

NITROGLYCERINE/ GLYCERYL TRINITRATE

Indications/Uses

Listed in Dosage.

Dosage/Direction for Use

Adult : PO Stable angina As modified-release tab/cap: 2.5-6.5 mg 3-4 times/day. Max: 26 mg 4 times/day. Sublingual Acute angina As tab: 300-600 mcg, repeat if necessary. Seek medical help if pain persists after 3 doses w/in 15 min. As aerosol spray (400 mcg/spray): 1-2 sprays onto or under the tongue. Max: 3 sprays. Buccal Acute angina 2 mg, increase to 3 mg if necessary. Severe angina: 5 mg. Stable angina 2-5 mg tid. Unstable angina Up to 5 mg. Heart failure 5 mg, repeat until symptoms are controlled. Chronic heart failure: 5-10 mg tid. IV Unstable angina Initial: 10 mcg/min, increase in increment of 10 mcg/min as required. Acute MI 10-100 mcg/min. Heart failure Initial: 5-25 mcg/min. Induction of hypotension or control of HTN during surgery Initial: 25 mcg/min, may be increased in increments of 25 mcg/min until BP is stabilised. Usual dose: 10-200 mcg/min (up to 400 mcg/min in some cases). Transdermal Stable angina As patch releasing 2.5-20 mg/24 hr: Apply 1 patch onto a fresh area of skin. Max: 20 mg/day. Prophylaxis of phlebitis and extravasation secondary to venous cannulation As patch releasing 2.5-20 mg/24 hr: Apply 5 mg patch distal to the IV site, replace patch at a different site daily or after 3-4 days depending on the patch; continue for as long as the IV infusion is maintained. Topical Stable angina As 2% oint: Apply 0.5-2 inches onto skin bid or 3-4 hrly. Rectal Pain due to chronic anal fissure As 0.4% oint: Apply approx 1.5 mg intra-anally 12 hrly for up to 8 wk.

Dosage Details

Buccal

Stable angina

Adult: 2-5 mg tid.

Buccal

Heart failure

Adult: 5 mg, repeat until symptoms are controlled. Chronic heart failure: 5-10 mg tid.

Buccal

Acute angina

Adult: 2 mg, placed between the gum and upper lip, increase to 3 mg if necessary. Severe angina: 5 mg may be given.

Buccal

Unstable angina

Adult: Up to 5 mg.

Intravenous

Unstable angina

Adult: Initially, 10 mcg/min, increase in increment of 10 mcg/min at approx 30-minute intervals, according to patient requirement.

Intravenous

Induction of hypotension or control of hypertension during surgery

Adult: Initially, 25 mcg/min. Dose may be increased in increments of 25 mcg/min at 5-minute intervals until BP is stabilised. Usual dose: 10-200 mcg/min (up to 400 mcg/min in some cases).

Intravenous

Acute myocardial infarction

Adult: 10-100 mcg/min, w/ the dose initially at the lower rate, then increase gradually according to response.

Intravenous

Heart failure

Adult: Initially, 5-25 mcg/min, adjust according to response.

Oral

Stable angina

Adult: As modified-release tab/cap: 2.5-6.5 mg 3-4 times daily, adjust according to response. Max: 26 mg 4 times daily.

Rectal

Pain due to chronic anal fissure

Adult: As 0.4% oint: Apply an equivalent of approx 1.5 mg intra-anally 12 hrly for up to 8 wk.

Sublingual

Acute angina

Adult: As tab: 300-600 mcg, repeat if necessary. Seek medical help if pain persists after a total of 3 doses w/in 15 min. As aerosol spray (400 mcg/spray): 1-2 sprays directed onto or under the tongue, may give further 1 spray after 5 minutes. Max: 3 sprays.

Topical/Cutaneous

Stable angina

Adult: As 2% oint: Apply 0.5-2 inches on a convenient area of the skin bid or 3-4 hrly if necessary; cover the area after application.

Transdermal

Stable angina

Adult: As patch releasing 2.5-20 mg/24 hr: Apply 1 patch onto a fresh area of skin (chest, upper arms, thigh or shoulder). Max: 20 mg daily.

Transdermal

Prophylaxis of phlebitis and extravasation secondary to venous cannulation

Adult: As patch releasing 2.5-20 mg/24 hr: Apply 5 mg patch distal to the IV site, replace patch at a different skin site either daily or after 3-4 days depending on the patch; continue for as long as the IV infusion is maintained.

Incompatibility

Adsorbed by some plastic IV admin sets, including PVC. Y-site: Caffeine citrate, levofloxacin. Syringe: Pantoprazole.

Contraindications

Uncorrected hypovolaemia, postural hypotension, hypotension, marked anaemia, hypertrophic obstructive cardiomyopathy, constrictive pericarditis or pericardial tamponade, aortic or mitral stenosis, raised intracranial pressure (e.g. cerebral haemorrhage, head trauma), migraine or recurrent headache, closed-angle glaucoma. Concomitant use w/ phosphodiesterase type 5 (PDE5) inhibitors, riociguat, other organic nitrates w/ nitric oxide (NO) donors, heparin.

Special Precautions

Patient w/ hypothyroidism, hypothermia, malnutrition, recent MI, arterial hypoxaemia due to severe anaemia, hypoxaemia or ventilation/perfusion imbalance due to lung disease or ischaemic heart failure. Severe renal or hepatic impairment. Pregnancy and lactation.

Adverse Reactions

Orthostatic hypotension, peripheral oedema, bradycardia, tachycardia, flushing, hypotension, syncope, dizziness, headache, light-headedness, nausea, vomiting, xerostomia, weakness, paraesthesia, diaphoresis, dyspnoea, rhinitis, pharyngitis.

Pregnancy Category (US FDA)

IV/Parenteral/PO/Rectal/SL/Topical/Transdermal: C

Patient Counseling Information

This drug may cause postural hypotension, dizziness, light-headedness, blurred vision, headache or tiredness, if affected, do not drive or operate machinery.

MonitoringParameters

Monitor heart rate and BP.

Overdosage

Symptoms: Hypotension, reflex tachycardia, pallor, sweating, diarrhoea, weak pulse, collapse, syncope, dizziness, headache, asthenia, nausea, vomiting, methaemoglobinaemia. Bradycardia, psychosis and resp depression may occur in severe poisoning. Management: Increase central fluid volume through passive elevation of patient's legs. IV infusion of normal saline or similar fluid may also be necessary. Methylene blue infusion may be given in case of methaemoglobinaemia. Administer oxygen if necessary.

Drug Interactions

Enhanced hypotensive effect w/ vasodilators and other hypotensive drugs. Reduced efficacy (oral/buccal preparations) w/ drugs that cause dry mouth (e.g. TCAs, other antimuscarinics). Increased vasodilatory effect w/ acetylcysteine. May reduce the thrombolytic activity of alteplase. May increase the bioavailability of dihydroergotamine which may lead to coronary vasoconstriction.

Potentially Fatal: Potentiation of hypotensive effect w/ PDE5 inhibitors (e.g. sildenafil, tadalafil, vardenafil), riociguat and other organic nitrates w/ nitric oxide (NO) donors. May reduce the anticoagulant effect of heparin.

Food Interaction

Alcohol may enhance the hypotensive effect of glyceryl trinitrate.

Lab Interference

May interfere w/ the measurement of catecholamines and vanilmandelic acid in urine. Triglyceride assays (dependent on glycerol oxidase) may be falsely elevated.

Action

Description: Glyceryl trinitrate forms free radical nitric oxide (NO), which stimulates guanylate cyclase in the vascular smooth muscle cells resulting in relaxation of smooth muscles. It reduces cardiac oxygen demand by decreasing preload and may modestly reduce afterload, dilates coronary arteries and improves collateral flow to ischaemic regions. It also decreases sphincter tone and intra-anal pressure when administered rectally.

Onset: W/in 1-3 min (sublingual, buccal); w/in 30-60 min (transdermal, topical); w/in 1-2 min (IV).

Duration: Approx 30-60 min (sublingual); 3-5 hr (modified-release buccal tab); 24 hr (transdermal); up to 12 hr (topical); approx 3-5 min (IV).

Pharmacokinetics:

Absorption: Rapidly absorbed from oral mucosa; well absorbed from the GI tract and through the skin. Bioavailability: <100%.

Distribution: Widely distributed; taken up by RBCs and smooth muscles cells of the blood vessels. Volume of distribution: Approx 3 L/kg. Plasma protein binding: 60%.

Metabolism: Rapidly metabolised in the liver by glutathione-organic nitrate reductase to form di- and mononitrate metabolites; undergoes hydrolysis in the plasma.

Excretion: Via urine (as inactive metabolites). Plasma half-life: Approx 3 min (glyceryl trinitrate); approx 30-60 min (dinitrate metabolites).

Chemical Structure

Click on icon to see table/diagram/image

Storage

Store between 15-30°C.

MIMS Class

Anti-Anginal Drugs

ATC Classification

C01DA02 - glyceryl trinitrate ; Belongs to the class of organic nitrate vasodilators. Used in the treatment of cardiac disease.

C05AE01 - glyceryl trinitrate ; Belongs to the class of muscle relaxants. Used in the topical treatment for the treatment of hemorrhoids and anal fissures.