 to 4 weeks.
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function: Adult</b> Caution and monitor effect. CrCl <10 mL/minute: Use not recommended due to lack of efficacy. <b>Dosing: Hepatic Impairment: Adult</b> Use chlorthalidone with caution in patients with hepatic disease.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Anuria</li> <li>• Sulfonamide hypersensitivity</li> <li>• Thiazide diuretic hypersensitivity</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions:</b></p> <p><b>Electrolyte disturbances</b> Reversible hypokalemia, hypomagnesemia, hypercalcemia, and hyponatremia may occur, particularly in high doses more than 25mg/day and elderly.</p> <p><b>Gout and hyperuricemia</b> may occur in high doses, long durations or with family history of gout.</p> <p><b>Hypersensitivity reactions (immediate and delayed):</b> within 1 hour to weeks</p> <p><b>Ocular effects:</b> Acute transient myopia and acute angle-closure glaucoma.</p> <p><b>Common or very common (&gt;1%):</b> Decreased Appetite, gastrointestinal discomfort</p> <p><b>Uncommon (0.1%-1%):</b> Gout</p> <p><b>Rare or very rare:</b> Arrhythmia, diabetes mellitus, glycosuria, hepatic disorders, nephritis tubulointerstitial, pulmonary oedema, respiratory disorder</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Serum electrolytes</li> <li>• Fluid intake and output</li> <li>• Kidney function</li> <li>• Blood glucose</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Aminolevulinic Acid (Systemic), Bromperidol, Levosulpiride, Promazine</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Arsenic Trioxide, Bile Acid Sequestrants, Dofetilide, Lithium, Mecamylamine, Obinutuzumab</p>

<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Diuretic use may decrease placental perfusion. Potential risks from thiazide use include electrolyte imbalances in the newborn, pancreatitis, jaundice, or neonatal complications resulting from such maternal complications such as hyperglycemia, electrolyte imbalance, or hypotension.</p> <p><b>Lactation:</b> Potential risk to infant. Thiazide diuretics have the potential to decrease milk volume and suppress lactation. Use should be avoided when possible</p>
<b>Administration</b>	<p>Oral: Administer as a single dose in the morning with food. Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Sulfonamide allergy</li> <li>• Adrenal insufficiency: Avoid use of diuretics for treatment of hypertension in patients with primary adrenal insufficiency (Addison disease).</li> <li>• Diabetes: Hyperglycemia, reduced glucose tolerance, and glycosuria can occur during Chlorthalidone therapy. Use with caution in patients with prediabetes or diabetes mellitus.</li> <li>• Hepatic impairment: Use with caution in patients with severe hepatic impairment; electrolyte imbalances might lead to hepatic encephalopathy.</li> <li>• Hypercholesterolemia: Use with caution in moderate or high cholesterol concentrations patients; increased cholesterol and triglyceride levels have been reported with thiazide diuretics.</li> <li>• Renal impairment: Cumulative effect. Avoid in severe renal disease (ineffective).</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from light. Refer to manufacturer PIL for specific considerations.</p>

## Hydrochlorothiazide

<b>Generic Name</b>	Hydrochlorothiazide
<b>Dosage form/strengths</b>	Tablet: 12.5mg, 25mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Thiazide ATC: C03AA03
<b>Indications</b>	<b>Edema or general volume overload:</b> Treatment of edema due to heart failure, various forms of renal dysfunction or corticosteroid or estrogen therapy. <b>Note:</b> Hydrochlorothiazide may be used as an adjunctive agent for refractory edema. <b>Hypertension, chronic:</b> Management of mild to moderate hypertension.
<b>Dosage Regimen</b>	<b>Edema or general volume overload:</b> <b>Oral:</b> Initial: 25 to 50 mg once or twice daily; may increase dose as needed based on response and tolerability up to a maximum of 200 mg/day. Assess volume status frequently (eg, daily or at least every 2 to 3 days) <b>Hypertension, chronic (alternative agent):</b> <b>Oral:</b> Initial: 12.5 to 25 mg once daily; adjust dose after 2 to 4 weeks according to response up to 25 mg once daily
<b>Dosage adjustment</b>	<b>Dosing: Older Adult</b> Oral: Initial: 12.5 mg once daily; titrate as necessary in increments of 12.5 mg. Minimal increase in response and more electrolyte disturbances are seen with doses >50 mg daily. <b>Dosing: Altered Kidney Function: Adult</b> CrCl ≥30 mL/minute: No dosage adjustment necessary. CrCl <30 mL/minute: Use not recommended due to lack of efficacy. <b>Dosing: Hepatic Impairment: Adult</b> There are no dosage adjustments available. However, use with caution and monitor for precipitation of hepatic coma.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Anuria</li> <li>• Sulfonamide hypersensitivity</li> <li>• Thiazide diuretic hypersensitivity</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Adverse Reactions (Significant): Considerations</b> <b>Dermatologic toxicity:</b> Skin photosensitivity. 5 years use increases the risk for squamous cell carcinoma (SCC) of skin (lip) and basal cell carcinoma (BCC) of skin <b>Electrolyte disturbances:</b> Reversible hypokalemia, hypomagnesemia, hypercalcemia, and hyponatremia may occur with hydrochlorothiazide and may increase the risk of arrhythmias. minimized by using in combination with other electrolyte-sparing antihypertensives. <b>Gout:</b> may cause hyperuricemia <b>Hypersensitivity reactions (immediate and delayed):</b> within 1 hour to 6 weeks after drug exposure. <b>Ocular Effects:</b> rarely cause acute transient myopia and acute angle-closure glaucoma which is generally reversible. <b>Frequency not defined:</b>

	<p>Cardiovascular: Hypersensitivity angitis, hypotension (including orthostatic)</p> <p>Dermatologic: Alopecia, skin rash, toxic epidermal necrolysis, urticaria</p> <p>Endocrine and metabolic: Glycosuria, hypomagnesemia</p> <p>Gastrointestinal: Abdominal cramps, anorexia, constipation, diarrhea, gastric irritation, nausea, vomiting</p> <p>Hematologic and oncologic: Aplastic anemia, thrombocytopenia</p> <p>Hypersensitivity: Anaphylaxis</p> <p>Nervous system: Dizziness, headache, paresthesia, restlessness, vertigo</p> <p>Neuromuscular and skeletal: Asthenia, muscle spasm</p> <p>Ophthalmic: Blurred vision (transient), xanthopsia</p> <p>Renal: Acute kidney injury</p> <p>Miscellaneous: Fever</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Fluid intake and output</li> <li>• Serum electrolytes</li> <li>• Kidney functions</li> <li>• Skin to assess for photosensitivity and skin cancer</li> <li>• Visual acuity, ocular pain.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Aminolevulinic Acid (Systemic), Bromperidol, Dofetilide, Levosulpiride, Promazine</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Arsenic Trioxide, Bile Acid Sequestrants, Lithium, Mecamylamine, Obinutuzumab.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Maternal use may cause fetal or neonatal jaundice, thrombocytopenia, or other adverse events observed in adults. Monitor volume status and adjust dose to minimize risk of placental hypoperfusion.</p> <p><b>Breastfeeding:</b> Thiazide diuretics have the potential to decrease milk volume and suppress lactation; use should be avoided when possible. Hydrochlorothiazide is considered compatible with breastfeeding by WHO. Low dosages (25 mg per day or less) are compatible with lactation.</p>
<b>Administration</b>	<p>Oral: May administer with or without food; administer early in day to avoid nocturia; if multiple daily dosing unless instructed otherwise.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Sulfonamide allergy: There is a potential for cross-reactivity.</li> <li>• Adrenal insufficiency: Avoid use of diuretics for treatment of elevated blood pressure in patients with primary adrenal insufficiency (Addison disease).</li> <li>• Ascites due to cirrhosis: Use with extreme caution or avoid hydrochlorothiazide in the management of ascites due to cirrhosis; may lead to rapid development of hyponatremia when used in combination with spironolactone and furosemide.</li> <li>• Bariatric surgery: Dehydration: Avoid diuretics early after bariatric surgery; electrolyte disturbances and dehydration may occur. Resume, if indicated, once oral fluid intake goals are met.</li> <li>• Diabetes: Use with caution in patients with diabetes; increased blood glucose levels and hyperglycemia may occur. Monitor blood glucose periodically.</li> <li>• Hepatic impairment: Use with caution in patients with severe hepatic disorders, avoid electrolyte and acid/base imbalances that might lead to hepatic encephalopathy/coma.</li> </ul>

	<ul style="list-style-type: none"> <li>• Hypercholesterolemia: Use with caution in patients with moderate or high cholesterol concentrations; increased cholesterol and triglyceride levels have been reported.</li> <li>• Parathyroid disease: Thiazide diuretics reduce calcium excretion; pathologic changes in the parathyroid glands with hypercalcemia and hypophosphatemia have been observed with prolonged use; should be discontinued prior to testing for parathyroid function.</li> <li>• Renal impairment: Cumulative effect. Avoid in severe renal disease (ineffective).</li> <li>• Systemic lupus erythematosus (SLE): May cause SLE exacerbation or activation.</li> <li>• Surgical patients: Avoid in morning of surgery to avoid volume depleted and blood pressure may be labile during general anesthesia.</li> </ul>
<b>Storage</b>	Store at 15°C to 30°C. Protect from light and moisture. <b>N.B.</b> Refer to manufacturer PIL for specific considerations

## Indapamide

<b>Generic Name</b>	Indapamide
<b>Dosage form/strengths</b>	Tablets: 2.5 mg Sustained or extended Release Tablets: 1.5mg And in combinations
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antihypertensive; Diuretic, Thiazide-Related ATC: C03BA11
<b>Indications</b>	<b>Edema or general volume overload:</b> Treatment of edema in heart failure. <b>Hypertension, chronic:</b> Management of mild to moderate hypertension.
<b>Dosage Regimen</b>	<b>Edema or general volume overload (adjunctive to loop diuretic):</b> <b>Oral:</b> Initial: 2.5 mg once daily; may increase dose, as needed, up to 5 mg once daily depending on patient response; may administer every other day or on specific days of the week. <b>Hypertension, chronic:</b> <i>Immediate release:</i> Initial: 1.25 to 2.5 mg once daily; adjust dose after 2 to 4 weeks as needed, up to 5 mg once daily; if additional blood pressure control is needed, consider combination therapy. <i>Sustained release:</i> 1.5 mg once daily. <b>Note:</b> Dosages >1.5 mg/day (using sustained-release formulation) do not enhance antihypertensive effect but may increase saluretic effect.
<b>Dosage adjustment</b>	<b>Patients with Renal Impairment Dosing</b> CrCl ≥ 30 mL/min: No dosage adjustment needed. CrCl < 30 mL/min: Do not use, indapamide is less effective as renal function declines. <i>Intermittent Hemodialysis:</i> Avoid use. Indapamide is not removed by hemodialysis. <b>Dosing: Hepatic Impairment: Adult</b> Use with caution. Sustained release tablets are contraindicated in patients with severe hepatic impairment or hepatic encephalopathy.
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Anuria</li> <li>• Hypersensitivity to sulfonamide or any component in the formulation.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>&gt;10%:</b> Endocrine and metabolic: Hypokalemia. <b>1% to 10%:</b> Cardiovascular: Cardiac arrhythmia (<5%), chest pain (<5%), flushing (<5%), orthostatic hypotension (<5%), palpitations (<5%), peripheral edema (<5%), vasculitis (<5%), ventricular premature contractions (<5%) Dermatologic: Pruritus (<5%), skin rash (<5%), urticaria (<5%) Endocrine and metabolic: Decreased libido (<5%), glycosuria (<5%), hyperglycemia (<5%), hyperuricemia (<5%), hypochloremia (<5%), hyponatremia (<5%), weight loss (<5%) Gastrointestinal: Abdominal cramps (<5%), abdominal pain (<5%), anorexia (<5%), constipation (<5%), diarrhea (<5%), dyspepsia (<5%), gastric irritation (<5%), nausea (<5%), vomiting (<5%), xerostomia (<5%) Genitourinary: Impotence (<5%), nocturia (<5%), urinary frequency (<5%) Infection: Infection (≥5%)



	<p>Nervous system: Agitation (<math>\geq 5\%</math>), anxiety (<math>\geq 5\%</math>), depression (<math>&lt; 5\%</math>), dizziness, drowsiness (<math>&lt; 5\%</math>), fatigue (<math>\geq 5\%</math>), headache (<math>\geq 5\%</math>), hypertonia (<math>&lt; 5\%</math>), insomnia (<math>&lt; 5\%</math>), irritability (<math>\geq 5\%</math>), lethargy (<math>\geq 5\%</math>), malaise (<math>\geq 5\%</math>), nervousness, numbness of extremities (<math>\geq 5\%</math>), pain (<math>\geq 5\%</math>), tension (<math>\geq 5\%</math>), tingling of extremities (<math>&lt; 5\%</math>), vertigo (<math>&lt; 5\%</math>)</p> <p>Neuromuscular and skeletal: Asthenia, back pain (<math>\geq 5\%</math>), muscle cramps (<math>\geq 5\%</math>), muscle spasm (<math>\geq 5\%</math>)</p> <p>Ophthalmic: Blurred vision (<math>&lt; 5\%</math>), conjunctivitis (<math>&lt; 5\%</math>)</p> <p>Renal: Increased blood urea nitrogen (<math>&lt; 5\%</math>), increased serum creatinine (<math>&lt; 5\%</math>), polyuria (<math>&lt; 5\%</math>)</p> <p>Respiratory: Cough (<math>&lt; 5\%</math>), flu-like symptoms (<math>&lt; 5\%</math>), pharyngitis (<math>&lt; 5\%</math>), rhinitis (<math>\geq 5\%</math>), rhinorrhea (<math>&lt; 5\%</math>), sinusitis (<math>&lt; 5\%</math>)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Blood pressure</li> <li>• Blood glucose</li> <li>• Kidney functions</li> <li>• Hepatic Function</li> <li>• Serum electrolytes</li> <li>• Serum uric acid</li> <li>• Intake and output reports daily to determine fluid loss</li> <li>• Visual changes (to assess for ocular adverse effects).</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Aminolevulinic Acid (Systemic), Bromperidol, Fexinidazole, Levosulpiride, Promazine</p> <p><b>Risk D: Consider therapy modification</b> Amifostine, Arsenic Trioxide, Bile Acid Sequestrants, Dofetilide, Lithium, Mecamylamine, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Insufficient human data. Other agents are preferred.</p> <p><b>Lactation:</b> No human data.</p>
<b>Administration</b>	<p><b>Administration: Oral</b></p> <p>May be administered without regard to meals; however, administration with food or milk may decrease GI adverse effects. Administer early in day to avoid nocturia. Sustained release tablets should be swallowed whole (do not crush or chew).</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Electrolyte disturbances: Severe hyponatremia with hypokalemia has been reported at recommended doses (particularly in elderly women); risk may be dose dependent, therefore, use lowest dose possible. Hypochloremic alkalosis, hypomagnesemia, or hypercalcemia can also occur; monitor electrolytes periodically during therapy.</li> <li>• Ocular effects: may cause an idiosyncratic reaction resulting in acute angle-closure glaucoma and elevated intraocular pressure with or without a noticeable acute myopic shift and/or choroidal effusions. Symptom onset (eg, decreased visual acuity, ocular pain) typically occurs within hours to weeks after treatment initiation and may result in permanent vision loss if left untreated. Risk may be increased in patients with sulfonamide or penicillin allergy.</li> </ul>

- Photosensitivity: Photosensitization may occur.
- Sulfonamide allergy: In cases where prior reactions were severe (Stevens-Johnson syndrome/TEN), avoid exposure to these classes.

***Disease-related concerns:***

- Adrenal insufficiency: Avoid use of diuretics for treatment of elevated blood pressure in patients with primary adrenal insufficiency (Addison disease).
- Bariatric surgery: Dehydration: Avoid diuretics early after bariatric surgery; electrolyte disturbances and dehydration may occur.
- Diabetes: Use with caution in patients with prediabetes or diabetes mellitus; hyperglycemia may occur, monitor.
- Gout: In certain patients with a history of gout, or chronic renal failure, gout can be precipitated.
- Hepatic impairment: Use with caution in patients with severe hepatic dysfunction; in cirrhosis, avoid electrolyte and acid/base imbalances that might lead to hepatic encephalopathy.
- Hypercholesterolemia: Use with caution in patients with moderate or high cholesterol concentrations; thiazide diuretics have been shown to increase cholesterol concentrations; however, indapamide (a thiazide-like diuretic) has not been shown to adversely affected lipids.
- Hypokalemia: Use with caution in patients with hypokalemia; correct before initiating therapy.
- Renal impairment: Use with caution in severe renal disease.
- Systemic lupus erythematosus: Can cause systemic lupus erythematosus exacerbation or activation.

***Dosage forms specific issues:***

- Lactose: Formulation may contain lactose.

**Storage**

Store between 15°C to 30°C.

**N.B.** Refer to manufacturer PIL for specific considerations.

## Fibrinolytics Agent

## Alteplase

<b>Generic Name</b>	<b>Alteplase</b>
<b>Dosage form/strengths</b>	Powder and solvent for injection: 50 mg vial
<b>Route of administration</b>	IV
<b>Pharmacologic category</b>	Thrombolytic Agent ATC: B01AD02
<b>Indications</b>	<p>IV:</p> <p><b>1-Acute ischemic stroke:</b> administer as soon as possible within 4.5 hours of symptom onset and if intracranial haemorrhage has been excluded by appropriate imaging techniques.</p> <p><b>2-Pulmonary embolism:</b> Management of acute massive pulmonary embolism.</p> <p><b>3- Acute myocardial infarction:</b> Thrombolytic therapy</p> <ul style="list-style-type: none"> <li>• 90 minutes (accelerated)dose regimen: for patients in whom treatment can be started within 6 h after symptom onset</li> <li>• 3h dose regimen: for patients in whom treatment can be started between 6-12 h after symptom onset provided that diagnosis has been clearly confirmed.</li> </ul>
<b>Dosage Regimen</b>	<p><b>1-Acute ischemic stroke:</b></p> <p><u>Adult:</u> treatment must begin within 4.5 hours of symptom onset: 0.9mg/kg (max. per dose 90 mg), the initial 10% of dose is to be administered by intravenous injection and the remainder by intravenous infusion over 60 minutes. <b>N.B.</b> Not indicated for Acute ischemic stroke in elderly over 80 years.</p> <p><b>2-Acute myocardial infarction</b></p> <p><b>A. Accelerated regimen within 6 hours of symptom onset</b></p> <p><u>Adult (body-weight up to 65 kg):</u></p> <ul style="list-style-type: none"> <li>• Initially IV bolus 15 mg, to be initiated within 6 hours of symptom onset.</li> <li>• Followed by IV 0.75 mg/kg, to be given over 30 minutes (maximum 50mg)</li> <li>• Then IV 0.5 mg/kg (maximum 35mg), to be given over 60 minutes,</li> </ul> <p><b>N.B.</b> Maximum total dose of 100mg administered over 90 minutes</p> <p><u>Adult (body-weight 65 kg and above):</u></p> <ul style="list-style-type: none"> <li>• Initially IV bolus 15 mg, to be initiated within 6 hours of symptom onset.</li> <li>• Followed by IV 50mg, to be given over 30 minutes.</li> <li>• Then IV 35mg to be given over 60 minutes.</li> </ul> <p><b>N.B.</b> Maximum total dose of 100mg administered over 90 minutes</p> <p><b>B. 3-hour dose regimen for patients in whom treatment can be started between 6-12 hours after symptom onset:</b></p> <p><u>Adult:</u></p> <ul style="list-style-type: none"> <li>• Initially IV 10 mg, to be initiated within 6–12 hours of symptom onset,</li> </ul>

	<ul style="list-style-type: none"> <li>• Followed by IV 50 mg, to be given over 60 minutes.</li> <li>• Then IV 10 mg for 4 infusions, each 10 mg infusion dose to be given over 30 minutes, total dose of 100mg over 3 hours</li> </ul> <p>N.B. Maximum 1.5 mg/kg in patients less than 65 kg</p> <p><b>3-Pulmonary embolism (Massive):</b></p> <ul style="list-style-type: none"> <li>• Initial: IV 10 mg, to be given over 1–2 minutes</li> <li>• Followed by IV 90 mg, to be given over 2 hours.</li> </ul> <p>N.B. Maximum 1.5 mg/kg in patients less than 65 kg.</p> <p><b>Pediatrics:</b> Safety and efficacy have not been established in children and adolescents under 18years.</p>
<p><b>Dosage Adjustment</b></p>	<p><b>Dosing: Altered Kidney Function: Adult</b> There are no dose adjustments needed.</p> <p><b>Dosing: Hepatic Impairment: Adult</b> There are no dose adjustments needed.</p>
<p><b>Contra-Indications</b></p>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Alteplase and gentamicin.</li> <li>• Cases where there is a high risk of hemorrhage.</li> <li>• Recent delivery</li> <li>• <b>Additional contraindications in acute ischaemic stroke:</b> symptoms of ischaemic attack beginning more than 4.5 hours prior to infusion start or symptoms for which the onset time is unknown and could potentially be more than 4.5 hours ago, Convulsion accompanying stroke. history of stroke in patients with diabetes. severe stroke. stroke in last 3 months. Platelet count of below 100,000 /mm<sup>3</sup>, systolic blood pressure&gt;185 or diastolic BP&gt;110mm Hg, or aggressive management necessary to reduce BP to these limits, blood glucose&lt;50 or &gt;400mg/dl.</li> <li>• <b>Additional contraindications in acute pulmonary embolism and acute myocardial infarction:</b> Known history of ischaemic stroke or transient ischaemic attack in the preceding 6 months except current acute ischaemic stroke within 4.5 hours.</li> </ul>
<p><b>Adverse Drug Reactions</b></p>	<p><b>&gt;10%:</b> Cardiovascular: Intracranial hemorrhage (stroke: Within 90 days: 15%, within 36 hours: 6%; Acute Myocardial Infarction AMI: &lt;1%)</p> <p><b>1% to 10%:</b></p> <p>Dermatologic: Ecchymosis (AMI: 1%) Gastrointestinal: Gastrointestinal hemorrhage (AMI: 5%) Genitourinary: Genitourinary tract hemorrhage (AMI: 4%)</p> <p><b>Frequency not defined:</b></p> <p>Hematologic and oncologic: Arterial embolism, major hemorrhage, pulmonary embolism Infection: Sepsis</p>
<p><b>Monitoring</b></p>	<ul style="list-style-type: none"> <li>• Creatine phosphokinase (CPK)</li> </ul>

<b>Parameters</b>	<ul style="list-style-type: none"> <li>• ECG</li> <li>• Hemoglobin/hematocrit</li> <li>• Partial thromboplastin time (PTT)</li> <li>• CBC, prothrombin time (PT)</li> <li>• Thrombin time</li> </ul> <p><b>When used for acute ischaemic stroke:</b> Monitor for intracranial haemorrhage and blood pressure.</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Defibrotide, Tranexamic Acid</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy</b> Limited data. Evaluate benefit and risk.</p> <p><b>Lactation.</b> No sufficient data.</p>
<b>Administration</b>	<p><b>Preparation of administration:</b></p> <ul style="list-style-type: none"> <li>• Dissolve in water for injections to a concentration of 1 mg/mL or 2 mg/mL and give intravenously; or dilute the solution further by N.S 0.9% to a concentration of not less than 0.2 mg/mL; not to be infused in glucose solution.</li> <li>• Reconstitute immediately before administration. Dispose any unused solution.</li> <li>• Solution 1mg/1ml should be clear and colorless to pale yellow.</li> </ul> <p><b>N.B</b> Refer to PIL of product for more specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>Haemorrhages: If a potentially dangerous haemorrhage occurs, in particular cerebral haemorrhage, the fibrinolytic therapy must be discontinued. Higher intracranial bleeding risk is associated with high doses and Elderly.</p> <p>Concomitant use of GP IIb/IIIa antagonists increases the risk of bleeding.</p> <p>The therapeutic benefit is reduced in patients that had a prior stroke or in those with known uncontrolled diabetes, thus the benefit/risk ratio is considered less favourable, but still positive in these patients.</p> <p>The risk of haemorrhage is increased if coumarine derivatives, oral anticoagulants, platelet aggregation inhibitors, unfractionated heparin or LMWH or active substances which interfere with coagulation are administered (before, during or within the first 24 hours after treatment with Alteplase)</p>
<b>Storage</b>	<ul style="list-style-type: none"> <li>• Store intact vials between 15°C to 30°C; protect from light.</li> <li>• Discard any unused solution</li> </ul> <p><b>N.B</b> Refer to PIL of product for more specific considerations.</p>

## Streptokinase

<b>Generic Name</b>	Streptokinase
<b>Dosage form/strengths</b>	Vial: 1.500 M.I.U.
<b>Route of administration</b>	IV
<b>Pharmacologic category</b>	Thrombolytic Agent ATC: B01AD01
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Central retinal venous or arterial thrombosis</li> <li>• Deep vein thrombosis</li> <li>• Pulmonary embolism</li> <li>• Acute myocardial infarction</li> <li>• Occlusive peripheral arterial disease</li> </ul>
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b></p> <p><b>Central retinal venous or arterial thrombosis:</b> IV: 250,000 units over 30 minutes, followed by 100,000 units/hour for 12 hours.</p> <p><b>Deep vein thrombosis:</b> IV: 250,000 units over 30 minutes, followed by 100,000 units/hour for 72 hours. Note: Some guidelines recommend against routine systemic or catheter-directed thrombolysis compared to anticoagulation alone for deep vein thrombosis.</p> <p><b>Pulmonary embolism: IV:</b> <i>Accelerated regimen:</i> 1.5 million units administered over 1 to 2 hours.</p> <p><b>Acute myocardial infarction:</b> IV: 1.5 million units over 60 minutes.</p> <p><b>Occlusive peripheral arterial disease: IV:</b> 250 000 units, dose to be given over 30 minutes, then 100 000 units every 1 hour for up to 5 days</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Renal Impairment:</b> Mild or moderate impairment: There are no dose adjustments available. Severe impairment: Use is contraindicated.</p> <p><b>Dosing: Hepatic Impairment:</b> Mild or moderate impairment: There are no dose adjustments available Severe impairment: Use is contraindicated</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to streptokinase or any component of the formulation.</li> <li>• Active or recent internal bleeding.</li> <li>• Recent CVA, intracranial or intraspinal surgery or recent head trauma; recent (within 6 to 10 days) major operation or invasive operation.</li> <li>• Intracranial neoplasm or other neoplasm with risk of hemorrhage.</li> <li>• Arteriovenous malformation or aneurysm.</li> <li>• Known bleeding diathesis.</li> <li>• Spontaneous fibrinolysis and extensive clotting disorders.</li> <li>• Severe uncontrolled hypertension (systolic BP &gt;200 mm Hg and/or diastolic BP &gt;100 mm Hg); hypertensive retinopathy (grade III or IV).</li> <li>• Acute pancreatitis.</li> <li>• Severe renal impairment; severe hepatic impairment.</li> <li>• Endocarditis or pericarditis.</li> <li>• Concurrent or recent oral anticoagulant therapy (INR &gt;1.3)</li> </ul>



<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Immunologic: Antibody development</p> <p><b>1% to 10%:</b></p> <p>Cardiovascular: Bradycardia (at initiation), flushing, hypotension (most likely during drug initiation), tachycardia (at initiation)</p> <p>Central nervous system: Chills, headache, malaise</p> <p>Dermatologic: Ecchymoses, pruritus, skin rash, urticaria</p> <p>Gastrointestinal: Diarrhea, epigastric pain, gastrointestinal hemorrhage, nausea, vomiting</p> <p>Hematologic and oncologic: Genitourinary tract hemorrhage</p> <p>Hepatic: Increased serum bilirubin (transient), increased serum transaminases (transient)</p> <p>Hypersensitivity: Anaphylaxis, angioedema, nonimmune anaphylaxis, hypersensitivity reaction</p> <p>Local: Bleeding at injection site</p> <p>Neuromuscular and skeletal: Asthenia, back pain, musculoskeletal pain</p> <p>Respiratory: Bronchospasm, dyspnea, epistaxis</p> <p>Miscellaneous: Fever</p>
<b>Monitoring Parameters</b>	<p>Blood pressure, heart rate</p> <p>ECG, PT/INR</p> <p>Activated partial thromboplastin time</p> <p>CBC</p> <p>Signs of bleeding</p> <p>Fibrinogen levels, fibrinogen degradation products</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>Bromperidol, Heparin, Vitamin K Antagonists (eg, warfarin)</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Amifostine, Desirudin, Obinutuzumab</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> The risk of bleeding may be increased in pregnant women. Many guidelines consider pregnancy a relative contraindication to thrombolytic use. Thrombolytic therapy should not be withheld from pregnant women in life-threatening situations, but should be avoided when safer alternatives are available.</p> <p><b>Lactation:</b> It is not known if Streptokinase is excreted in breast milk. It is recommended to avoid breastfeeding for 24 hours following therapy.</p>
<b>Administration</b>	<p><b>Administration: IV</b></p> <p>If streptokinase administration is repeated between 5 days and 1 year after initial treatment efficacy may be reduced and risk of allergic reaction may increase; use alternative fibrinolytic agent during this period. Corticosteroids may be administered prophylactically to reduce the likelihood of infusion-related allergic reactions.</p> <p><b>Myocardial infarction:</b> Administer dose over 60 minutes.</p> <p><b>Pulmonary embolism:</b> Administer dose over 1 to 2 hours (accelerated regimen); alternatively, for non-accelerated regimen administer bolus infusion over 30 minutes followed by continuous infusion.</p> <p><b>Deep vein thrombosis:</b> Administer bolus infusion over 30 minutes followed by continuous infusion. Alternatively, an intermittent maintenance infusion for 6 hours per day has been described.</p> <p><b>Peripheral arterial occlusion or central retinal venous or arterial occlusion:</b> Administer bolus infusion over 30 min. followed by continuous infusion.</p> <p><b>Administration: Intra-arterial</b></p>



	<p>Peripheral arterial occlusion: May administer doses every 3-5 minutes for up to 10 hours, or administer as prolonged continuous low-dose infusion (using infusion pump).</p> <p><b>Administration: Other</b></p> <p>Intracoronary: Myocardial infarction: Administer bolus dose followed by infusion over 30 to 90 minutes.</p> <p><b>Preparation for Administration:</b></p> <p>Reconstitute with 4 to 5 mL of NS or SWFI. Swirl gently but avoid foaming. Reconstituted solution may have a slight yellow color.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<p><b>Warnings/ Precautions</b></p>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Anaphylaxis: Rare anaphylactic reactions may occur. Discontinue streptokinase immediately and institute supportive measures; do not rechallenge. May switch to alternative fibrinolytic therapy if needed.</li> <li>• Arrhythmias: Coronary thrombolysis may result in reperfusion arrhythmias (eg, accelerated idioventricular rhythm).</li> <li>• Bleeding: Risk of bleeding is increased with use; fatal hemorrhage has been reported. Monitor carefully. Discontinue if serious bleeding occurs. Concomitant or recent use of oral anticoagulants (INR &gt;1.3) is contraindicated.</li> <li>• Hypotension: Hypotension, tachycardia, and/or bradycardia may commonly occur with initial infusion; severe hypotension or bradycardia may rarely occur (not from bleeding or anaphylaxis).</li> </ul> <p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Conditions that increase bleeding risk: For conditions the risk of bleeding is higher with use of thrombolytics should be weighed against the benefits of therapy</li> </ul> <p><b>Special populations:</b></p> <ul style="list-style-type: none"> <li>• Elderly: Use with caution in patients with advanced age (eg, &gt;75 years); thrombolytics may increase bleeding risk. However, risk of intracranial hemorrhage may be less with streptokinase compared to fibrin specific agents.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Administration: Intramuscular injections and nonessential handling of the patient should be avoided. Venipunctures should be performed carefully and only when necessary. If arterial puncture is necessary, use an upper extremity vessel that can be manually compressed.</li> <li>• Antistreptokinase antibodies: Increased antistreptokinase antibodies may decrease efficacy and increase likelihood of an allergic reaction. Avoid use immediately after streptococcal infections which have produced a high antistreptokinase titer (eg, acute rheumatic fever, acute glomerulonephritis, and streptococcal pharyngitis). If streptokinase administration is repeated between 5 days and 1 year after initial treatment efficacy may be reduced and risk of allergic reaction may increase; use alternative fibrinolytic agent during this period.</li> <li>• Appropriate use: Not indicated for restoration of patency of intravenous catheters. Alternative thrombolytics are preferred for occluded catheters due to higher risk of allergic reaction with streptokinase</li> </ul>
<p><b>Storage</b></p>	<p>Store intact vials between 15°C to 30°C. Do not freeze vials. Reconstituted solution is stable for 24 hours when stored between 2°C and 8°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Lipid Modifying Agents, Bile Acid Sequestrants

## Cholestyramine

<b>Generic Name</b>	<b>Cholestyramine</b>
<b>Dosage form/strengths</b>	Powder for Oral Suspension: 4mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, Bile Acid Sequestrant ATC: C10AC01
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Dyslipidemia: Adjunct in the management of primary hypercholesterolemia; regression of arteriosclerosis</li> <li>• Primary prevention of coronary heart disease in men aged 35–59 years with primary hypercholesterolemia who have not responded to diet and other appropriate measures.</li> <li>• Diarrhea associated with Crohn’s disease, ileal resection, vagotomy, diabetic vagal neuropathy, and radiation</li> <li>• Treatment of pruritus associated with partial biliary obstruction and primary biliary cirrhosis</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>Dyslipidemia, Diarrhea and for Primary prevention of coronary heart disease:</b></p> <p>-Oral: Initially 4 g daily, increased weekly if necessary to 12–24 g daily in 1–4 divided doses, maximum 36 g per day.</p> <p>-If no response to diarrhea within 3 days an alternative therapy should be initiated.</p> <p><b>Treatment of pruritus associated with partial biliary obstruction and primary biliary cirrhosis</b></p> <p>-Oral: 4–8 g once daily</p> <p><b>Pediatric dosing:</b></p> <p><b>familial hypercholesterolemia</b></p> <p>Oral: Child 6–12 years: initial dose: weight of child (kgs) * adult dose/70 Then adjust according to response.</p>
<b>Dosage Adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b></p> <p>There are no dosage adjustments needed; however, use with caution in renal impairment; may cause hyperchloremic acidosis.</p> <p><b>Dosing: Hepatic Impairment:</b></p> <p>No dosage adjustment necessary; not absorbed from the gastrointestinal tract.</p> <p><b>Dosing elderly:</b></p> <p>Doses may be reduced to avoid adverse effects.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to bile acid sequestering resins or components of the formulation.</li> <li>• Complete Biliary obstruction.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><u>Constipation</u>: The most common adverse. Most cases of constipation are mild and self-limiting or may require dosage adjustment or discontinuation of therapy.</p> <p><u>Fat-soluble vitamin/folate deficiency</u>: Chronic use may cause reversible fat-soluble vitamin (A, D, K) and/or folate deficiencies in adult and pediatric resulting in various clinical issues. Supplementation of folic acid and parenteral vitamin K is recommended.</p>

	<p>Hemorrhage: due to vitamin K deficiency</p> <p><u>Hyperchloremic metabolic acidosis</u>: Because it is a chloride containing anion exchange resin, particularly in prolonged use or in children.</p> <p><u>Hypertriglyceridemia</u>: Bile acid resins have been reported to increase serum triglyceride concentrations and should be used with caution in patients with hypertriglyceridemia. Bile acid resins such as cholestyramine are contraindicated in patients with a <i>serum triglyceride concentration &gt; 400 mg/dl</i>.</p> <p><b>Uncommon adverse effects</b>: Bleeding tendency, hypoprothrombinaemia, night blindness, osteoporosis, skin reactions, tongue irritation, vitamin deficiencies.</p>
<b>Monitoring Parameters</b>	Serum lipid profile (baseline and periodically)
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Mycophenolate, Taurursodiol</p> <p><b>Risk D: Consider therapy modification</b> Amiodarone, Chenodiol, Cholic Acid, Deferasirox, Ethinyl Estradiol-Containing Products, Ezetimibe, Fibric Acid Derivatives, Fluvastatin, Leflunomide, Lomitapide, Maralixibat, Multivitamins/Fluoride (with ADE), Niacin, Obeticholic Acid, Odevixibat, Phenobarbital, Pravastatin, Raloxifene, Rosiglitazone, Sincalide, Teriflunomide, Thiazide and Thiazide-Like Diuretics, Thyroid Products, Ursodiol, Valproic Acid and Derivatives, Vitamin D Analogs, Vitamin K Antagonists (eg, warfarin)</p>
<b>Pregnancy and Lactation</b>	<b>Pregnancy and Lactation</b> : Not absorbed systemically but may interfere with absorption of vital vitamins which may harm fetus.
<b>Administration</b>	<p><b>Preparation for Administration</b>: Mix powder with at least 150ml water, juice or skimmed milk.</p> <p>-Administer prepared suspension orally at mealtime.</p> <p>-Administer other oral medications <math>\geq 1</math> hour before or 4 to 6 hours after cholestyramine.</p> <p>-Supplementation of vitamins A, D, E, and K, folic acid, and iron may be required with high-dose, long-term therapy.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Bleeding: Chronic use may be associated with bleeding problems (especially in high doses) due to vitamin K deficiency.</li> <li>• Constipation: May produce or exacerbate constipation; initiate at a reduced dose in patients with a history of constipation. Hemorrhoids may be worsened.</li> <li>• Hypertriglyceridemia: May increase serum triglyceride concentrations and should be used with caution in patients with hypertriglyceridemia. Bile acid resins such as cholestyramine are contraindicated in patients with a <i>serum triglyceride concentration &gt; 400 mg/dl</i> <ul style="list-style-type: none"> <li>• Renal impairment: Use caution in patients with renal impairment.</li> <li>• Decreased absorption (orally administered drugs): Separate administration of other medicines and oral vitamins several hours to minimize the risk of an interaction.</li> <li>• Phenylalanine: Some products may contain phenylalanine.</li> <li>• Secondary causes of hyperlipidemia should be ruled out prior to therapy.</li> </ul> </li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Colesevelam

<b>Generic Name</b>	Colesevelam
<b>Dosage form/strengths</b>	Tablets: 625mg Powder for Oral Suspension: 1.875 gm, 3.75 gm
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, Bile Acid Sequestrant ATC: C10AC04
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Monotherapy for primary hypercholesterolaemia as an adjunct to dietary measures</li> <li>• Primary hypercholesterolaemia as an adjunct to dietary measures [in combination with a statin or ezetimibe]</li> <li>• For the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult Dosing:</b>  <b>Monotherapy for primary hypercholesterolaemia as an adjunct to dietary measures,</b>  <b>Primary hypercholesterolaemia as an adjunct to dietary measures [in combination with a statin or ezetimibe], For the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise:</b>                      Oral: 3.75 g daily in 1–2 divided doses</p> <p>Use in pediatrics has not been proved for efficacy and safety.</p>
<b>Dosage Adjustment</b>	<p><b>Dosing: Altered Kidney Function:</b>                      No dosage adjustments necessary; not absorbed from the gastrointestinal tract.</p> <p><b>Dosing: Hepatic Impairment:</b>                      No dosage adjustments necessary; not absorbed from the gastrointestinal tract.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Colesevelam or any component of the formulation.</li> <li>• Biliary or bowel obstruction</li> <li>• Hypertriglyceridemia</li> <li>• Pancreatitis</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>&gt;10%:</b> Gastrointestinal: Constipation (3% to 11%)</p> <p><b>1% to 10%:</b>                      Cardiovascular: Cardiovascular toxicity (2%, including myocardial infarction, aortic stenosis, bradycardia), hypertension (2% to 3%)                      Central nervous system: Headache (children and adults 4% to 8%), fatigue (children 4%)                      Endocrine and metabolic: Hypertriglyceridemia (4% to 5%; &gt;500 mg/dL: &lt;1%; &gt;1,000 mg/dL: &lt;1%), hyperglycemia (3%), hypoglycemia (3%)                      Gastrointestinal: Dyspepsia (3% to 8%), diarrhea (4%), nausea (children and adults 3% to 4%), gastroesophageal reflux disease (2%), periodontal abscess (2%), vomiting (children 2%)                      Hematologic and oncologic: C-reactive protein increased (3%)                      Infection: Influenza (children and adolescents 4%)                      Neuromuscular and skeletal: Weakness (4%), back pain (2%), increased creatine phosphokinase (children and adults 2%), myalgia (2%)</p>

	Respiratory: Nasopharyngitis (children 5% to 6%), upper respiratory tract infection (children and adults 3% to 5%), flu-like symptoms (children 4%), pharyngitis (3%), rhinitis (children 2%)
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Serum Lipid profile baseline and periodically.</li> <li>• Blood glucose</li> <li>• Serum triglycerides</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Mycophenolate, Taurursodiol</p> <p><b>Risk D: Consider therapy modification</b> Amiodarone, Chenodiol, Cholic Acid, Cyclosporine (Systemic), Deferasirox, Ethinyl Estradiol-Containing Products, Ezetimibe, Glimepiride, Glipizide, Glyburide, Leflunomide, Lomitapide, Maralixibat, Multivitamins/Minerals (with ADEK, Folate, Iron), Niacin, Norethindrone, Obeticholic Acid, Odevixibat, Olmesartan, Phenytoin, Pravastatin, Raloxifene, Teriflunomide, Thiazide and Thiazide-Like Diuretics, Thyroid Products, Ursodiol, Vitamin D Analogs</p>
<b>Pregnancy and Lactation</b>	<b>Pregnancy and Lactation:</b> Not absorbed systemically but may interfere with absorption of vital vitamins which may harm fetus.
<b>Administration</b>	<p><b>Administration: Oral</b></p> <p>Granules for oral suspension: Administer with meal(s). Powder is not to be taken in dry form (to avoid esophageal distress).</p> <p>Tablets: Administer with meal(s) and a liquid.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Gastrointestinal disease: Use is not recommended in patients with gastroparesis, other severe GI motility disorders, a history of major GI tract surgery, or patients at risk for bowel obstruction. Use tablets with caution in patients with dysphagia or swallowing disorders; use the oral suspension form of colesevelam due to large tablet size and risk for esophageal obstruction. Discontinue if symptoms of bowel obstruction occur (eg, severe abdominal pain, severe constipation).</li> <li>• Hypertriglyceridemia: Bile acid sequestrants can increase serum triglyceride concentrations; severely elevated triglycerides can cause acute pancreatitis. Discontinue if symptoms of acute pancreatitis occur (eg, severe abdominal pain with or without nausea and vomiting).</li> <li>• Patients susceptible to fat-soluble vitamin deficiencies: Use with caution in patients susceptible to fat-soluble vitamin deficiencies. Absorption of fat soluble vitamins A, D, E, and K may be decreased; patients should take vitamins <math>\geq 4</math> hours before colesevelam.</li> <li>• Phenylalanine: Some products may contain phenylalanine.</li> </ul>
<b>Storage</b>	<p>Store below 15°C to 30° C. protect from moisture.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Lipid Modifying Agents, Cholesterol Absorption Inhibitor



## Ezetimibe

<b>Generic name</b>	<b>Ezetimibe</b>
<b>Dosage form/strengths</b>	Ezetimibe 10 mg tablets
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, 2-Azetidinone ATC: C10AX09
<b>Indications</b>	<ul style="list-style-type: none"> <li>• <b>Homozygous familial hypercholesterolemia:</b> In combination with a high-intensity statin.</li> <li>• <b>Homozygous sitosterolemia:</b> As adjunctive therapy to diet.</li> <li>• <b>Primary and mixed hyperlipidemia:</b> As adjunctive therapy to diet and an HMG-CoA reductase inhibitor or as monotherapy if an HMG-CoA reductase inhibitor is not tolerated.</li> </ul>
<b>Dosage Regimen</b>	<p><b>-Adults:</b>  <b>-Homozygous familial hypercholesterolemia, Homozygous sitosterolemia, Primary hyperlipidemia:</b>                      10 mg once daily</p> <p><b>-Pediatric:</b>  <b>-Hyperlipidemia:</b>                      - Children <math>\geq 10</math> years and Adolescents: Oral: 10 mg once daily in combination with Simvastatin.</p>
<b>Dosage adjustment</b>	<p><b>-Renal Impairment:</b>                      No dosage adjustment necessary</p> <p><b>-Hepatic Impairment:</b>                      -Mild impairment: No dosage adjustment necessary.                      -Moderate to severe impairment: Use not recommended</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to ezetimibe or any component of the formulation</li> <li>• Concomitant use with an HMG-CoA reductase inhibitor (statin) in patients with active hepatic disease or unexplained persistent elevations in serum transaminases</li> <li>• Pregnancy and breastfeeding (when used concomitantly with a statin)</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>-1% to 10%:</b>                      -Hepatic: Increased serum transaminases (monotherapy, <math>\geq 3</math> x ULN: &lt;1%; with HMG-CoA reductase inhibitors; <math>\geq 3</math> x ULN: 1%)                      -Neuromuscular and skeletal: Arthralgia (3%)                      -Respiratory: Sinusitis (3%), upper respiratory tract infection (4%)</p>
<b>Monitoring Parameters</b>	<p>- Signs or symptoms of myopathy, CPK.</p> <p>- Lipid panel (total cholesterol, HDL, LDL, triglycerides): Lipid profile (fasting or nonfasting) before initiating treatment. Fasting lipid profile should be rechecked 4 to 12 weeks after starting therapy and every 3 to 12 months thereafter</p> <p>- Hepatic transaminase levels: Baseline Liver function tests (LFTs); when used in combination with statin therapy, monitor LFTs when clinically indicated; discontinue use of ezetimibe if ALT elevations <math>&gt;3</math> times upper limit of normal persist. When used</p>



	in combination with fenofibrate, monitor LFTs and signs and symptoms of cholelithiasis.
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Fibric Acid Derivatives</p> <p><b>Risk D: Consider therapy modification</b> Bile Acid Sequestrants, Trofinetide</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b> -Limited human data. Adverse effects in animal studies. Ezetimibe should be used during pregnancy only if the potential benefit justifies the risk to the fetus. -Use is contraindicated in pregnant women who require combination therapy with an HMG-CoA reductase inhibitor</p> <p><b>-Lactation:</b> -Avoid use. The decision to continue or discontinue breastfeeding during therapy should consider the risk of exposure to the infant and the benefits of treatment to the mother.</p>
<b>Administration</b>	<p>-May be administered without regard to meals. -May be taken at the same time as a statin or fenofibrate. -Administer <math>\geq 2</math> hours before or <math>\geq 4</math> hours after bile acid sequestrants. Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>- Use with caution in patients with mild hepatic impairment; use is not recommended in patients with moderate or severe hepatic impairment. - In patients with severe kidney impairment (<math>\text{CrCl} \leq 30 \text{ mL/minute/1.73 m}^2</math>) systemic exposure is increased <math>\sim 1.5</math>-fold.</p>
<b>Storage</b>	<p>- Store between <math>15^\circ\text{C}</math> to <math>30^\circ\text{C}</math> Refer to manufacturer PIL if there are specific considerations.</p>

## Lipid Modifying Agents, Fibrates

## Fenofibrate

<b>Generic Name</b>	<b>Fenofibrate</b>
<b>Dosage form/strengths</b>	Capsules 67mg, 100mg, 200mg, 250mg (retard), 300mg Tablets 145mg, 160mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, Fibric Acid ATC: C10AB05
<b>Indications</b>	<b>Hypertriglyceridemia:</b> Adjunctive therapy to diet for treatment of adult patients with severe hypertriglyceridemia
<b>Dosage Regimen</b>	<b>Dosing Adults:</b> Fenofibrate and Derivative Hypertriglyceridemia dosing: differ according to formulation. refer to PIL of product. Capsules: Initially 200 mg daily, then increased if necessary to 267 mg daily, maximum 200 mg daily with concomitant statin. Tablets: 160 mg daily
<b>Dosage adjustment</b>	<b>Dosing: Altered kidney function:</b> Mild disease: Use lowest strength CrCl $\leq$ 30 mL/minute: Use contraindicated.  <b>Dosing: Hepatic Impairment:</b> Use is contraindicated
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to fenofibrate or fenofibric acid or any component of the formulation.</li> <li>• Active liver disease.</li> <li>• Severe kidney impairment or end-stage kidney disease, including those receiving dialysis.</li> <li>• Preexisting gallbladder disease.</li> <li>• Pregnancy and Breastfeeding.</li> </ul>
<b>Adverse Drug Reactions</b>	<b>Adverse Reactions (Significant): Considerations</b> Hepatic Effects Hypersensitivity Reactions (Delayed) Myopathy/Rhabdomyolysis Photosensitivity Renal effects <b>&gt;10%:</b> Hepatic: Increased serum alanine aminotransferase ( $\geq$ 3), increased serum aspartate aminotransferase ( $\geq$ 3) <b>1% to 10%:</b> Cardiovascular: Pulmonary embolism (1%) Dermatologic: Skin rash (1%), urticaria (1%) Gastrointestinal: Abdominal pain (5%), constipation (2%), diarrhea ( $\geq$ 3%), dyspepsia ( $\geq$ 3%) Nervous system: Dizziness ( $\geq$ 3%), pain ( $\geq$ 3%) Neuromuscular and skeletal: Arthralgia ( $\geq$ 3%), increased creatine phosphokinase in blood specimen (3%), limb pain ( $\geq$ 3%), myalgia ( $\geq$ 3%) Respiratory: Nasopharyngitis ( $\geq$ 3%), rhinitis (2%), sinusitis ( $\geq$ 3%), upper respiratory

	infection ( $\geq 3\%$ )
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Periodic blood counts.</li> <li>• Lipid profile periodically.</li> <li>• Liver functions at baseline and periodically during therapy.</li> <li>• Monitor kidney function in patients with kidney impairment or in those at increased risk for developing kidney impairment.</li> <li>• Monitor for signs/symptoms of myopathy, myositis, or rhabdomyolysis (eg, CPK elevation; muscle pain, tenderness, weakness, especially if accompanied with malaise or fever; brown urine).</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Aminolevulinic Acid (Systemic), Ciprofibrate</p> <p><b>Risk D: Consider therapy modification</b> Bile Acid Sequestrants, Cyclosporine (Systemic), Vitamin K Antagonists (eg, warfarin)</p>
<b>Pregnancy and Lactation</b>	Avoid use in pregnancy and breastfeeding. Toxicity in animal studies.
<b>Administration</b>	Oral administration. Dietary Considerations differ according to formulation. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Cholelithiasis: May cause cholelithiasis; discontinue if gallstones are found upon gallbladder studies.</li> <li>• HDL cholesterol: A paradoxical, severe, and reversible decrease in HDL-C (as low as 2 mg/dL) with a simultaneous decrease in apolipoprotein A1 has been reported within 2 weeks to years after initiation of fibrate therapy; clinical significance unknown.</li> <li>• Hematologic effects: May cause mild to moderate decreases in hemoglobin, hematocrit, and WBC upon initiation of therapy, which usually stabilizes with long-term therapy. Agranulocytosis and thrombocytopenia have been reported.</li> <li>• Pancreatitis: Pancreatitis has been reported with fenofibrate use; may be secondary to a failure of efficacy in patients with severe hypertriglyceridemia, medication side effect, or due to biliary tract stone or sludge formation from bile duct obstruction.</li> <li>• Venous thromboembolism: Use has been associated with pulmonary embolism and deep vein thrombosis. Use with caution in patients with risk factors for venous thromboembolism.</li> </ul> <p><b>Disease-related concerns:</b></p> <ul style="list-style-type: none"> <li>• Cardiovascular disease: Fibric acid derivatives have not demonstrated significant efficacy in aging cardiovascular disease mortality in major clinical studies.</li> <li>• Hepatic impairment: Contraindicated in patients with active liver disease, including primary biliary cirrhosis and unexplained persistent liver function abnormalities.</li> <li>• Kidney impairment: use with caution in patients with mild to moderate kidney impairment; dosage adjustment required. Contraindicated in patients with severe kidney impairment, including those receiving dialysis.</li> </ul> <p><b>Concurrent drug therapy issues:</b></p> <ul style="list-style-type: none"> <li>• HMG-CoA reductase inhibitors: Use caution with HMG-CoA reductase inhibitors. No incremental benefit of combination therapy on cardiovascular morbidity and mortality over statin monotherapy has been established.</li> </ul> <p><b>Special populations:</b></p>

Storage	<ul style="list-style-type: none"> <li>• Older adults: Use with caution in older adults; dosage adjustment may be required.</li> </ul> <p><b>Dosage form specific issues:</b></p> <ul style="list-style-type: none"> <li>• Peanut, arachis oil, Soya lecithin: Some products may contain peanut, arachis oil or Soya lecithin; caution in allergic patients.</li> </ul> <p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Optimal response: Therapy should be withdrawn if an adequate response is not obtained after 2 to 3 months of therapy at the maximum daily dose.</li> </ul>
	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Lipid Modifying Agents, Statins

## Atorvastatin

<b>Generic Name</b>	Atorvastatin
<b>Dosage form/strengths</b>	Tablets: 10mg, 20mg, 40mg, 80mg Chewable Tablets 10mg, 20mg, 40mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, HMG-CoA Reductase Inhibitor ATC: C10AA05
<b>Indications</b>	<p><b>Heterozygous familial hypercholesterolemia (adults and pediatrics from 10 years of age):</b> To reduce elevated total cholesterol, LDL cholesterol, apolipoprotein B, and triglyceride levels, and to increase HDL cholesterol in patients with primary hypercholesterolemia.</p> <p><b>Homozygous familial hypercholesterolemia:</b> To reduce total-C and LDL-C as an adjunct to other lipid-lowering treatments or if such treatments are unavailable.</p> <p><b>Prevention of atherosclerotic cardiovascular disease</b></p>
<b>Dosage Regimen</b>	<p><b>Heterozygous (adults and pediatrics from 10 years of age) or Homozygous familial hypercholesterolaemia in patients who have not responded adequately to diet and other appropriate measures:</b> Initially 10 mg once daily, then increased to 40 mg once daily, dose to be increased at intervals of at least 4 weeks; maximum 80 mg per day</p> <p><b>Primary hypercholesterolaemia or Combined (mixed) hyperlipidaemia in patients who have not responded adequately to diet and other appropriate measures:</b> Usual dose 10 mg once daily; increased if necessary up to 80 mg once daily, dose to be increased at intervals of at least 4 weeks</p> <p><b>Primary prevention of cardiovascular events in patients at high risk of a first cardiovascular event:</b> 20 mg once daily, dose can be increased if necessary</p> <p><b>Secondary prevention of cardiovascular events:</b> 80 mg once daily</p>
<b>Dosage adjustment</b>	<p><b>Renal Impairment dosing:</b> No dose adjustment necessary.</p> <p><b>Hepatic Impairment dosing:</b> Contraindicated in active liver failure or decompensated cirrhosis.</p> <p><b>Dosing: Adjustment for Toxicity: Adult</b></p> <p><b>Severe muscle symptoms or fatigue:</b> Promptly discontinue use; evaluate creatine kinase level.</p> <p><b>Mild to moderate muscle symptoms:</b> Discontinue use until symptoms can be evaluated; evaluate patient for conditions that may increase the risk for muscle symptoms. Upon resolution, resume the original or lower dose of atorvastatin. If muscle symptoms recur, discontinue atorvastatin use. After muscle symptom resolution, may use a low dose of a different statin; gradually increase if tolerated.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to atorvastatin or any component of the formulation</li> <li>• Acute liver failure or decompensated cirrhosis.</li> <li>• Pregnancy or Lactation</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Adverse Reactions</b></p> <p>Hepatic effects</p> <p>Muscle-related effects</p> <p><b>&gt;10%:</b></p> <p>Gastrointestinal: Diarrhea (7% to 14%)</p>

	<p>Neuromuscular and skeletal: Arthralgia (9% to 12%) Respiratory: nasopharyngitis (13%) <b>1% to 10%:</b> Cardiovascular: Hemorrhagic stroke (2%) Endocrine and metabolic: Diabetes mellitus (6%) Gastrointestinal: dyspepsia (6%), nausea (7%) Genitourinary: Urinary tract infection (7% to 8%) Hepatic: Increased serum transaminases (<math>\leq 2\%</math>) Nervous system: Insomnia (5%) Neuromuscular and skeletal: Limb pain (3% to 9%), muscle spasm (2% to 5%), musculoskeletal pain (2% to 5%), myalgia (3% to 8%) Respiratory: Pharyngolaryngeal pain (3% to 4%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Lipid panel (total cholesterol, HDL, LDL, triglycerides)</li> <li>• Hepatic transaminase levels</li> <li>• Monitor closely for myopathy/rhabdomyolysis</li> <li>• Baseline Creatine phosphokinase (CPK) in patients with risk or symptoms suggestive of myopathy.</li> <li>• Blood glucose</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Antihepaciviral combinations, Asunaprevir, Cyclosporine (Systemic), Fexinidazole Fusidic Acid (Systemic), Gemfibrozil, Glecaprevir and Pibrentasvir, Leniolisib, Lonafarnib, Posaconazole, Red Yeast Rice, Sparsentan, Taurursodiol, Tipranavir</p> <p><b>Risk D: Consider therapy modification</b> Atazanavir, Bezafibrate, Ciprofibrate, Clarithromycin, Cobicistat, Daptomycin, Darunavir, Elbasvir and Grazoprevir, Fosamprenavir, Fostemsavir, Grapefruit Juice, Grazoprevir Indinavir, Itraconazole, Ketoconazole, Lanthanum, Letermovir, Lopinavir, Lomitapide, Nelfinavir, Rifampin, Ritonavir, Saquinavir, Simeprevir, St John's Wort, Telithromycin, Trofinetide, Verapamil, Voxilaprevir</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Contraindicated. Because there is potential for fetal harm, statins should be discontinued once pregnancy is recognized.</p> <p><b>Lactation:</b> Due to the potential for adverse events in the breastfed infant, breastfeeding is not recommended.</p>
<b>Administration</b>	<p><b>Oral:</b> Administer with or without food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Diabetes mellitus: Increases in HbA<sub>1c</sub> and fasting blood glucose occurred</li> <li>• Hepatic impairment and/or ethanol use: Use with caution in patients who consume large amounts of ethanol or have a history of liver disease; use is contraindicated in patients with active liver disease or unexplained persistent elevations of serum transaminases.</li> <li>• Myasthenia gravis: May rarely worsen or precipitate myasthenia gravis; monitor</li> <li>• Hemorrhagic stroke: Patients with recent stroke receiving long-term therapy with high-dose (ie. 80 mg/day) Atorvastatin may be at high risk for hemorrhagic stroke.</li> <li>• Polysorbate 80: Some dosage forms may contain polysorbate 80 (also known as Tweens). Risk of Hypersensitivity reactions, usually a delayed reaction.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>



## Pitavastatin

<b>Generic Name</b>	<b>Pitavastatin</b>
<b>Dosage form/strengths</b>	Tablets: 1mg, 2mg, 4mg
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antilipemic Agent, HMG-CoA Reductase Inhibitor ATC: C10AA08
<b>Indications</b>	Reduction of elevated total cholesterol and LDL-C, in patients with primary hypercholesterolaemia and combined (mixed) dyslipidaemia, when response to diet and other non-pharmacological measures is inadequate
<b>Dosage Regimen</b>	<b>Treatment of dyslipidaemia and hypercholesterolaemia in adjunct to diet control.</b> -Adult, adolescents and children over 9 years: Oral: 1 to 4 mg once daily Evaluate lipids after 4 weeks and titrate dose accordingly; maximum daily dose: 4 mg/day -Children 6-9 years: Oral: 1-2mg once daily
<b>Dosage adjustment</b>	<b>Dosing: Altered Kidney Function:</b> Moderate to Severe renal impairment: Maximum dose is 2 mg with close monitoring <b>Dosing: Hepatic Impairment:</b> Contraindicated in active liver disease or decompensated cirrhosis
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to Pitavastatin or any component of the formulation</li> <li>• Active liver disease or decompensated cirrhosis</li> <li>• Pregnancy or Lactation</li> </ul>
<b>Adverse Drug Reactions</b>	<b>1% to 10%:</b> Gastrointestinal: Constipation (4%), diarrhea (3%) Neuromuscular and skeletal: Back pain (4%), myalgia (2% to 3%) <b>Frequency not defined:</b> Infection: Influenza Nervous system: Headache Neuromuscular and skeletal: Arthralgia Respiratory: Nasopharyngitis
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Lipid profile</li> <li>• Renal and hepatic functions</li> <li>• CPK in patients with risk or symptoms suggestive of myopathy.</li> <li>• Monitor closely for myopathy/rhabdomyolysis</li> </ul>
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Cyclosporine (Systemic), Fusidic Acid (Systemic), Gemfibrozil, Leniolisib, Letemovir, Voxilaprevir <b>Risk D: Consider therapy modification</b> Bezafibrate, Ciprofibrate, Daptomycin, Erythromycin (Systemic), Fostemsavir, Lanthanum, Rifampin, Trofinetide

<b>Pregnancy and Lactation</b>	Pregnancy: Contraindicated Lactation: Contraindicated
<b>Administration</b>	<b>Administration:</b> Oral: Administer without regard to food; take at the same time each day. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Diabetes mellitus: Small increases in HbA<sub>1c</sub> and fasting blood glucose occurred; however, the benefits of statin outweigh this risk.</li> <li>• Hepatotoxicity: Elevations in liver enzymes have been reported; elevations may be reversible after a brief interruption in therapy in most cases. Ethanol may enhance the potential of adverse hepatic effects.</li> <li>• Hypersensitivity: Hypersensitivity reactions, including angioedema, rash, pruritus, and urticaria, occurred.</li> <li>• Myopathy/Rhabdomyolysis: Discontinue therapy if markedly elevated CPK levels occur or myopathy is diagnosed/suspected; Use with caution in patients with renal impairment. immune mediated necrotizing myopathy occurred rarely which is persistent even with discontinuation. consider treatment with immunosuppressants and additional neuromuscular and serologic testing.</li> <li>• Older adult: Use with caution in patients ≥65 years of age; these patients are predisposed to myopathy and rhabdomyolysis.</li> <li>• Appropriate use: The cardiovascular protective effect has not been established.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Protect from light. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Rosuvastatin

<b>Generic Name</b>	<b>Rosuvastatin</b>
<b>Dosage form/strengths</b>	Tablets: 5mg, 10mg, 20mg, 40mg And in combinations
<b>Route of administration</b>	<i>Oral</i>
<b>Pharmacologic category</b>	Antilipemic Agent, HMG-CoA Reductase Inhibitor ATC: C10AA07
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Primary (including heterozygous familial) and Homozygous Familial Hypercholesterolemia</li> <li>• Hyperlipidemia and Mixed Dyslipidemia (type IIb)</li> <li>• Primary Prevention of Cardiovascular Disease and Slowing of the Progression of Atherosclerosis</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b>  <b>Primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia), homozygous familial Hypercholesterolaemia, or mixed dyslipidaemia (type IIb) in patients who have not responded adequately to diet and other measures:</b>                      Adult 18 to over 70 years: Initially 5 mg once daily, then increased gradually if necessary up to 20 mg once daily at intervals of 4 weeks. (and up to 40mg in severe cases at high cardiovascular events risk) .</p> <p><b>Prevention of cardiovascular events in patients at high risk of a first cardiovascular event</b>                      Adult 18–69 years: 20 mg once daily                      Adult 70 years and over, or patients at risk of myopathy or rhabdomyolysis: Initially 5 mg once daily, then increased if tolerated to 20 mg once daily, dose to be increased gradually at intervals of at least 4 weeks.</p> <p><b>Pediatric dosing:</b>  <b>Heterozygous familial hypercholesterolemia:</b>                      Children 6 to &lt;10 years: Oral: 5 to 10 mg once daily.                      Children ≥10 years and Adolescents: Oral: 5 to 20 mg once daily.  <b>Homozygous familial hypercholesterolemia:</b>                      Children ≥6 years and Adolescents: Oral: 5 to 10 mg once daily increased up to 20 mg once daily.</p>
<b>Dosage adjustment</b>	<p><b>Altered kidney function:</b>                      CrCl 30-60 mL/minute/1.73 m<sup>2</sup>: initial 5mg, avoid high doses.                      CrCl≤30 mL/minute/1.73 m<sup>2</sup>: Avoid use</p> <p><b>Dosing: Hepatic Impairment:</b>                      Monitor closely. Use is contraindicated in patients with active liver disease or decompensated cirrhosis.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Patients with a known hypersensitivity to any component of this product.</li> <li>• Patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels</li> <li>• Severe renal impairment</li> <li>• Pregnancy or Lactation</li> </ul>

<b>Adverse Drug Reactions</b>	<p><b>Hepatic effects:</b> Statins are associated with increased serum transaminases and hepatotoxicity, usually reversible Upon dose reduction or discontinuation. Onset vary from 2 month-2 years.</p> <p><b>Statins are associated with several muscle-related effects, including:</b> Myalgia, Myopathy, Rhabdomyolysis, Immune-mediated necrotizing myopathy. <i>Onset:</i> Delayed after few months. Risk factors: Hypothyroidism, Kidney impairment, Low body mass index, Heavy exercise.</p> <p><b>&gt;10%:</b> Neuromuscular and skeletal: Myalgia (2% to 13%)</p> <p><b>1% to 10%:</b></p> <p>Endocrine and metabolic: Diabetes mellitus (new onset: 3%)                  Gastrointestinal: Constipation (3% to 5%), nausea (4% to 6%)                  Hepatic: Increased serum transaminases (&gt;3 × ULN; including increased serum alanine aminotransferase, serum alkaline phosphatase and serum bilirubin)                  Nervous system: Asthenia (5%), dizziness (4%), headache (6% to 9%)                  Neuromuscular and skeletal: Arthralgia (4% to 10%), increased creatine phosphokinase in blood specimen (3%)</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Lipid profile</li> <li>• Renal and hepatic functions</li> <li>• CPK in patients with risk or symptoms suggestive of myopathy.</li> <li>• Monitor closely for myopathy/rhabdomyolysis</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Fusidic Acid (Systemic), Ledipasvir, Leniolisib, Pacritinib, Red Yeast Rice, Sparsentan, Taurursodiol, Voxilaprevir</p> <p><b>Risk D: Consider therapy modification</b>                  Atazanavir, Bezafibrate, Capmatinib, Ciprofibrate, Cobicistat, Cyclosporine (Systemic), Daptomycin, Darolutamide, Dasabuvir, Elbasvir And Grazoprevir, Eltrombopag, Febuxostat, Fostamatinib, Fostemsavir, Gemfibrozil, Glecaprevir and Pibrentasvir, Lanthanum, Leflunomide, Lopinavir, Regorafenib, Simeprevir, Tafamidis, Teriflunomide, Trofinetide</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy, Lactation:</b> Contraindicated</p>
<b>Administration</b>	<p>Oral: Administer whole with or without food. May be taken at any time of day.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Diabetes mellitus: Small increases in HbA<sub>1c</sub> (~0.1%) and fasting blood glucose occurred; however, the benefits of statin outweigh this risk.</li> <li>• Hepatic impairment: Use with caution in patients who consume alcohols and/or have a history of liver disease; may require dosage adjustment in some patients.</li> <li>• East Asian population: Dosage adjustment should be considered.</li> <li>• Older adult: Use with caution in patients with advanced age; these patients are more predisposed to myopathy.</li> <li>• Surgical patients: Perioperative discontinuation of statin therapy is associated with an increased risk of cardiac morbidity and mortality.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Protect from moisture.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Simvastatin

<b>Generic Name</b>	Simvastatin
<b>Dosage form/strengths</b>	Tablets: 10 mg, 20 mg, 40 mg, 80 mg Capsules 10mg, 20mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antilipemic Agent, HMG-CoA Reductase Inhibitor ATC: C10AA01
<b>Indications</b>	<p><b>Heterozygous familial hypercholesterolemia:</b> To reduce elevated total cholesterol (total-C), LDL-C, apoB, and triglyceride levels, and to increase HDL-C in patients with primary hypercholesterolemia.</p> <p><b>Homozygous familial hypercholesterolemia:</b> To reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (eg, LDL apheresis) or if such treatments are unavailable.</p> <p><b>Primary hypercholesterolaemia, or combined hyperlipidaemia</b> in patients who have not responded adequately to diet and other appropriate measures</p> <p><b>Prevention of atherosclerotic cardiovascular disease</b></p>
<b>Dosage Regimen</b>	<p><b>Notes:</b> Use in conjunction with lifestyle modification (eg, diet and exercise). Simvastatin is considered a moderate-intensity statin at doses of 20 to 40 mg/day (generally reduces LDL-C by ~30% to 45%). If LDL-C must be lowered <math>\geq 50\%</math>, select an alternative high-intensity statin (atorvastatin or rosuvastatin). Assess response ~1 to 3 months after initiation of therapy or dose adjustment and every 3 to 12 months thereafter.</p> <p><b>Safety: Dosing limitations:</b> Increased risk of myopathy associated with 80 mg/day dose of Simvastatin. The 80 mg dose should be considered only in patients with severe hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits outweigh the potential risks.</p> <p><b>Dosage: adult</b>  <b>Heterozygous familial hypercholesterolemia (alternative agent):</b>                      Moderate-intensity therapy: <b>Oral:</b> 20 to 40 mg once daily in the evening.  <b>Homozygous familial hypercholesterolemia (alternative agent):</b>                      Moderate-intensity therapy: <b>Oral:</b> 20 to 40 mg once daily in the evening  <b>Prevention of atherosclerotic cardiovascular disease:</b>                      Moderate-intensity therapy: <b>Oral:</b> 20 to 40 mg once daily in the evening  <b>Primary hypercholesterolaemia, or combined hyperlipidaemia</b> in patients who have not responded adequately to diet and other appropriate measures: 10–20 mg once daily</p> <p><b>Pediatric Dosing</b>  <b>Hyperlipidemia or heterozygous familial hypercholesterolemia and nonfamilial hypercholesterolemia</b>  <b>Oral</b>                      Children 10–17 years of age: Initially, 10 mg once daily.</p>

	Adjust dosage at intervals of $\geq 4$ weeks until the desired effect on lipoprotein concentrations is observed. Recommended dosage range is 10–40 mg daily.
<b>Dosage Adjustment</b>	<p><b>Dosing: Renal Impairment:</b>                  Initial: No dosage adjustment necessary for any degree of kidney dysfunction.                  Maximum dose: 40 mg once daily                  CrCl <math>\leq 30</math> mL/minute: Use with caution.</p> <p><b>Dosing: Hepatic Impairment:</b>                  Contraindicated in active liver disease or in patients with unexplained persistent elevations of serum transaminases.</p> <p><b>Dosing: Adjustment for Toxicity: Adult</b>  <b>Severe muscle symptoms or fatigue:</b> Promptly discontinue use; evaluate CPK, creatinine, and urinalysis for myoglobinuria  <b>Mild to moderate muscle symptoms:</b> Discontinue use until symptoms can be evaluated; evaluate patient for conditions that may increase the risk for muscle symptoms (eg, hypothyroidism, reduced renal or hepatic function, rheumatologic disorders, steroid myopathy, vitamin D deficiency, or primary muscle diseases). After symptoms resolved, resume the original or lower dose of simvastatin. If muscle symptoms recur, discontinue simvastatin use.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>• Hypersensitivity to simvastatin or any component of the formulation</li> <li>• Active liver disease</li> <li>• Pregnancy or women who may become pregnant; breastfeeding</li> <li>• Concomitant use of strong CYP3A4 inhibitors (Itraconazole, Ketoconazole, Posaconazole, Voriconazole, Erythromycin, Clarithromycin, Nelfinavir, Ritonavir, Darunavir/Ritonavir, Boceprevir, Telaprevir, Cobicistat-containing products, and Nefazodone), Cyclosporine, Danazol, and Gemfibrozil</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b>                  Hepatic effects: Statins are associated with increased serum transaminases and hepatotoxicity                  Muscle-related effects: Statins are associated with several muscle-related effects, including: Myalgia Myopathy Rhabdomyolysis Immune-mediated necrotizing myopathy</p> <p><b>1% to 10%:</b>                  Cardiovascular: Atrial fibrillation (6%), edema (<math>\leq 3\%</math>)                  Dermatologic: Eczema (5%)                  Gastrointestinal: Abdominal pain (7%), constipation (7%), gastritis (5%), nausea (5%)                  Genitourinary: cystitis (interstitial; Huang 2015)                  Hepatic: Increased serum transaminases (<math>\leq 2\%</math>)                  Nervous system: Headache (3% to 7%), vertigo (5%)                  Neuromuscular and skeletal: Increased creatine phosphokinase in blood specimen (<math>&gt;3 \times</math> normal: 5%), myalgia (4%)                  Respiratory: bronchitis (7%), upper respiratory infection (9%)                  Miscellaneous: Swelling (<math>\leq 3\%</math>)</p> <p><b>Frequency not defined:</b>                  Dermatologic: Skin rash                  Endocrine and metabolic: Increased gamma-glutamyl transferase                  Gastrointestinal: diarrhea, dyspepsia, flatulence                  Hepatic: Increased serum alkaline phosphatase                  Nervous system: Asthenia</p>



<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Lipid profile</li> <li>• Hepatic functions baseline and periodic</li> <li>• CPK in patients with risk or symptoms suggestive of myopathy.</li> <li>• Monitor closely for myopathy/rhabdomyolysis</li> </ul> <p><b>Lipid panel (total cholesterol, HDL, LDL, triglycerides):</b> lipid profile (fasting or nonfasting) before initiating treatment. Fasting lipid profile should be rechecked 4 to 12 weeks after starting therapy and every 3 to 12 months thereafter. If 2 consecutive LDL levels are &lt;40 mg/dL, consider decreasing the dose.</p>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Abametapir, Cyclosporine (Systemic), Strong CYP3A4 Inhibitors, Danazol, Daptomycin, Erythromycin (Systemic), Erdafitinib, Fexinidazole, Fusidic Acid (Systemic), Gemfibrozil, Glecaprevir and Pibrentasvir, Grapefruit Juice, Leniolisib, Letemovir, Lonafarnib, Pacritinib, Red Yeast Rice, Tipranavir, Treosulfan</p> <p><b>Risk D: Consider therapy modification</b>                  Amiodarone, Amlodipine, Bempedoic Acid, Bezafibrate, Ciprofibrate, Cyproterone, Diltiazem, Dronedarone, Fostemsavir, Lanthanum, Lercanidipine, Levamlodipine, Lomitapide, Niacin, Ranolazine, St John's Wort, Ticagrelor, Verapamil, Voxilaprevir</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy Category X:</b> Contraindicated because there is potential for fetal harm. Statins should be discontinued once pregnancy is recognized</p> <p><b>Lactation:</b> Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is contraindicated.</p>
<b>Administration</b>	<p>Oral: Administered without regard to meals. Administer in the evening for maximal efficacy.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Diabetes mellitus: Increases in HbA<sub>1c</sub> and fasting blood glucose have been reported; however, the benefits of statin therapy far outweigh the risk of dysglycemia.</li> <li>• Hepatic impairment: use with caution in patients who consume large amounts of ethanol and/or have a history of liver disease; may require dosage adjustment in some patients with hepatic impairment.</li> <li>• Myasthenia gravis: May rarely worsen or precipitate myasthenia gravis (MG); monitor for worsening MG if treatment is initiated.</li> <li>• Renal impairment: use with caution in patients with severe renal impairment; monitor closely.</li> <li>• Elderly: Use with caution in patients ≥65 years of age; these patients are predisposed to myopathy.</li> </ul>
<b>Storage</b>	<p>Tablets: Store between 15°C to 30°C.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Selective Sinus Node I(f) Inhibitors



## Ivabradine

<b>Generic Name</b>	Ivabradine
<b>Dosage form/strengths</b>	Tablets: 5mg; 7.5mg
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Cardiovascular Agent, Miscellaneous ATC: C01EB17
<b>Indications</b>	<p><b>-Heart failure with reduced ejection fraction:</b> To reduce the risk of hospitalization in adult patients with stable, symptomatic (NYHA class II to III) heart failure with left ventricular ejection fraction <math>\leq 35\%</math>, who are in sinus rhythm with resting heart rate <math>\geq 70</math> beats per minute despite being on a maximally tolerated dose of beta blocker or if there is a contraindication to beta-blocker use</p>
<b>Dosage Regimen</b>	<p><b>-Adult:</b> <b>-Heart failure with reduced ejection fraction (adjunctive agent):</b> -Oral: Initial: 5 mg twice daily or 2.5 mg twice daily in patients with a history of conduction defects or who may experience hemodynamic compromise due to bradycardia. Adjust dose every <math>\geq 2</math> weeks as needed. -Dosage adjustment based on resting heart rate: -If heart rate <math>&gt; 60</math> bpm: Increase dose by 2.5 mg twice daily; maximum dose: 7.5 mg twice daily. -If heart rate 50 to 60 bpm: Maintain dose. -If heart rate <math>&lt; 50</math> bpm or signs and symptoms of bradycardia: Decrease dose by 2.5 mg twice daily; if current dose is 2.5 mg twice daily, discontinue therapy.</p> <p><b>-Pediatric:</b> <b>-Heart failure, dilated cardiomyopathy:</b> -Infants <math>\geq 6</math> months, Children, and Adolescents <math>&lt; 18</math> years: -<math>&lt; 40</math> kg: Oral: Initial: 0.05 mg/kg/dose twice daily; may increase dose every 2 weeks by 0.05 mg/kg/dose as tolerated to achieve a 20% reduction in heart rate without inducing bradycardia. -Maximum dose: Age-dependent: -<math>\geq 6</math> months to <math>&lt; 1</math> year: 0.2 mg/kg/dose twice daily. -<math>\geq 1</math> year: 0.3 mg/kg/dose twice daily, not to exceed 7.5 mg/dose twice daily.</p> <p>-Dosage adjustment for bradycardia: -Initial dose: Decrease dose to 0.02 mg/kg/dose twice daily. -During titration: Decrease dose to previous dose.</p> <p>-<math>\geq 40</math> kg: Oral: Initial: 2.5 mg twice daily; may increase dose every 2 weeks by 2.5 mg as tolerated to achieve a 20% reduction in heart rate without inducing bradycardia; maximum dose: 7.5 mg/dose twice daily. -Dosage adjustment for bradycardia: Decrease dose to previous dose.</p>
<b>Dosage adjustment</b>	<p><b>-Adult:</b> <b>-Renal Impairment:</b> -CrCl <math>\geq 15</math> mL/minute: No dosage adjustment necessary. -CrCl <math>&lt; 15</math> mL/minute: There are no dosage adjustments provided in the</p>

	<p>manufacturer's labeling (has not been studied).</p> <p><b>-Hepatic Impairment:</b></p> <ul style="list-style-type: none"> <li>-Mild or moderate impairment: No dosage adjustment necessary.</li> <li>-Severe impairment: Use is contraindicated (has not been studied; increase in systemic exposure anticipated).</li> </ul>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>-Acute decompensated heart failure.</li> <li>- Clinically significant hypotension.</li> <li>- Sick sinus syndrome, sinoatrial block, or third-degree AV block (unless a functioning pacemaker is present).</li> <li>-Clinically significant bradycardia.</li> <li>-Severe hepatic impairment.</li> <li>- Pacemaker dependence (heart rate maintained exclusively by the pacemaker)</li> <li>-Concomitant use with strong CYP3A4 inhibitors.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>-1% to 10%:</b></p> <ul style="list-style-type: none"> <li>-Cardiovascular: Bradycardia (4% to 10%), hypertension (9%), atrial fibrillation (8%)</li> <li>-Central nervous system: Phosphene (3%)</li> </ul> <p><b>Frequency not defined:</b> Cardiovascular: Heart block, sinoatrial arrest</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>-Heart rate (prior to initiation, prior to increasing dose, or after decreasing dose); monitor heart rate more closely if receiving other negative chronotropes (eg, amiodarone, beta-blockers, digoxin).</li> <li>- Blood pressure.</li> <li>-Cardiac rhythm (assessing for atrial fibrillation).</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b></p> <p>CYP3A4 Inducers (Moderate, Strong including Barbiturates (phenobarbital), Carbamazepine, Corticosteroids, Phenytoin, Rifampicin, St John's wort), CYP3A4 Inhibitors (Moderate or Strong including Amiodarone, Aprepitant, Cimetidine, Ciprofloxacin, Clarithromycin, Diltiazem, Erythromycin, Fluconazole, Grapefruit juice, Itraconazole, Ketoconazole, Posaconazole, Voriconazole, Verapamil), Fexinidazole</p> <p><b>Risk D: Consider therapy modification</b></p> <p>Fingolimod, Ponesimod, Siponimod</p>
<b>Pregnancy and Lactation</b>	<p><b>-Pregnancy:</b></p> <p>Adverse events have been observed in animal reproduction studies, and fetal harm may occur if Ivabradine is administered to pregnant women. If treatment is needed during pregnancy, closely monitor for destabilization of heart failure that could potentially result from heart rate slowing caused by ivabradine, especially during the first trimester. Pregnant women with chronic heart failure should also be monitored for preterm birth</p> <p><b>-Lactation:</b></p> <p>No human data. Due to the potential risk from exposure in the breastfed infant, breastfeeding is not recommended.</p>
<b>Administration</b>	<p>Administer with food.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>- Use increases the risk of atrial fibrillation; monitor cardiac rhythm. Discontinue if atrial fibrillation develops.</li> <li>-Bradycardia, sinus arrest, and heart block may occur; monitor heart rate prior to initiation and with any dosage adjustment. Bradycardia may increase the risk of QT</li> </ul>

	<p>prolongation, which may lead to severe ventricular arrhythmias, including torsade de pointes, especially in patients with risk factors such as use of QTc prolonging drugs. Risk factors for bradycardia include sinus node dysfunction, conduction defects (eg, first- or second-degree AV block, bundle branch block), ventricular dyssynchrony, and use of other negative chronotropes (eg, Digoxin, Diltiazem, Verapamil, Amiodarone).</p> <ul style="list-style-type: none"> <li>-Avoid concurrent use with Verapamil and Diltiazem.</li> <li>-Avoid use in patients with second-degree AV block (unless a functioning demand pacemaker is present).</li> <li>- Phosphenes (described as transient enhanced brightness in a limited area of the visual field, halos, image decomposition, colored bright lights, or multiple images) may occur with use. Onset is generally within the first 2 months of therapy and is reported to be of mild to moderate intensity; most cases resolve during or after treatment discontinuation.</li> </ul>
<b>Storage</b>	Store between 15°C and 30°C. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.

## Sodium-glucose Cotransporter 2 (SGLT2) Inhibitors

## Dapagliflozin

<b>Generic Name</b>	<b>Dapagliflozin</b>
<b>Dosage form/strengths</b>	Tablets: 5mg, 10mg And in combinations.
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antidiabetic Agent, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitor ATC: A10BK01
<b>Indications</b>	<ul style="list-style-type: none"> <li>Type 2 diabetes mellitus [in combination with insulin or other antidiabetic drugs or as monotherapy if metformin is inappropriate]</li> <li>Chronic heart failure with reduced ejection fraction to reduce hospitalization and death.</li> <li>Chronic kidney disease.</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult Dosing</b></p> <p><u>Type 2 diabetes mellitus:</u></p> <ul style="list-style-type: none"> <li>Oral: 5mg may be increased to 10 mg if more glycemic control is needed.</li> <li>Dose of 10 mg is recommended for patients with type 2 diabetes mellitus and cardiovascular disease or multiple risk factors.</li> </ul> <p><u>Chronic heart failure with reduced ejection fraction to reduce hospitalization and death:</u></p> <p>Oral: 10mg</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b></p> <ul style="list-style-type: none"> <li>eGFR more than 45 mL/minute/1.73 m<sup>2</sup>: No adjustments required.</li> <li>eGFR 25-45: hypoglycemic effect is reduced, not recommended for this use. Combination therapy is recommended.</li> <li>eGFR less than 25 mL/minute/1.73 m<sup>2</sup>: Do not initiate therapy; may continue if patient is already on Dapagliflozin.</li> <li>Dialysis: use is not contraindicated.</li> </ul> <p><b>Dosing: Hepatic Impairment: Adult</b></p> <p>No dosage adjustment is needed. Use in severe hepatic impairment is not studied but exposure is increased.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>History of serious hypersensitivity to Dapagliflozin or any component of the formulation</li> <li>Patients on dialysis.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><b>Ketoacidosis:</b> serious and life-threatening cases of diabetic ketoacidosis (DKA) have been reported rarely in patients taking an SGLT2 inhibitor.</p> <p>To minimize risk, follow these advices:</p> <ul style="list-style-type: none"> <li>Inform patients of the signs and symptoms of DKA, (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a different breath smell, metallic taste), and advise them to seek immediate medical advice if they develop any of these signs.</li> <li>Test for raised ketones in patients with signs and symptoms of DKA, even if plasma glucose levels are near-normal</li> <li>Use Dapagliflozin with caution in patients with risk factors for ketoacidosis.</li> </ul>

- Discontinue treatment if DKA is suspected or diagnosed.
- Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved.
- Interrupt SGLT2 inhibitor treatment in patients who are hospitalized for major surgery or acute serious illnesses; treatment may be restarted once the patient condition is stabilized.

**Hypersensitivity:**

Occurs in hours to days after treatment initiation. Hypersensitivity reactions including **angioedema**, **asthma**, **urticaria**, and **skin rash**, have been reported in patients receiving sodium-glucose cotransporter 2 (SGLT2) inhibitors.

**Hypotension/volume depletion:**

Intravascular volume depletion which manifest as symptomatic hypotension or acute transient changes in creatinine (severe acute kidney injury have been reported). Interrupt treatment temporarily until the depletion is corrected.

*Risk factors are:*

Kidney impairment, elderly, concomitant use of diuretics or antihypertensive, initial low systolic blood pressure, low oral fluid intake or increased loss.

**Infection:**

Associated with an increased risk of urinary tract infections (sometimes severe) or genital fungal Infections have occurred. Monitor symptoms and treat promptly.

**Fournier's Gangrene:**

Necrotizing fasciitis of the perineum is rare but serious and potentially life-threatening event. Either uro-genital infection or perineal abscess may precede necrotizing fasciitis. If Fournier's gangrene is suspected, Dapagliflozin should be discontinued and prompt treatment (including antibiotics and surgical intervention) should be taken. Patient should be informed to seek medical advice in case symptoms of severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise.

**Adverse Reactions**

**1% to 10%:**

Endocrine and metabolic: Dyslipidemia (3%), hypovolemia (1% to 3%)

Gastrointestinal: Nausea (3%)

Genitourinary: Dysuria (2%), increased urine output (3% to 4%), urinary tract infection (6%)

Hematologic and oncologic: Increased hematocrit (1%)

Infection: Genitourinary fungal infection (3% to 8%), influenza (3%)

Neuromuscular and skeletal: Back pain (4%), limb pain (2%)

Respiratory: Nasopharyngitis (7%)

**Monitoring Parameters**

- Renal function (baseline and periodically during treatment)
- Volume status (blood pressure, hematocrit, risk of volume depletion): correct prior to initiation.
- Monitor for genital mycotic infections and urinary tract infection; assess patients presenting with fever or malaise along with genital or perianal pain, tenderness, erythema, or swelling for necrotizing fasciitis;
- Signs/symptoms of ketoacidosis (eg, nausea/vomiting, abdominal pain, malaise,

	<p>shortness of breath), confirm diagnosis by direct measurement of blood ketones.</p> <ul style="list-style-type: none"> <li>• Blood glucose</li> <li>• Glycosylated hemoglobin A1c (HbA1c)</li> <li>• Serum cholesterol profile</li> <li>• Hypersensitivity reactions</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk D: Consider therapy modification</b> Insulins, Sulfonylureas.</p>
<b>Pregnancy and Lactation</b>	<p>Pregnancy: Avoid. Toxicities may occur. Lactation: Avoid due to potential serious reactions. No human data.</p>
<b>Administration</b>	<p>Oral: Administer in the morning with or without food. Refer to manufacturer PIL if there are specific considerations.</p>
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Infection, acute: Discontinue therapy if any of the following occur: signs and symptoms of new infection (including osteomyelitis), new pain or tenderness, or sores/ulcers involving the lower limbs.</li> <li>• Renal impairment: Glycemic efficacy may be decreased in patients with renal impairment.</li> <li>• Older adults: Older adults may be predisposed to renal impairment or failure.</li> <li>• Appropriate use: Not for use in patients with diabetic ketoacidosis or patients with type 1 diabetes mellitus.</li> <li>• Hospitalized patients: Use of SGLT2 inhibitors for glycemic control is not routinely recommended for hospitalized patients.</li> <li>• Surgical procedures: In patients with diabetes mellitus, consider temporary discontinuation at least 3 days prior to surgery; ensure risk factors for ketoacidosis are resolved prior to reinitiating therapy.</li> </ul>
<b>Storage</b>	<p>Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.</p>



## Empagliflozin

<b>Generic Name</b>	Empagliflozin
<b>Dosage form/strengths</b>	Tablets: 10mg, 25 mg And in combinations
<b>Route of administration</b>	Oral
<b>Pharmacologic category</b>	Antidiabetic Agent, Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitor ATC: A10BK03
<b>Indications</b>	<p><b>Diabetes mellitus, type 2, treatment:</b> As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus; risk reduction of cardiovascular mortality in adults with type 2 diabetes mellitus and established cardiovascular disease.</p> <p><b>Heart failure:</b> Risk reduction of cardiovascular mortality and hospitalization for heart failure in adults with heart failure.</p>
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b></p> <p><b>Diabetes mellitus, type 2, treatment: Oral:</b> Initial: 10 mg once daily; may increase to 25 mg once daily after 4 to 12 weeks if needed to achieve glycemic goals</p> <p><b>Heart failure: Oral:</b> 10 mg once daily</p>
<b>Dosage adjustment</b>	<p><b>Dosing: Altered Kidney Function: Adult</b></p> <p><b>When used for type 2 diabetes mellitus:</b> eGFR &lt; 60 L/minute/1.73m<sup>2</sup>: Avoid initiation eGFR is persistently &lt; 45 mL/minute/1.73m<sup>2</sup>: Avoid use.</p> <p><b>When used for symptomatic chronic heart failure with reduced ejection fraction:</b> eGFR &lt; 20 L/minute/1.73m<sup>2</sup>: Avoid use.</p> <p><b>Hemodialysis, Peritoneal dialysis:</b> Use is contraindicated.</p> <p><b>Dosing: Hepatic Impairment: Adult</b> No dosage adjustments are needed.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to Empagliflozin or any component of the formulation.</li> <li>End-stage renal disease, patients on dialysis.</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Significant Adverse Reactions:</b></p> <p><b>Ketoacidosis:</b> serious and life-threatening cases of diabetic ketoacidosis (DKA) have been reported rarely in patients taking an SGLT2 inhibitor. To minimize risk, follow these advices:</p> <ul style="list-style-type: none"> <li>Inform patients of the signs and symptoms of DKA, (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a different breath smell, metallic taste), and advise them to seek immediate medical advice if they develop any of these signs.</li> <li>Test for raised ketones in patients with signs and symptoms of DKA, even if plasma glucose levels are near-normal</li> <li>Use Empagliflozin with caution in patients with risk factors for ketoacidosis.</li> <li>Discontinue treatment if DKA is suspected or diagnosed.</li> <li>Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved.</li> <li>Interrupt SGLT2 inhibitor treatment in patients who are hospitalized for major</li> </ul>



surgery or acute serious illnesses; treatment may be restarted once the patient condition is stabilized.

**Hypersensitivity:**

Occurs in hours to days after treatment initiation. Hypersensitivity reactions including **angioedema**, **asthma**, **urticaria**, and **skin rash**, have been reported in patients receiving sodium-glucose cotransporter 2 (SGLT2) inhibitors.

**Hypotension/volume depletion:**

Intravascular volume depletion which manifest as symptomatic hypotension or acute transient changes in creatinine (severe acute kidney injury have been reported). Interrupt treatment temporarily until the depletion is corrected.

*Risk factors* are:

Kidney impairment, elderly, concomitant use of diuretics or antihypertensive, initial low systolic blood pressure, low oral fluid intake or increased loss.

**Infection:**

Associated with an increased risk of urinary tract infections (sometimes severe) or genital fungal Infections have occurred. Monitor symptoms and treat promptly.

**Fournier's Gangrene:**

Necrotizing fasciitis of the perineum is rare but serious and potentially life-threatening event. Either uro-genital infection or perineal abscess may precede necrotizing fasciitis. If Fournier's gangrene is suspected, Empagliflozin should be discontinued and prompt treatment (including antibiotics and surgical intervention) should be taken. Patient should be informed to seek medical advice in case symptoms of severe pain, tenderness, erythema, or swelling in the genital or perineal area, accompanied by fever or malaise.

**1% to 10%:**

Endocrine and metabolic: Dyslipidemia (4%), increased thirst (2%)

Gastrointestinal: Nausea (2%)

Genitourinary: Genitourinary fungal infection (2% to 6%) (See Table 1), increased urine output (3%), urinary tract infection (8% to 9%; incidence higher in females) (See Table 2)

Hematologic and oncologic: Increased hematocrit (3% to 4%)

<1%: Genitourinary: Phimosis

**Monitoring Parameters**

- Renal function (baseline and periodically during treatment)
- Volume status (blood pressure, hematocrit, risk of volume depletion): correct prior to initiation.
- Monitor for genital mycotic infections and urinary tract infection; assess patients presenting with fever or malaise along with genital or perianal pain, tenderness, erythema, or swelling for necrotizing fasciitis;
- Signs/symptoms of ketoacidosis (eg, nausea/vomiting, abdominal pain, malaise, shortness of breath), confirm diagnosis by direct measurement of blood ketones.
- Blood glucose
- Glycosylated hemoglobin A1c (HbA1c)
- Serum cholesterol profile
- Hypersensitivity reactions

<b>Drug Interactions</b>	<b>Risk D: Consider therapy modification</b> Insulins, Sulfonylureas.
<b>Pregnancy and Lactation</b>	<b>Pregnancy:</b> use is not recommended. Toxicity in animals. <b>Lactation:</b> use is not recommended. No Human Data.
<b>Administration</b>	Oral: Administer once daily in the morning, with or without food. Refer to manufacturer PIL if there are specific considerations.
<b>Warnings/ Precautions</b>	<ul style="list-style-type: none"> <li>• Infection, acute: Discontinue therapy if any of the following occur: signs and symptoms of new infection (including osteomyelitis), new pain or tenderness, or sores/ulcers involving the lower limbs.</li> <li>• Volume depletion: Correct hypovolemia before starting treatment. Consider interrupting treatment if volume depletion occurs.</li> <li>• Renal impairment: Glycemic efficacy may be decreased in patients with renal impairment.</li> <li>• Elderly: Older adults may be predisposed to renal impairment or failure.</li> <li>• Appropriate use: Not for use in patients with diabetic ketoacidosis or patients with type 1 diabetes mellitus.</li> <li>• Hospitalized patients: Use of SGLT2 inhibitors for glycemic control is not routinely recommended for hospitalized patients.</li> <li>• Surgical procedures: In patients with diabetes mellitus, consider temporary discontinuation at least 3 days prior to surgery; reinstate therapy after condition is stabilized.</li> </ul>
<b>Storage</b>	Store between 15°C to 30°C. Refer to manufacturer PIL if there are specific considerations.

## Sympathomimetics

## Adrenaline (Epinephrine)

<b>Generic Name</b>	<b>Adrenaline (Epinephrine)</b>
<b>Dosage form/strengths</b>	Solution for Injection: 0.25 mg/ml, 1mg/ml and in combinations
<b>Route of administration</b>	IM, IV, SC
<b>Pharmacologic category</b>	Sympathomimetics; vasoconstrictor, alpha/beta agonist ATC: as sympathomimetic: C01CA24
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Anaphylaxis and other severe immediate hypersensitivity reactions</li> <li>• Acute hypotension or shock</li> <li>• Cardiopulmonary resuscitation</li> <li>• Bradycardia unresponsive to atropine</li> </ul>
<b>Dosage Regimen</b>	<p><b>Adult dosing:</b></p> <p><b>1. <u>Anaphylaxis and other severe immediate hypersensitivity reactions:</u></b></p> <ul style="list-style-type: none"> <li>– <b>IM:</b> 0.3 or 0.5 mg (use 0.5 mg in patients &gt;50 kg) using the 1 mg/mL solution given in the anterolateral thigh; may repeat every ~5 to 15 minutes if no response. Most patients will respond after 1 – 2 doses. If inadequate response, additional measures should be instituted (eg, IV fluids and continuous IV epinephrine infusion).</li> <li>– <b>IV:</b> This route should be reserved for patients who are unresponsive to the intramuscular therapy.                     <ul style="list-style-type: none"> <li>▪ Continuous infusion: Start with 0.06 – 0.02 mcg/kg/min and titrate to the usual dosing range 0.01 – 2 mcg/kg/min based on response.</li> <li>▪ Slow IV bolus: 0.05 – 1 mg/ml (0.1 mg/ml solution) given over 5 – 10 minutes. This dose can be repeated once if the patient does not respond.</li> </ul> </li> </ul> <p><b>2. <u>Hypotension and shock:</u></b></p> <ul style="list-style-type: none"> <li>• <b>Post cardiac arrest shock:</b> <ul style="list-style-type: none"> <li>– <b>IV infusion:</b> <ul style="list-style-type: none"> <li>▪ Usual range: 0.01 – 0.5 mcg/kg/min.</li> <li>▪ Maximum dose: 2 mcg/kg/min.</li> </ul> </li> </ul> </li> <li>• <b>Septic shock:</b> Epinephrine is given as an adjunctive treatment when initial vasoconstrictor therapy fails to achieve target blood pressure.                     <ul style="list-style-type: none"> <li>– <b>IV infusion:</b> <ul style="list-style-type: none"> <li>▪ Initial: 0.01 – 0.2 mcg/kg/min.</li> <li>▪ Usual range: 0.01 – 0.5 mcg/kg/min.</li> <li>▪ Maximum: 0.5 – 2 mcg/kg/min by IV infusion.</li> </ul> </li> </ul> </li> <li>• <b>Cardiopulmonary resuscitation: (specialist use only)</b></li> </ul>

	<ul style="list-style-type: none"> <li>– <b>Slow IV injection:</b> 1 mg every 3–5 minutes as required, 0.1 mg/mL solution is recommended.</li> <li>• <b>Bradycardia or atrioventricular block, symptomatic (unresponsive to atropine):</b> IV injection: 2–10 micrograms/minute, adjusted according to response</li> </ul> <p><b>Dosage: Pediatric</b></p> <p><b>Intravenous route should be used with extreme care by specialists only</b></p> <ul style="list-style-type: none"> <li>• <b>Anaphylaxis and other severe immediate hypersensitivity reactions</b></li> </ul> <p><b>Note:</b> IM administration in the anterolateral aspect of the middle third of the thigh is preferred; repeat dose after 5 minutes if no response; if life-threatening features persist, further doses can be given every 5 minutes until specialist critical care available</p> <p>SUBQ administration results in slower absorption and is less reliable.</p> <p><b>IM:</b></p> <p>Child up to 6 months: 100–150 micrograms, using adrenaline (1 mg/mL) injection          Child 6 months–5 years: 150 micrograms, using adrenaline (1 mg/mL) injection          Child 6–11 years: 300 micrograms, using adrenaline (1 mg/mL) injection          Child 12–17 years: 500 micrograms, using adrenaline (1 mg/mL) injection.</p> <ul style="list-style-type: none"> <li>• <b>Hypotension/shock, fluid-resistant: Infants, Children, and Adolescents:</b></li> </ul> <p><b>Continuous IV:</b> 0.1 to 1 mcg /kg/ minute; rates &gt;0.3 mcg /kg/ minute associated with vasopressor activity.</p> <ul style="list-style-type: none"> <li>• <b>Bradycardia:</b></li> </ul> <p><b>Infants, Children, and Adolescents:</b></p> <p><b>IV:</b> 0.01 mg/kg (maximum dose: 1 mg/dose); may repeat every 3 to 5 minutes as needed.</p>
<p><b>Dosage adjustment</b></p>	<p><b>Dosing: Altered Kidney Function:</b> No dose adjustments are needed.</p> <p><b>Dosing: Hepatic Impairment:</b> No dose adjustments are needed.</p>
<p><b>Contra-indications</b></p>	<p>There are no absolute contraindications to the use of epinephrine in a life-threatening situation.</p>
<p><b>Adverse Drug Reactions</b></p>	<p><b>Frequency not defined:</b></p> <p>Cardiovascular: Angina pectoris, cardiac arrhythmia, cardiomyopathy (stress), cerebrovascular accident, chest pain, hypertension, increased cardiac work, ischemic heart disease, limb ischemia, localized blanching, myocardial infarction, palpitations, peripheral vasoconstriction, supraventricular tachycardia, tachyarrhythmia, tachycardia, vasoconstriction, ventricular arrhythmia, ventricular ectopy, ventricular fibrillation</p> <p>Central nervous system: Anxiety, apprehension, cerebral hemorrhage, disorientation, dizziness, drowsiness, exacerbation of Parkinson's disease, headache, memory impairment, panic, paresthesia, psychomotor agitation, restlessness, tingling sensation</p> <p>Dermatologic: Diaphoresis, gangrene of skin or other tissue (at injection site), pallor, piloerection</p> <p>Endocrine and metabolic: Hyperglycemia, hypoglycemia, hypokalemia, insulin resistance, lactic acidosis</p> <p>Gastrointestinal: Nausea, vomiting</p> <p>Local: Tissue necrosis at injection site</p>

	<p>Neuromuscular and skeletal: Asthenia, tremor                  Renal: Renal insufficiency                  Respiratory: dyspnea, pulmonary edema, rales</p>
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• Heart rate, blood pressure</li> <li>• Monitor site of infusion for extravasation</li> <li>• ECG</li> <li>• Intravascular volume if used to treat hypotension, prior to and during therapy; support as needed</li> <li>• Monitor for hyperlactatemia, and hyperglycemia.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b>                  Blonanserin, Bromperidol, Ergot Derivatives, Isoproterenol, Kratom, Lisuride.</p> <p><b>Risk D: Consider therapy modification</b>                  Benzylpenicilloyl Polylysine, Bromocriptine, Cocaine (Topical), Haloperidol, Hyaluronidase, Inhalational Anesthetics, Linezolid, Promethazine, Serotonin/Norepinephrine Reuptake Inhibitors, Tricyclic Antidepressants.</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Epinephrine is recommended for the treatment of anaphylaxis in pregnant women. Use with caution and monitor hemodynamic response.  <b>Lactation:</b> Epinephrine is generally considered compatible in breastfeeding and is recommended for the treatment of anaphylaxis in breastfeeding women</p>
<b>Administration</b>	<p><b>Administration: IM</b>                  IM administration in the anterolateral aspect of the middle third of the thigh is preferred in the setting of anaphylaxis. Administer through clothing if necessary. Do not administer repeated injections at the same site. Do not inject into the buttocks or into digits, hands, or feet.</p> <p><b>Administration: IV</b>  <b>Usual Infusion Concentrations: Pediatric</b>                  IV infusion: 16 mcg /mL, 20 mcg /mL, 32 mcg /mL, 40 mcg /mL, or 64 mcg /mL.  <b>Usual Infusion Concentrations: Adult</b>  <b>IV infusion:</b> 1 mg in 250 mL (concentration: 4 mcg /mL) or 4 mg in 250 mL (concentration: 16 mcg /mL) of D<sub>5</sub> W; 1 mg in 1,000 mL (concentration: 1 mcg /mL) in D<sub>5</sub> W or D<sub>5</sub> NS</p> <p><b>Direct IV:</b> 1 mg/mL concentration must be further diluted to 0.1 mg/mL  <b>Continuous IV infusion:</b> Concentration may vary by use. IV infusions require an infusion pump. When administering as a continuous infusion, central line administration is preferred; extravasation may cause severe ischemic necrosis. If central line is not available, may administer for a short duration (&lt;72 hours) through a peripheral IV catheter placed in a large vein, at a proximal site (eg, in or proximal to antecubital fossa). Frequent monitoring of the IV catheter site is recommended to rapidly identify extravasation</p> <ul style="list-style-type: none"> <li>– shock/hypotension; cardiac output maintenance/stabilization, postresuscitation: Dilute to a maximum concentration of 64 mcg/mL</li> <li>– Hypersensitivity/anaphylaxis (refractory): Prepare a 1 mcg/mL solution (eg, add 1 mg of the 1 mg/mL solution to 1,000 mL of D5W)</li> </ul> <p><b>Rate of infusion (mL/hour) =</b> dose (mcg/kg/minute) x weight (kg) x 60 minutes/hour divided by the concentration (mcg/mL)</p> <p><b>Extravasation management:</b> If extravasation occurs, stop infusion immediately and</p>

disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevated extremity. Initiate phentolamine (or alternative antidote). Apply dry warm compresses.

*Phentolamine*: Dilute 5 to 10 mg in 10 to 20 mL NS and administer into extravasation site as soon as possible after extravasation; may readminister if patient remains symptomatic

**SUBQ** administration results in slower absorption and lower peak concentrations. IM administration is preferred.

**N.B.** Refer to manufacturer PIL for specific considerations.

### Warnings/ Precautions

#### **Concerns related to adverse effects:**

- Cardiac effects: May precipitate or aggravate angina pectoris or induce cardiac arrhythmias; use with caution.
- Extravasation: IV administration: Vesicant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation.
- Pulmonary edema: Due to peripheral constriction and cardiac stimulation, pulmonary edema may occur.
- Renal effects: Due to renal blood vessel constriction, decreased urine output may occur.

#### **Disease-related concerns:**

- Cardiovascular disease: Use with caution in patients with cardiovascular diseases (eg, arrhythmias, cerebrovascular disease, coronary artery disease, heart disease, hypertension).
- Diabetes: Use with caution in patients with diabetes mellitus; may transiently increase blood glucose levels.
- Hypovolemia: Correct blood volume depletion before administering any vasopressor.
- Parkinson's disease: Use with caution in patients with Parkinson's disease; psychomotor agitation or temporary worsening of symptoms may occur.
- Pheochromocytoma: Use with caution in patients with pheochromocytoma.
- Thyroid disease: Use with caution in patients with thyroid disease.

#### **Special populations:**

- Older adults: Use with caution in older adults.
- Pediatric: Lacerations, bent needles, and embedded needles have been reported in young children who are uncooperative during injection for hypersensitivity reaction. To minimize risk, hold the child's leg firmly in place and limit movement prior to and during injection.

#### **Dosage form specific issues:**

- Intraocular use: Not all formulations of epinephrine injection are suitable for intraocular use; consult the prescribing information prior to selecting a product. Appropriate products should have an indication for induction and maintenance of mydriasis during intraocular surgery and should not contain any sulphites or preservatives. Prior to intraocular use of an appropriate product, must dilute single-use 1 mg/mL (1 mL) solution to a concentration of 1 **mcg** /mL to 10 **mcg** /mL. Corneal endothelial damage has occurred when products containing sodium bisulfite have been used undiluted; Therefore, dilution is advised prior to any intraocular use. In addition, products containing chlorobutanol must also not be used intraocularly (may be harmful to corneal endothelium).
- Sulfites: Some products may contain sulfites as preservatives. The presence of sulphites in some products should not be prevent administration during a serious allergic or other emergency situation even if the patient is sulphite-sensitive.

	<p><b>Other warnings/precautions:</b></p> <ul style="list-style-type: none"> <li>• Appropriate use: Hypersensitivity reactions: Do not inject into the buttock; may not effectively treat anaphylaxis and has been associated with Clostridial infections (gas gangrene). Preferred injection site is anterolateral aspect of the thigh. Do not administer repeated injections at the same site (tissue necrosis may occur). Monitor for signs/symptoms of injection-site infection.</li> </ul>
<p><b>Storage</b></p>	<p>Store between 15°C to 30°C; do not freeze or refrigerate.  <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>



## Dobutamine

<b>Generic Name</b>	Dobutamine
<b>Dosage form/strengths</b>	Ampoules: 12.5mg/ml; 250mg/20ml; 250 mg/5ml
<b>Route of administration</b>	IV
<b>Pharmacologic category</b>	Adrenergic Agonist Agent; Inotrope ATC: C01CA07
<b>Indications</b>	<b>-Acute decompensated heart failure:</b> Short-term management of patients with cardiac decompensation.
<b>Dosage Regimen</b>	<b>-Adults dosing:</b> Continuous infusion: IV: Initial: 2 to 5 mcg/kg/minute; titrate based on clinical end point (eg, systemic perfusion or end-organ perfusion); usual dosage range: 2 to 10 mcg/kg/minute; maximum dose: 20 mcg/kg/minute.  <b>-Pediatric dosing:</b> Hemodynamic support: Infants, Children, and Adolescents: Continuous IV or intraosseous infusion: Initial: 0.5 to 1 mcg/kg/minute; titrate gradually every few minutes until desired response achieved; usual range: 2 to 20 mcg/kg/minute.
<b>Dosage adjustment</b>	<b>-Adult:</b> <b>-Renal Impairment:</b> -No dose adjustments needed. <b>- Hepatic Impairment:</b> - No dose adjustments needed.
<b>Contra-indications</b>	-Hypersensitivity to dobutamine or sulfites (some contain sodium metabisulfate), or any component of the formulation. -Hypertrophic cardiomyopathy with outflow tract obstruction (formerly known as idiopathic hypertrophic subaortic stenosis). -Pheochromocytoma
<b>Adverse Drug Reactions</b>	<b>-1% to 10%:</b> -Cardiovascular: Increased heart rate (10%), increased systolic blood pressure (8%), ventricular premature contractions (5%), angina pectoris (1% to 3%), chest pain (1% to 3%), palpitations (1% to 3%) -Central nervous system: Headache (1% to 3%) -Gastrointestinal: Nausea (1% to 3%) -Respiratory: Dyspnea (1% to 3%)
<b>Monitoring Parameters</b>	-BP, heart rate, ECG. - Intravascular volume status. - Serum-potassium concentration. - Kidney function. -Urine output.
<b>Drug Interactions</b>	<b>Risk X: Avoid combination</b> Kratom <b>Risk D: Consider therapy modification</b> Linezolid, Cocaine (Topical)
<b>Pregnancy and Lactation</b>	<b>-Pregnancy:</b> No evidence of harm. Use only if potential benefit outweighs risk. Appropriate

	<p>medications should not be withheld due to concerns of fetal teratogenicity.</p> <p><b>-Lactation:</b> No human data. Avoid.</p>
<b>Administration</b>	<p>Always administer via infusion device; administer into large vein. Central line administration is preferred</p> <p>-Adult: IV infusion: 250 mg in 500 mL (concentration: 500 mcg/mL), 500 mg in 250 mL (concentration: 2,000 mcg/mL), or 1,000 mg in 250 mL (concentration: 4000 mcg/mL) of D<sub>5</sub>W or NS.</p> <p>Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p>-Arrhythmias: Ventricular arrhythmias, including nonsustained ventricular tachycardia and supraventricular arrhythmias, have been reported. Observe closely for arrhythmias in patients with decompensated heart failure; sudden cardiac death has been observed. Ensure that ventricular rate is controlled in atrial fibrillation/flutter before initiating; may increase ventricular response rate.</p> <p>- An increase in BP is more common due to augmented cardiac output, but hypotension secondarily to vasodilation may occur at higher doses.</p> <p>-An increased risk of hospitalization and death has been observed with prolonged use in New York Heart Association Class III/IV heart failure patients.</p> <p>- May cause dose-related increases in heart rate.</p> <p>- May exacerbate ventricular ectopy (dose related).</p> <p>- Ineffective therapeutically in the presence of mechanical obstruction such as severe aortic stenosis.</p> <p>-Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy to minimize the risk of arrhythmias.</p> <p>- If needed, correct hypovolemia first to optimize hemodynamics.</p> <p>-Use with caution in patients with active myocardial ischemia or recent myocardial infarction; can increase myocardial oxygen demand.</p>
<b>Storage</b>	<p>-Store between 15°C to 30°C.</p> <p>-Following dilution in a compatible solution, use within 24 hours.</p> <p><b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>

## Dopamine

<b>Generic Name</b>	Dopamine
<b>Dosage form/strengths</b>	Concentrate for Solution For I.V Infusion: 200mg
<b>Route of administration</b>	IV
<b>Pharmacologic category</b>	Adrenergic Agonist Agent; Inotrope ATC: C01CA04
<b>Indications</b>	<b>Cardiogenic shock:</b> Treatment of severe hypotension or shock (eg, septic shock and other vasodilatory shock states, cardiogenic shock, decompensated heart failure, post–cardiac arrest, cardiac surgery) that persists during and after adequate fluid volume replacement.
<b>Dosage Regimen</b>	<p><b>Dosing: Adult</b> Dopamine is a cardiac stimulant which acts on beta1 receptors in cardiac muscle, and increases contractility with little effect on rate.</p> <p><b>Hypotension or shock:</b></p> <p><b>Septic shock and other vasodilatory shock states (alternative agent):</b> <b>Continuous infusion: IV:</b> Initial: 2 to 5 mcg/kg/minute; titrate up to a dose of 20 mcg/kg/minute</p> <p><b>Cardiogenic shock (alternative agent):</b> <b>Continuous infusion: IV:</b> Usual dosage range: 0.5 to 20 mcg/kg/minute; titrate based on clinical end point (eg, end-organ perfusion)</p> <p><b>Post–cardiac arrest shock (alternative agent):</b> <b>Continuous infusion: IV:</b> Usual dosage range: 5 to 20 mcg/kg/minute; titrate based on clinical end points</p> <p><b>Dosing: Pediatric: offlabel</b></p> <ul style="list-style-type: none"> <li><b>Hemodynamic support:</b> Infants, Children, and Adolescents: Continuous IV or intraosseous infusion: 2 to 20 mcg/kg/minute; titrate gradually by 5 to 10 mcg/kg/minute increments until optimal response is obtained</li> </ul>
<b>Dosage adjustment</b>	<p><b>Patients with Renal Impairment Dosing</b> No dosage adjustments are needed.</p> <p><b>Patients with hepatic impairment dosing</b> No dosage adjustments are needed.</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to sulfites (commercial preparation contains sodium bisulfite);</li> <li>Pheochromocytoma;</li> <li>Uncorrected tachyarrhythmias</li> <li>Ventricular fibrillation</li> </ul>
<b>Adverse Drug Reactions</b>	<p><b>Postmarketing:</b></p> <p>Cardiovascular: Angina pectoris, atrial fibrillation, bradycardia, cardiac conduction disorder, ectopic beats, hypertension, hypotension, palpitations, tachycardia, vasoconstriction, ventricular arrhythmia, widened QRS complex on ECG</p> <p>Dermatologic: Peripheral gangrene (with prolonged or high dose, can occur with low doses with concomitant occlusive vascular disease), piloerection</p> <p>Gastrointestinal: Nausea, vomiting</p>

	Genitourinary: Azotemia Nervous system: Anxiety, headache Respiratory: Dyspnea
<b>Monitoring Parameters</b>	<ul style="list-style-type: none"> <li>• BP, heart rate, ECG</li> <li>• End-organ perfusion (eg, urine output, mental status)</li> <li>• Infusion site for blanching/extravasation;</li> <li>• Intravascular volume status.</li> </ul>
<b>Drug Interactions</b>	<p><b>Risk X: Avoid combination</b> Ergot Derivatives, Kratom</p> <p><b>Risk D: Consider therapy modification</b> Benzylpenicilloyl Polylysine, Bromocriptine, Cocaine (Topical), Hyaluronidase, Linezolid, Monoamine Oxidase Inhibitors, Serotonin/Norepinephrine Reuptake Inhibitors, Tricyclic Antidepressants</p>
<b>Pregnancy and Lactation</b>	<p><b>Pregnancy:</b> Use dopamine during pregnancy only if the potential benefit justifies the potential risk of the fetus. Animal studies have shown maternal toxicity including mortality, decreased weight gain, and pharmacotoxic signs</p> <p><b>Lactation:</b> Use caution when administering dopamine to a breast-feeding woman. It is not known whether dopamine is excreted in human milk</p>
<b>Administration</b>	<p><b>Usual Infusion Concentrations: Pediatric</b> <b>IV infusion:</b> 200mg, 400mg or 800mg in 250 mL of D<sub>5</sub>W or NS.</p> <p><b>Usual Infusion Concentrations: Adult</b> <b>IV infusion:</b> 400 mg in 250 mL (concentration: 1600 mcg/mL) or 800 mg in 250 (or 500 mL) (concentration: 3200 mcg/mL) of D<sub>5</sub>W or NS Do not administer unless solution is clear. Avoid contact or simultaneous administration with alkalis (including sodium bicarbonate), oxidizing agents, or iron salts.</p> <p><b>Administration: IV</b> <b>Administer as a continuous infusion via an infusion pump.</b> Central line administration is preferred; extravasation may cause severe ischemic necrosis. If central line is not available, may administer for a short duration (&lt;72 hours) through a peripheral IV catheter placed in a large vein at a proximal site (eg, in or proximal to antecubital fossa). Frequent monitoring of the IV catheter site is recommended to rapidly identify extravasation. Vesicant; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation. <b>Extravasation management:</b> If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity. Initiate phentolamine antidote. Apply dry warm compresses. <i>Phentolamine:</i> Dilute 5 to 10 mg in 10 to 20 mL NS and administer into extravasation site as soon as possible after extravasation; may readminister if patient remains symptomatic. Pediatric dosage of phentolamine should be 0.1 to 0.2 mg/kg up to a maximum of 10 mg per dose. <b>N.B.</b> Refer to manufacturer PIL for specific considerations.</p>
<b>Warnings/ Precautions</b>	<p><b>Concerns related to adverse effects:</b></p> <ul style="list-style-type: none"> <li>• Arrhythmias: May cause increases in heart rate, increasing the risk of tachycardia and other tachyarrhythmias including ventricular arrhythmias. In heart transplant candidates, institute appropriate measures to protect patient against risks of</li> </ul>

sudden cardiac death.

- Extravasation: Vesicant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation; infuse into a large vein if possible. Avoid infusion into leg veins. Watch IV site closely. If extravasation occurs, infiltrate the area with diluted phentolamine (5 to 10 mg in 10 to 15 mL of saline) with a fine hypodermic needle. Phentolamine should be administered as soon as possible after extravasation is noted to prevent sloughing/necrosis.

***Disease-related concerns:***

- Cardiovascular disease: Use with caution in patients with cardiovascular disease, cardiac arrhythmias and/or occlusive vascular disease.
- Active myocardial ischemia/post-myocardial infarction: Use with caution in patients with active myocardial ischemia or recent myocardial infarction; may increase myocardial oxygen consumption.
- Electrolyte imbalance: Correct electrolyte disturbances, especially hypokalemia or hypomagnesemia, prior to use and throughout therapy to minimize the risk of arrhythmias.
- Shock: The use of dopamine in adult patients with shock (majority of patients had septic shock) demonstrated a higher incidence of adverse events (eg, tachyarrhythmias). Higher 28-day mortality was also seen in patients with septic shock with the use of dopamine as compared to norepinephrine.

***Concurrent drug therapy issues:***

- Monoamine oxidase inhibitors (MAO-I): Use with extreme caution in patients taking MAO inhibitors; prolong hypertension may result from concurrent use.

***Dosage form specific issues:***

- Sodium metabisulfite: Product may contain sodium metabisulfite.

***Other warnings/precautions:***

- Appropriate use: Assure adequate circulatory volume to minimize need for vasoconstrictors when used in hemodynamic support. Avoid hypertension; monitor blood pressure closely and adjust infusion rate.

**Storage**

Store between 15°C to 30°C. Protect from light. Avoid excessive heat; Protect from freezing. Dopamine has been found to be stable for a minimum of 24 hours after dilution.

Refer to manufacturer PIL for specific considerations.

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36	Hydralazine	91	73	Verapamil	137
37	Hydrochlorothiazide	168			

## Sources

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