

FINAL PACKAGE INSERT: MONICOR 60 mg SR

SCHEDULING STATUS:

Ⓢ3

PROPRIETARY NAME AND DOSAGE FORM:

MONICOR 60 mg SR slow release tablets

COMPOSITION:

Active ingredients:

Each slow release tablet contains 60 mg isosorbide-5-mononitrate.

Inactive ingredients:

Carnauba wax, ferric oxide, hydroxypropylmethylcellulose, macrogol, magnesium stearate, silica anhydrous colloidal, stearic acid, titanium dioxide.

MONICOR 60 mg SR also contains lactose monohydrate. (see **WARNINGS** and **SPECIAL PRECAUTIONS**).

PHARMACOLOGICAL CLASSIFICATION:

A 7.1.4 Vasodilators – coronary and other medicines used in angina pectoris.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Isosorbide-5-mononitrate is an active metabolite of isosorbide dinitrate. It relaxes vascular smooth muscle, producing vasodilation of both the arteries and veins (predominantly in the veins). This effect is dose-dependent. 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-5-mononitrate may also have a direct dilatory effect on the coronary arteries. By reducing the end diastolic pressure and volume, isosorbide-5-mononitrate lowers the intramural pressure, thereby leading to an improvement in the subendocardial blood flow. The net effect is therefore a reduced workload of the heart and an improved oxygen supply/demand balance in the myocardium.

Pharmacokinetic properties:

Isosorbide-5-mononitrate is almost completely absorbed, though it does not undergo first pass metabolism in the liver, elimination takes place primarily in the liver by denitration and conjugation. The elimination half-life is about 5 hours, volume of distribution is 0,6 l/kg and total clearance is approximately 115 ml/minute. The metabolites of isosorbide-5-mononitrate are excreted mainly via the kidneys. Only about 2 % of the isosorbide-5-mononitrate dose ingested is excreted unchanged in the urine.

Impaired liver or kidney function does not have a major influence on the pharmacokinetics of isosorbide-5-mononitrate. **MONICOR 60 mg SR** is a slow release formulation of isosorbide-5-mononitrate. The active substance is released independently of pH over a 10 hour period. The absorption phase of **MONICOR 60 mg SR** is prolonged and the duration of effect is extended. After repeated per oral administration with 60 mg once daily, a maximal plasma concentration (of about 3000 nmol/l) is achieved after around four hours. The plasma concentration then steadily falls to around 500 nmol/l at the end of the dosage interval (which is twenty-four hours after dose intake). Absorption is not significantly affected

by food intake.

INDICATIONS:

MONICOR 60 mg SR is indicated for the prophylactic treatment of angina pectoris.

CONTRA INDICATIONS:

- Hypersensitivity to any of the ingredients
- Severe hypotension, hypovolaemia, marked anaemia, heart failure due to obstruction (including constrictive pericarditis), or raised intracranial pressure due to head trauma or cerebral haemorrhage.
- Patients with angle closure glaucoma as **MONICOR 60 mg SR** may increase intra-ocular pressure.
- Sildenafil and other phosphodiesterase type 5 inhibitors (PDE₅) must not be given with **MONICOR 60 mg SR** (see **INTERACTIONS**).

WARNINGS and SPECIAL PRECAUTIONS:

Caution should be observed in patients with severe cerebral arteriosclerosis and hypotension (see **CONTRA INDICATIONS**). **MONICOR 60 mg SR** tablets are not indicated for the relief of acute anginal attacks. Sublingual or buccal nitroglycerin tablets should be used in these situations (see **DOSAGE AND DIRECTIONS FOR USE**).

MONICOR 60 mg SR may increase intra-ocular pressure in patients with angle closure glaucoma, (see **CONTRA INDICATIONS**). It should be used with caution in patients with severely impaired renal or hepatic function, hypothyroidism, malnutrition or hypothermia.

MONICOR 60 mg SR contains lactose. Patients with rare hereditary problems or a history of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **MONICOR 60 mg SR**.

Effects on ability to drive and use machinery:

MONICOR 60 mg SR may cause drowsiness and impair your ability to drive and use machinery. Caution is advised while performing these tasks, especially if other blood pressure lowering medications are taken at the same time.

INTERACTIONS:

The hypotensive effects of **MONICOR 60 mg SR** may be enhanced by alcohol, and by vasodilators and other medicines with hypotensive actions.

Concomitant administration with sildenafil and other phosphodiesterase type 5 inhibitors (PDE₅) can potentiate the effect of **MONICOR 60 mg SR** with the potential result of serious adverse effects such as hypotension, syncope or myocardial infarction.

PREGNANCY AND LACTATION:

The safety of **MONICOR 60 mg SR** during pregnancy and lactation has not been established. It is not known whether **MONICOR 60 mg SR** is secreted in human milk.

DOSAGE AND DIRECTIONS FOR USE:

The recommended dosage is 60 mg daily (one tablet), in the morning.

This dosage may be increased to 120 mg (two tablets), once daily in the morning.

Treatment may be initiated with 30 mg (half a tablet) for the first two to four days, to minimize the possibility of headache. **MONICOR 60 mg SR** tablets may be broken in half, but should not be chewed or crushed and should be taken with half a glass of water.

MONICOR 60 mg SR may be used effectively in monotherapy as well as in combination with chronic beta-blocker therapy.

NOTE:

MONICOR 60 mg SR tablets are not indicated for the relief of acute anginal attacks.

Sublingual or buccal nitroglycerin tablets should be used in these situations (see **WARNINGS and SPECIAL PRECAUTIONS**).

Tablets are divisible, but should not be chewed or crushed.

SIDE EFFECTS:

System Organ Class	Frequency	Undesirable effects
<i>Blood and the lymphatic system disorders:</i>	<i>Less frequent:</i>	Methaemoglobinaemia
<i>Nervous system disorders:</i>	<i>Frequent:</i>	Dizziness, restlessness
<i>Eye disorders:</i>	<i>Less frequent:</i>	Blurred vision
<i>Cardiac disorders:</i>	<i>Frequent:</i>	Tachycardia
	<i>Less frequent:</i>	Bradycardia
<i>Vascular disorders:</i>	<i>Frequent:</i>	Hypotension, syncope, headache
	<i>Less frequent:</i>	Severe or prolonged headache

<i>Respiratory, thoracic and mediastinal disorders:</i>	<i>Less frequent:</i>	Impairment of respiration
<i>Gastro-intestinal disorders:</i>	<i>Frequent:</i> <i>Less frequent:</i>	Nausea Vomiting, diarrhoea
<i>Skin and subcutaneous tissue disorders:</i>	<i>Frequent:</i> <i>Less frequent:</i>	Flushing of the face Cyanosis, rash, pruritus
<i>Musculoskeletal, connective tissue and bone disorders:</i>	<i>Less frequent:</i>	Myalgia

Note that the following side effects generally disappear with continued treatment:

- headache which occurs when treatment has just been started
- hypotension which may manifest as dizziness and nausea.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of overdose are pulsing headache, excitation, flushing, cold perspiration, nausea, vomiting, vertigo, syncope, tachycardia and hypotension. Treatment should include induction of emesis and the use of activated charcoal. If the patient presents with pronounced hypotension, they should be placed in the supine position with legs raised and if necessary intravenous fluid can be administered.

Treatment is symptomatic and supportive.

IDENTIFICATION:

Cream oval tablets, half-scored on both sides, marked with “60” on one side.

PRESENTATION:

White polypropylene securitainers containing 30 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25°C. Keep well closed. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

RSA S3 37/ 7.1.4/ 0340 NAM NS2 08/ 7.1.4/ 0181

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF
REGISTRATION:**

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