APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

MONICOR 60 mg SR slow release film coated tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

MONICOR 60 mg SR also contains sugar (lactose monohydrate 38,17 mg per tablet), see section 4.4.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Slow release film coated tablets.

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

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 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 section 4.4).

Special populations

Elderly

There is no evidence for routine dosage adjustment in the elderly, however, special care may be needed in those with increased susceptibility to hypotension or marked hepatic or renal insufficiency.

Paediatric population

The safety and efficacy of this medicine in children has not been established.

Method of administration

Tablets are divisible.

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.

Missed dose:

Doctors should advise patients who forget to take MONICOR 60 mg SR to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- hypersensitivity to isosorbide-5-mononitrate or to any of the ingredients of MONICOR 60 mg SR (see section 6.1)
- severe hypotension, hypovolaemia, marked anaemia, heart failure due to obstruction (including constrictive pericarditis, aortic or mitral stenosis), cardiac tamponade, 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 (PDE_5) must not be given with MONICOR 60 mg SR (see section 4.5).

Severe cerebrovascular insufficiency or hypotension are relative contraindications to the use of MONICOR 60 mg SR.

4.4 Special warnings and precautions for use

The lowest effective dose should be used.

There is a risk of tolerance developing to modified release preparations. In such patients intermittent therapy may be more appropriate.

Therapy should not be discontinued suddenly. Both dosage and frequency should be tapered gradually (see section 4.2).

Symptoms of circulatory collapse may arise after the first dose, particularly in patients with labile circulation.

Hypotension induced by nitrates may be accompanied by paradoxical bradycardia and increased angina.

Severe postural hypotension with light-headedness and dizziness is frequently observed after the consumption of alcohol.

The administration of isosorbide mononitrate causes a decrease of effective renal plasma flow (eRPF) in cirrhotic patients and should be used with caution.

Caution should be observed in patients with severe cerebral arteriosclerosis and hypotension.

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 section 4.2).

MONICOR 60 mg SR may increase intra-ocular pressure in patients with angle closure glaucoma, (see section 4.3).

MONICOR 60 mg SR should be used with caution in patients who have a recent history of myocardial infarction and in patients suffering from hypothyroidism, hypothermia, malnutrition, and severely impaired renal or hepatic function. Oral nitrates should also be used with caution in patients with angina due to other causes, or pre-existing hyperdynamic conditions.

Since oral nitrates can cause venous dilatation, they should not be used in patients with increased intracranial pressure.

Excipients

MONICOR 60 mg SR contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

The hypotensive effects of MONICOR 60 mg SR may be enhanced by alcohol, and by vasodilators and other medicines with hypotensive actions (antihypertensives, calcium channel blockers, and diuretics).

Concomitant administration with sildenafil and other phosphodiesterase type 5 inhibitors (PDE_5) can potentiate the effect of MONICOR 60 mg SR leading to life threatening cardiovascular complications such as hypotension, syncope or myocardial infarction.

Concomitant administration of MONICOR 60 mg SR may increase the blood level of dihydroergotamine and its hypertensive effect.

Alcohol can attenuate cerebral ischaemia associated with postural hypotension.

MONICOR 60 mg SR can act as a physiological antagonist to noradrenaline, acetylcholine and histamine.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of MONICOR 60 mg SR during pregnancy has not been established.

Breastfeeding

The safety of MONICOR 60 mg SR during lactation has not been established.

It is not known whether MONICOR 60 mg SR is secreted in human milk.

Fertility

There is no data on fertility with MONICOR 60 mg SR.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

a. Summary of the safety profile

Most of the adverse reactions are pharmacodynamically mediated and dose dependent. Headache may occur when treatment is initiated but usually disappears after 1-2 weeks of treatment. The dose can be titrated to minimize the possibility of headache, by initiating treatment with 30mg. Hypotension which may manifest as dizziness and nausea with syncope in isolated cases, has occasionally been reported.
These symptoms generally disappear during continued treatment.

b. Tabulated list of adverse effects

System Organ Class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Less frequent	Methaemoglobinaemia
Immune system disorders	Frequency unknown	Allergic dermatitis, exfoliative dermatitis
Nervous system disorders	Frequent Frequency unknown	Dizziness, restlessness Somnolence, pituitary haemorrhage
Eye disorders	Less frequent	Blurred vision

Cardiac disorders	Frequent Less frequent	Tachycardia Bradycardia
Vascular disorders	Frequent Less frequent Frequency unknown	Hypotension, syncope, headache Severe or prolonged headache Flushing, orthostatic hypotension, pallor, circulatory collapse (sometimes accompanied by brady-dysrhythmia, bradycardia and syncope), severe hypotension may lead to enhanced angina pectoris symptoms
Respiratory, thoracic and mediastinal disorders	Less frequent Frequency unknown	Impairment of respiration Hypoxia
Gastrointestinal disorders	Frequent Less frequent	Nausea Vomiting, diarrhoea
Skin and subcutaneous tissue disorders	Frequent Less frequent	Flushing of the face Cyanosis, rash, pruritus
Musculoskeletal, connective tissue and bone disorders	Less frequent	Myalgia
General disorders and administrative site conditions	Frequency unknown	Asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org)

found on SAHPRA website.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

Symptoms of overdosage are pulsing headache, excitation, flushing, cold perspiration, nausea, vomiting, vertigo, syncope, tachycardia and hypotension.

A rise in intracranial pressure with confusion and neurological deficits can sometimes occur.

Methaemoglobinaemia (cyanosis, hypoxaemia, change in mental status, respiratory depression, convulsions, cardiac dysrhythmias, circulatory failure and raised intracranial pressure) occurs rarely.

Management of overdose:

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.

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.

If methaemoglobinaemia occurs seek expert advice. Treat with supplemental oxygen and methylene blue.

In cases not responding to methylene blue or where methylene blue is contraindicated consider exchange transfusion or red blood cell concentrates. In case of cerebral convulsions, consider diazepam or
clonazepam IV or, if therapy fails, phenobarbital, phenytoin or propofol anaesthesia. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Organic nitrates

ATC code: C01DA14

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

Mechanism of action

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.

5.2 Pharmacokinetic properties

Absorption:

Isosorbide-5-mononitrate is almost completely absorbed. 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 a slow release formulation of isosorbide-5-mononitrate is prolonged and the duration of effect is extended. Absorption is not significantly affected by food intake.

Distribution:

The extent of bioavailability of the medicine is about 90 % compared to immediate release tablets.

The tablets are divisible. Volume of distribution is 0,6 L/kg and total clearance is approximately 115 mL/minute.

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).

Biotransformation:

Isosorbide-5-mononitrate does not undergo first pass metabolism in the liver.

Elimination:

Elimination takes place primarily in the liver by denitration and conjugation. Impaired liver or kidney function does not have a major influence on the pharmacokinetics of isosorbide-5-mononitrate. The elimination half-life is about 5 hours. 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.
About 96 % of an administered dose of isosorbide mononitrate is excreted in urine and about 1 % in faeces within 5 days; most excretion (about 93 %) occurs within 48 hours.

In placebo-controlled studies, isosorbide mononitrate once daily has been shown to effectively control angina pectoris both in terms of exercise capacity and symptoms, and also in reducing signs of myocardial ischaemia. The duration of the effect is at least 12 hours, at this point the plasma concentration is at the same level as at around 1 hour after dose intake (around 1300 nmol/L).

The medicine is effective as monotherapy, as well as in combination with chronic β-blocker therapy.

The clinical effects of nitrates may be attenuated during repeated administration owing to high and/or even plasma levels. This can be avoided by allowing low plasma levels for a certain period of the dosage interval. The medicine, when administered once daily in the morning, produces a plasma profile of high levels during the day and low levels during the night. With 60 mg or 120 mg once daily, no development of tolerance with respect to

antianginal effect has been observed. Rebound phenomenon between doses as described with intermittent nitrate patch therapy has not been seen with the medicine.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Carnauba wax

Hypromellose

Lactose monohydrate

Magnesium stearate

Silica colloidal anhydrous

Stearic acid

Film coating:

Ferric oxide (Yellow iron oxide)

Hypromellose

Macrogol

Magnesium stearate

Talc

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 °C.

Store in original container.

Protect from light.

Keep the container tightly closed.

6.5 Nature and contents of container

White polypropylene securitainers containing 30 tablets.

MONICOR 60 mg SR is also packed in hard silver-coloured aluminium foil/ clear transparent PVC/ PVDC/ film blister strips, available in a pack size of 30 tablets inside an outer carton.

*Not all pack types may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER(S)

A37/7.1.4/0340

9. DATE OF FIRST AUTHORISATION

Date of registration: 06 October 2006

10. DATE OF REVISION OF THE TEXT

17 February 2026

NAMIBIA:

NS2 08/7.1.4/0181