

METOPROLOL TARTRATE

CARDIOSTAT

50 mg Film-Coated Tablet

BETA ADRENOCEPTOR BLOCKER

FORMULATION:

Each film-coated tablet contains:
Metoprolol Tartrate, USP 50 mg

PRODUCT DESCRIPTION:

Metoprolol is white to off-white film coated tablet, round, biconvex, bisected on one side and plain on the other side.

PHARMACODYNAMICS:

Metoprolol is a beta-1 selective beta blocker. It has a relatively greater blocking effect on beta receptors (i.e. those mediating adrenergic stimulation of heart rate and contractility and release of the fatty acids from fat stores) than on beta receptors which are chiefly involved in broncho and vasodilation.

Metoprolol only exhibits insignificant membrane stabilizing effect and has no agonist effect.

Metoprolol reduces or blocks the stimulating effect of catecholamines (particularly released in case of physical or mental stress) on the heart. Metoprolol reduces tachycardia, decreases the cardiac output and the contractility, and lowers the blood pressure.

PHARMACOKINETICS:

Metoprolol is readily and completely absorbed from the gastrointestinal tract but is subject to considerable first-pass metabolism. Peak plasma concentrations vary widely and occur about 1.5 to 2 hours after a single oral dose. It is moderately lipid-soluble.

Metoprolol is metabolised by hepatic enzyme cytochrome (CYP) 2D6. Individuals with poor metabolic capacity (approx. 7-8%) exhibit higher plasma concentrations and slower elimination than individuals with good metabolic capacity.

More than 95% of an oral dose is excreted in urine. Approximately 5% of the dose is excreted in unchanged form; in single cases, up to an entire 20%. The elimination half-life of metoprolol in plasma is 3.5 hours on average (interval: 1-9 hours). Total clearance is approx. 1L/min. The systemic bioavailability and elimination of metoprolol is normal in renal failure patients. The elimination of metabolites is slower than normal, however. Significant accumulation of metabolites has been observed in patients with a glomerular filtration rate of less than 5 mL/min. The metabolite accumulation does not potentiate the beta blocking action of metoprolol.

Patients with hepatic cirrhosis may experience an increase in the bioavailability of metoprolol and a decline in total clearance. In patients with portocaval shunt, the total clearance is approx. 0.3 L/min, and the AUC values are approx. six times larger than healthy individuals.

INDICATIONS:

For the treatment of hypertension, angina pectoris, cardiac arrhythmia, myocardial infarction and heart failure. It is also used in the management of hyperthyroidism and migraine.

DOSAGE & ROUTE OF ADMINISTRATION:

Adult dose:

For Hypertension:

Oral: Initial dose of 2 tablets daily, increased weekly according to the response of the patient to 8 tablets; can be taken twice daily or as prescribed by the physician. Usual maintenance dose is 2 to 4 tablets daily taken with or immediately following a meal or as prescribed by the physician.

For Angina Pectoris:

Oral: 50 mg Tablet: 1 to 2 tablets, 2 or 3 times daily in divided doses or as prescribed by the physician.

For Cardiac Arrhythmias:

Oral: 50 mg Tablet: 1 tablet to be taken 2 or 3 times daily, increased if necessary to 6 tablets daily in divided doses or as prescribed by the physician.

CONTRAINDICATIONS:

Sinus bradycardia; second and third degree A-V block; right ventricular failure secondary to pulmonary hypertension; congestive heart failure and cardiogenic shock.

PRECAUTIONS:

Metoprolol should not be given to patients with bronchospasm or asthma or to those with history of obstructive airway disease.

ADVERSE EFFECTS:

Metoprolol is well tolerated, and the adverse effects are generally mild and reversible. The most commonly reported adverse reactions during treatment is fatigue. Gangrene (in patients with severe peripheral circulatory disorder), thrombocytopenia and agranulocytosis may occur very rarely (less than 1 case per 10,000 patients). The following adverse effects have been reported during the course of clinical studies or have been reported after routine use. Frequency estimates: very common, common, uncommon, rare to very rare.

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to <1/10)	Uncommon (≥ 1/1,000 to <1/100)	Rare (≥ 1/10,000 to <1/1,000)	Very rare (< 1/10,000)
Blood and lymphatic system disorders					Thrombocytopenia, leukopenia
Endocrine disorders				Deterioration of latent diabetes mellitus	
Metabolism and nutrition disorders			Weight gain		
Psychiatric disorders			Depression, concentration problems, drowsiness or insomnia, nightmares	Nervousness, anxiety	Forgetfulness or memory impairment, confusion, hallucinations, personality changes
Nervous System Disorders		Dizziness, headache	Paresthesia		
Eye disorders				Visual disturbances, dry or irritated eyes, conjunctivitis	
Ear and labyrinth disorders					Tinnitus, hearing problems
Cardiac disorders		Bradycardia, balance disturbances (very rare associated syncope, palpitations)	Temporary exacerbation of symptoms of heart failure, first-degree atrioventricular block, precordial pain	Functional heart symptoms, heart arrhythmia, conductivity disturbances.	
Vascular disorders	Pronounced blood pressure drop & orthostatic hypotension, very rare with syncope	Cold hands and feet			Necrosis in patients with severe peripheral vascular disorders prior to treatment, exacerbation of claudication intermittent or Raynaud's syndrome
Respiratory, thoracic & mediastinal disorders		Functional dyspnea	Bronchospasms	Rhinitis	
Gastrointestinal disorders		Nausea, abdominal pain, diarrhoea, constipation	Vomiting	Dryness of mouth	Taste disturbances
Hepatobiliary disorders				Abnormal LFT values	Hepatitis
Skin and subcutaneous tissue disorders			Rash (psoriasis like urticaria and dystrophic cutaneous lesions), increased perspiration	Hair loss	Light hypersensitivity reactions, exacerbation of psoriasis, new psoriasis manifestation, psoriasis-like dermatological changes
Musculoskeletal and connective tissue disorders			Muscle spasms		Arthralgia, muscle weakness
Reproductive system and breast disorders				Impotence and other sexual dysfunctions, induratio penis plastica (Peyronie's syndrome)	
General disorders and administration site conditions	Fatigue		Oedema		

OVERDOSAGE AND MANAGEMENT:

Overdosage of Metoprolol may cause severe hypotension, sinus bradycardia,atrioventricular block,heart failure, cardiogenic shock, cardiac arrest, asystole, QT-prolongation(isolated cases), poor peripheral perfusion, bronchospasms,loss of consciousness (even coma),nausea,vomiting or cyanosis. Respiratory depression, apnea,fatigue,fine tremor, seizures,sweating,paraesthesias, possible oesophageal spasm, hypoglycaemia (especially in children) or hyperglycaemia,hyperkalaemia,renal effects,transient symptoms of myasthenia.The symptoms may be exacerbated by concomitant ingestion of alcohol, antihypertensive agents, quinidine or barbiturates.

The first signs of an overdose present within 20 minutes to 2 hours after taking the medicinal product. The effects of massive overdose may persist several days, despite declining plasma concentrations.

Overdosed patient should be admitted to hospital and generally ,should be managed in an intensive care setting, with continuous monitoring of cardiac function, blood gases, and blood biochemistry.

TREATMENT:

Active charcoal, gastric lavage if necessary. NOTE: Atropine(0.25-0.5 mg I.V. to adults, 10-20 micrograms/kg to children) should be administered prior to gastric lavage (due to the risk of vagal stimulation). Intubation and assisted ventilation should occur based on a very wide indication. Adequate volume substitution. Glucose infusion. ECG monitoring. Atropine sulphate may be administered (0.5-2.0 mg intravenously) for blocking the vagus nerve. This can be repeated.

In case of severe hypotension, bradycardia or in risk of heart failure, the patient could be given a beta-1 agonist(e.g. prenalterol or isoprenaline) intravenously at intervals of 2-5 minutes or as continuous infusion until achieving the desired effect. If a selective beta-1 agonist is unavailable, dopamine may be used. If the desired effect is not achieved, another sympathomimetic agent may be used, e.g. dobutamine or noradrenaline.

Note: (1) The doses required for managing overdoses are much higher than the therapeutic doses usually applied as the beta blocker has blocked the beta receptors.(2) In case of cardiac arrest after overdosage with a beta-blocker,cardiopulmonary resuscitation during several hours may be required.

DRUG INTERACTIONS:

IV Ca-antagonist of verapamil and diltiazem type. Class I antiarrhythmics, antihistamines, H2 blockers, antidepressants, antipsychotics. Sympathomimetic ganglion-blocking agent, other β -blockers. MAOIs, clonidine, inhalation anesthetics, rifampicin, alcohol, hydralazine, indomethacin and other prostaglandin synthetase inhibitor. Oral antidiabetics. Digitalis glycosides.

FERTILITY, PREGNANCY AND LACTATION:

There are no well -controlled studies of the use of Metoprolol in pregnant women. Metoprolol may only be used during pregnancy if the benefits to the mother outweigh the risk to the embryo/foetus.

Beta blockers reduce placental perfusion and may cause foetal death and premature birth. Intrauterine growth retardation has been observed after long term treatment of pregnant women with mild to moderate hypertension. Beta blockers have been reported to cause prolonged delivery and bradycardia in the foetus and the newborn child.

The concentration of Metoprolol in breast milk is approximately three times higher than the one in the mother's plasma.Breastfeeding babies should be monitored for signs of beta blocking.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

CAUTION:

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING STATEMENT:

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph".Seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY:

Alu/Clear PVDC Blister Pack x 10's (Box of 100's)

REGISTRATION NUMBER:

DR-XY37399

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Manufactured by:

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Manufactured for:

 **ONE PHARMA**

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