Isosorbide Mononitrate Tablets 20 mg

Summary of Product Characteristics Updated 01-Jan-2018 | Dexcel Pharma Ltd

▼ 1. Name of the medicinal product

Isosorbide Mononitrate Tablets 20 mg

▼ 2. Qualitative and quantitative composition

Each tablet contains Isosorbide Mononitrate, 20 mg.

Excipients with a known effect:

Each tablet contains approximately 109 mg of lactose and approximately 59 mg sucrose.

For the full list of excipients, see Section 6.1.

▼ 3. Pharmaceutical form

Tablets

White round tablets with an embossment "IM 20" on one side.

▼ 4. Clinical particulars

▼ 4.1 Therapeutic indications

Isosorbide Mononitrate Tablets is indicated for the prophylaxis of angina pectoris.

▼ 4.2 Posology and method of administration

Posology

Dosage should be reduced in patients with renal or hepatic impairment.

Adults

One tablet to be taken asymmetrically (to allow a nitrate low period) two or three times a day. Patients already accustomed to prophylactic nitrate therapy may normally be transferred directly to a therapeutic dose of isosorbide mononitrate. For patients not already receiving prophylactic nitrate therapy it is recommended that the initial dose be one tablet of Isosorbide Mononitrate Tablets 20 mg twice a day.

The maintenance dose in individual patients is usually between 20- 120 mg daily.

The lowest effective dose should be used.

Elderly

No evidence of a need for routine dosage adjustment in older people has been found, but special care may be needed in those with increased susceptibility to hypotension or marked hepatic or renal insufficiency.

Children

The safety and efficacy of Isosorbide Mononitrate Tablets 20 mg has yet to be established in children.

Treatment with Isosorbide Mononitrate Tablets, as with any other nitrates, should not be stopped suddenly. Both the dosage and frequency should be tapered gradually (see section 4.4)

Method of administration

It is recommended that the tablets should be swallowed whole with a drink of water.

▼ 4.3 Contraindications

Isosorbide Mononitrate Tablets 20 mg should not be used in cases of acute myocardial infarction with low filling pressures, acute circulatory failure (shock, vascular collapse), or very low blood pressure, hypertrophic obstructive cardiomyopathy (HOCM), constrictive pericarditis, cardiac tamponade, low cardiac filling pressures, aortic/mitral valve stenosis and diseases associated with a raised intra-cranial pressure e.g. following a head trauma and including cerebral haemorrhage.

This product should not be given to patients with a known hypersensitivity to isosorbide dinitrate or mononitrate, to other nitrates or to any of the excipients.

Isosorbide Mononitrate Tablets 20 mg should not be used in patients with marked anaemia, sever hypotension, closed angle glaucoma, toxic pulmonary oedema or hypovolaemia.

Phosphodiesterase Type 5 Inhibitors (e.g. sildenafil, tadalafil, vardenafil) have been shown to potentiate the hypotensive effects of nitrates and their co-administration with nitrates or nitric oxide donors is therefore contraindicated (see section 4.5).

Severe cerebrovascular insufficiency or hypotension are relative contraindications to the use of Isosorbide Mononitrate Tablets 20 mg.

▼ 4.4 Special warnings and precautions for use

Isosorbide Mononitrate Tablets 20 mg should be used with caution in patients who have a recent history of myocardial infarction, or who are suffering from closed-angle glaucoma, hypothyroidism, hypothermia, malnutrition and sever liver or renal disease.

Symptoms of circulatory collapse may arise after first dose in patients with labile circulation and in patients already taking ACE inhibitors.

This product may give rise to postural hypotension and syncope in some patients. Severe postural hypotension with light headedness and dizziness is frequently observed after the consumption of alcohol, therefore alcohol should be avoided during treatment. Hypotension induced by nitrates may be accompanied by paradoxical bradycardia and increased angina.

In the event of an acute angina attack, sublingual treatment such as a GTN spray or tablet should be used instead of isosorbide mononitrate tablets.

Isosorbide Mononitrate Tablets contain sucrose and lactose and therefore patients with rare hereditary problems of galactose or fructose intolerance, total lactase deficiency, sucrase-isomaltase insufficiency glucose-galactose malabsorption should not take this medicine.

If the tablets are not taken as indicated (see section 4.2) tolerance to the medication and cross-tolerance to other nitrates may occur. The lowest effective dose should be used.

Treatment with isosorbide mononitrate tablets, as with any other nitrate, should not be stopped suddenly. Both the dosage and frequency should be tapered gradually (see section 4.2).

▼ 4.5 Interaction with other medicinal products and other forms of interaction

Isosorbide mononitrate can act as a physiological antagonist to noradrenaline, acetylcholine, histamine and other agents.

Concurrent administration of drugs with blood pressure lowering properties, e.g, beta-blockers, calcium channel blockers, vasodilators, alprostadil, aldesleukin, angiotensin II receptor antagonist, ACE inhibitors etc. may potentiate the hypotensive effect of Isosorbide Mononitrate Tablets. This may also occur with neuroleptics and tricyclic antidepressants.

Alcohol can accentuate cerebral ischaemia associated with postural hypotension.

Any blood pressure lowering effect of Isosorbide Mononitrate Tablets will be increased if used together with phosphodiesterase type 5 inhibitors (e.g. sildenafil, tadalafil and verdenafil) which are used for erectile dysfunction (see special warnings and contraindications). This might lead to life threatening cardiovascular complications. Patients who are on Isosorbide Mononitrate Tablets therapy therefore must not use phosphodiesterase type-5 inhibitors.

Reports suggest that concomitant administration of Isosorbide Mononitrate Tablets may increase the blood level of dihydroergotamine and its hypertensive effect.

▼ 4.6 Fertility, pregnancy and lactation

The safety and efficacy of Isosorbide Mononitrate Tablets during pregnancy or lactation has not been established.

▼ 4.7 Effects on ability to drive and use machines

Dizziness, tiredness or blurred vision might occur at the start of treatment. The patients should therefore be advised that if affected, they should not drive or operate machinery. This effect may be increased by alcohol.

▼ 4.8 Undesirable effects

A very common (>10% of patients) adverse reaction to Isosorbide Mononitrate Tablets is throbbing headache. The

incidence of headache diminishes gradually or disappears after 1-3 weeks and optimum dosage of isosorbide mononitrate may be achieved.

At the At the start of therapy or when the dosage is increased, hypotension and/or light headedness in the upright position are commonly observed (i.e in 1-10% of patients). These symptoms may be associated with cutaneous vasodilatation with flushing, dizziness, drowsiness, reflex tachycardia and occasionally unexplained bradycardia and a feeling of weakness.

Infrequently (i.e. in less than 1% of patients) nausea, vomiting, flushing and allergic skin reaction (e.g. rash) may occur sometimes severely. In single cases exfoliative dermatitis may occur.

Severe hypotensive responses have been reported for organic nitrates and include nausea, vomiting, restlessness, pallor and excessive perspiration. Uncommonly collapse may occur (sometimes accompanied by bradyarrhythmia and syncope). Uncommonly severe hypotension may lead to enhanced angina symptoms.

Very rarely (i.e. in less than 0.01%) myalgia may occur.

A few reports of heartburn most likely due to a nitrate induced sphincter relaxation have been recorded.

Tachycardia and paroxysmal bradycardia have been reported.

Nitrate-induced pituitary apoplexy has been reported in patients with undiagnosed pituitary tumours.

Reporting suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medical product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

▼ 4.9 Overdose

Symptoms and signs:

Pulsing headache, hypotension, nausea, vomiting, flushing, cold perspiration, sweating, tachycardia, vertigo, restlessness, excitation, warm flushed skin, blurred vision and syncope. A rise in intracranial pressure with confusion and neurological deficits can sometimes occur. Methaemoglobinaemia (cyanosis, hypoxaemia, restlessness, respiratory depression, convulsions, cardiac arrhythmias, circulatory failure, raised intracranial pressure) occurs rarely.

Management:

Induction of emesis, consider oral activated charcoal if ingestion of a potentially toxic amount has occurred within 1 hour. Observe for at least 12 hours after the overdose. Monitor blood pressure and pulse. Correct hypotension by raising the foot of the bed and/or by expanding the intravascular volume. Other measures as indicated by the patient's clinical condition. If severe hypotension persists despite the above measures consider use of inotropes or intravenous administration of fluid.

If methaemoglobinaemia (symptoms or > 30% methaemoglobin), IV administration of methylene blue 1-2 mg/kg body weight. If therapy fails with second dose after 1 hour or contraindicated, consider red blood cell concentrates or exchange transfusion. In case of cerebral convulsions, diazepam or clonazepam IV, or if therapy fails, phenobarbital, phenytoin or propofol anaesthesia.

▼ 5. Pharmacological properties

▼ 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vasodilators used in cardiovascular disease (organic nitrates). ATC Code: C01D A.

The principal pharmacological action of isosorbide mononitrate, an active metabolite of isosorbide dinitrate, is relaxation of vascular smooth muscle, producing vasodilation of both arteries and veins with the latter effect predominating. The effect of the treatment is dependent on the dose. Low plasma concentrations lead to venous dilatation, resulting in peripheral pooling of blood, decreased venous return and reduction in left ventricular end-diastolic pressure (preload). High plasma concentrations also dilate the arteries reducing systemic vascular resistance and arterial pressure leading to a reduction in cardiac afterload. Isosorbide mononitrate may also have a direct dilatory effect on the coronary arteries. By reducing the end diastolic pressure and volume, the preparation lowers the intramural pressure, thereby leading to an improvement in the subendocardial blood flow.

The net effect when administering isosorbide mononitrate is therefore a reduced workload of the heart and an improved oxygen supply/demand balance in the myocardium.

▼ 5.2 Pharmacokinetic properties

Isosorbide-5-mononitrate is rapidly absorbed and peak plasma levels occur approx. 1 hour following oral dosing.

Isosorbide-5-mononitrate is completely bioavailable after oral doses and is not subjected to pre-systemic elimination processes.Isosorbide-5-mononitrate is eliminated from the plasma with half-life of about 5.1 hours. It is metabolized to Isosorbide-5MN-2-glucoronide, which has a half-life of approximately 2.5 hours. As well as being excreted unchanged in the urine.

After multiple oral dosing plasma concentrations are similar to those that can be predicted from single dose kinetic parameters.

▼ 5.3 Preclinical safety data

The accessible data indicate that isosorbide mononitrate has expected pharmacodynamic properties of an organic nitrate ester, has simple pharmacokinetic properties, and is devoid of toxic, mutagenic or oncogenic effects.

▼ 6. Pharmaceutical particulars

▼ 6.1 List of excipients

Lactose monohydrate, Compressible sugar, Sodium starch glycollate, Magnesium stearate, Silica colloidal anhydrous.

▼ 6.2 Incompatibilities

Not applicable.

▼ 6.3 Shelf life

5 years

▼ 6.4 Special precautions for storage

Store in a dry place, below 25° C.

▼ 6.5 Nature and contents of container

Aluminium foil/UPVC blister packs: 28, 50, 56, 60 or 100 tablets.

Recloseable polyethylene jars: 100, 500 tablets.

▼ 6.6 Special precautions for disposal and other handling

No specific statement.

▼ 7. Marketing authorisation holder

Dexcel-Pharma Ltd,

7 Sopwith Way, Drayton Fields,

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UK

▼ 8. Marketing authorisation number(s)

PL 14017/0011

▼ 9. Date of first authorisation/renewal of the authorisation

30 September 1996 / 28 May 2005

▼ 10. Date of revision of the text

22/12/2017

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