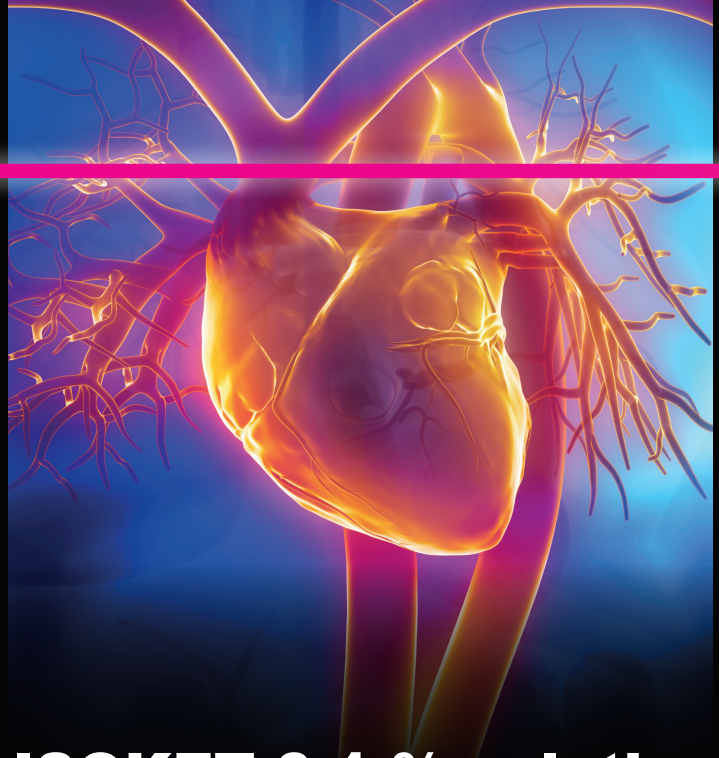

ISOKET 0,1 % solution

isosorbide dinitrate 1 mg /ml

Intravenous infusion solution

For severe angina pectoris, acute myocardial infarction and acute left ventricular failure

Available in 10 mg /10 ml ampoules

- Isosorbide dinitrate (ISDN) causes a relaxation of vascular smooth muscle thereby inducing vasodilatation. Both peripheral arteries and veins are relaxed by ISDN.
  The latter effect promotes venous pooling of blood and decreases venous return to the heart, thereby reducing ventricular end-diastolic pressure and volume (preload).
- The action on arterial, and at higher dosages arteriolar vessels, reduces the systemic vascular resistance (afterload). This in turn reduces the cardiac work.
- The effects on both preload and afterload lead to a reduced oxygen consumption by the heart.
- ISOKET is a concentrated solution and must be diluted prior to use.
- ISOKET should **Never** be injected directly as a bolus.
- Administer ISOKET as an intravenous admixture with a suitable vehicle such as 0,9 % sodium chloride injection or 5 % dextrose and water injection BP (exchange required volume of ISOKET with an equal volume of infusion vehicle).
- When 0,9 % sodium chloride is given, the effect of sodium overload should be taken into consideration.
- Always administer as IV infusion, or with the aid of a syringe pump incorporating a glass or rigid plastic syringe, in hospital under constant cardiovascular monitoring.
- The safety and efficacy of ISOKET in children has not yet been established.

BP = British Pharmacopoeia; IV = Intravenous

Dosage and directions for use

Recommended dose in adults	**Initial dose** • 1 mg /hour to 2 mg /hour • Adjust to individual requirements thereafter
Refer to package insert for maximum dose	

Special precautions:

- ISOKET should be used with caution and under medical supervision in patients who are suffering from hypothyroidism, hypothermia, malnutrition, severe liver disease, renal disease or orthostatic hypotension.

CONTRAINDICATIONS:

ISOKET solution must not be used in:

- hypersensitivity to ISOKET, to any of the other ingredients, or to other nitrates or nitrites
- low left ventricular filling pressure
- hypertrophic obstructive cardiomyopathy (HOCM)
- cardiogenic shock (unless a sufficient end-diastolic pressure is maintained by appropriate measures e.g. unless medicines with positive inotropic effect or intra-aortic balloon counterpulsation are simultaneously used)
- severe hypotension (systolic blood pressure less than 90 mmHg)
- marked anaemia
- head trauma
- cerebral haemorrhage
- hypovolaemia
- closed angle glaucoma
- diseases associated with an increased intracranial pressure
- constrictive pericarditis
- cardiac tamponade
- circulatory collapse
- aortic and/or mitral valve stenosis
- patients receiving phosphodiesterase-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil)

Interactions with other medication and other forms of interaction:

- Concurrent intake of medicines with blood pressure lowering properties and/or alcohol may potentiate the hypotensive effect of ISOKET. This might also occur with neuroleptics and tricyclic antidepressants.
- Phosphodiesterase-5 inhibitors e.g. sildenafil, potentiate the hypotensive effects of ISOKET. This might lead to life-threatening cardiovascular complications. Therefore, ISOKET must not be given to patients receiving phosphodiesterase-5 inhibitors.
- ISOKET may increase the blood level of dihydroergotamine and its toxic effect.

All adverse events should be reported by calling the Ethicare Medical Careline number or directly to GlaxoSmithKline on +27 11 745 6000.

S3 **ISOKET 0,1% Solution (infusion solution)**. Reg. No.: W/7.1.4/0360. Each 10 ml ampoule contains 10 mg of isosorbide dinitrate in sterile isotonic saline. Contains 1 mg/1 ml isosorbide dinitrate in sterile isotonic saline. PHARMACOLOGICAL CLASSIFICATION: A 7.1.4 Vasodilators – coronary and other medicines used in angina pectoris. INDICATIONS: Severe angina pectoris (e.g. unstable or vasospastic angina). Acute myocardial infarction. Acute left ventricular failure. CONTRA-INDICATIONS: Hypersensitivity to ISDN or other ingredients, cardiogenic shock, severe hypotension, marked anaemia, cerebral haemorrhage, uncorrected hypovolaemia, increased intra-ocular pressure, increased intracranial pressure, constrictive pericarditis, vascular collapse, severely impaired renal or hepatic function. Should not be given to patients within a 48 hour period after taking phosphodiesterase 5 inhibitors, e.g. sildenafil. Pregnancy and lactation: Should only be used during pregnancy if clearly needed and solely under the direction and continuous supervision of a physician. Caution should be exercised when administered to a nursing woman. WARNINGS: In cases with initial hypotension and low filling pressures, ISOKET should be used simultaneously with either positive inotropic drugs or assisted circulation (balloon pump) when absolutely needed. Continuous haemodynamic monitoring is required. Should be used with particular caution in low filling pressures e.g. in acute myocardial infarction, impaired left ventricular function (left ventricular failure); hypertrophic obstructive cardiomyopathy; pericardiac tamponade; aortic and/or mitral stenosis; tendency towards orthostatic disturbance of circulatory regulation; diseases associated with an increased intracranial pressure. DOSAGE AND DIRECTIONS FOR USE: Dosage should be adjusted to suit the patient's needs and the response of clinical and haemodynamic variables should be monitored. Recommended starting dose is 1-2 mg per hour; then the dose can be adjusted to the individual requirements. The maximum dose does not normally exceed 8 (-10) mg/hour. Patients suffering from heart failure may require higher doses: Up to 10 mg per hour and in individual cases up to 50 mg per hour. The safety and efficacy of ISOKET in children has not yet been established. Administration: Should never be injected directly in the form of a bolus. Can be administered as an intravenous admixture with a suitable vehicle such as Sodium Chloride Injection BP or Dextrose Injection BP. When saline is given, the effect of sodium overload should be taken into consideration. Prepared ISOKET admixtures are always given by intravenous infusion or with the aid of a syringe pump incorporating a glass or rigid plastic syringe, in a hospital setting under constant cardiovascular monitoring. Depending on the type and the severity of the disease, the usual follow-up examinations (symptoms, blood pressure, heart rate, urine) should be completed using invasive haemodynamic measurements. For preparation of admixtures please refer to package insert. SIDE EFFECTS AND SPECIAL PRECAUTIONS: Headache, hypotension and/or light-headedness on standing associated with dizziness, drowsiness, reflex tachycardia, and a feeling of weakness; nausea, vomiting, flush and allergic skin reaction (e.g. rash), which may be severe and exfoliative dermatitis; severe hypotensive responses including nausea, vomiting, restlessness, pallor and, excessive perspiration; collapse (sometimes accompanied by bradyarrhythmia and syncope); enhanced angina symptoms, heartburn, temporary hypoxaemia may occur. Symptoms of cerebral ischaemia, marked blood pressure drop, cyanosis, methaemoglobinaemia, coldness of the skin, impairment of respiration and bradycardia. If severe hypotension occurs, administration should be stopped immediately. If the symptoms do not subside spontaneously, appropriate measures should be undertaken (e.g. raising legs, administration of volume expanding drugs). Patients may develop postural hypotension with faintness upon rising suddenly. There is a theoretical hazard of rapid withdrawal following chronic exposure, which might be expected to produce non-exertional ischaemic cardiac pain or peripheral ischaemia. Special Precautions: Development of tolerance and cross-tolerance to other nitro compounds has been described. May affect the patient's reactivity to an extent that her/his ability to drive or operate machinery is impaired. This effect is increased in combination with alcohol. Interactions: Concurrent intake of medicines with blood pressure lowering properties, e.g. beta-blockers, calcium antagonists, vasodilators etc., and/or alcohol, phosphodiesterase type 5 inhibitors, e.g. sildenafil, neuroleptics and tricyclic antidepressants, dihydroergotamine. Pharmaceutical precautions: Compatible with all commonly employed infusion solutions (e.g. 5-30% Glucose infusion, Sodium Chloride Solution 0,9% (Isotonic); Ringer's solution, solutions containing protein, Heparin Solution 5 000 U per ml) and with glass infusion bottles. Infusion material made of polyvinyl chloride (PVC) or polyurethane (PU) has been shown to induce a loss of the active ingredient due to adsorption. If these materials are used the dosage should be adjusted to suit the patient's needs. MANAGEMENT OF OVERDOSAGE: General procedures:In the event of nitrate-related hypotension include patient should be kept horizontal with the head lowered and legs raised, supply oxygen, expand volume, specific shock treatment (admit patient to intensive care unit). Special procedure: Raising the blood pressure if the blood pressure is very low (additional administration of a sympathomimetic, e.g. etilefrine HCl or norfenefrine HCl), treatment of methaemoglobinaemia (reduction therapy of choice with vitamin C, methylene-blue, or toluidine-blue; administer oxygen (if necessary); initiate artificial ventilation; exchange blood (if necessary), Resuscitation measures.
For full prescribing information refer to the professional information approved by the medicines regulatory authority (07/2017). Trade marks are owned by or licensed to the GSK Group of companies.
HCR: GlaxoSmithKline South Africa (Pty) Ltd. (Co. Reg. No.: 1948/030135/07), 39 Hawkins Ave, Epping Industria 1, 7460. Marketed by Ethicare, a division of Pharmacare Limited. Healthcare Park, Woodlands Drive, Woodmead, 2191. ZAR-ISD-11-20-00001 07/2021

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