Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sormon 60 mg Prolonged-release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains 60 mg isosorbide mononitrate.

Excipient with known effect:
Each tablet contains 0.8 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet (tablet).

Pale yellow, elliptical, film-coated tablets (13.1 x 7.1 mm), embossed with 'IM' breakline '60' on one side and breakline on the reverse.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prophylactic treatment of angina pectoris.

4.2 Posology and method of administration

Posology
Sormon are intended for prophylactic therapy. Dosage should be adjusted individually and monitored according to clinical response.

Adults
When initiating therapy in new patients, the dose can be titrated to reduce the frequency of headache by administering 30 mg (half a tablet) for the first 2-4 days.

The usual dosage is 60 mg to be taken in the morning. When necessary, the dose may be increased to 120 mg daily to be taken in the morning.

There is a risk of tolerance developing when nitrate therapy is given. For this reason, it is important that *Sormon* are taken once a day to achieve an interval with low nitrate concentration, thereby reducing the risk of tolerance development.

When necessary the product may be used in combination with beta-adrenoceptor blockers and calcium antagonists.

Paediatric population
The safety and efficacy of *Sormon* in children has not been established.

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

Method of administration

For oral use.

The tablet is divisible; however, whether administered whole or divided, it is not to be chewed or crushed and should be swallowed with half a glass of liquid.

4.3 Contraindications

Hypersensitivity to the active substance, other nitrates, or to any of the excipients listed in section 6.1.

Cardiogenic shock, unless a sufficiently high left ventricular enddiastolic pressure is ensured either by intra-aortic counterpulsation or positive inotropic drugs.

Acute circulatory collapse (shock, vascular failure).

Constrictive pericarditis, pericardial tamponade, and restrictive cardiomyopathy.

Concomitant treatment with preparations containing phosphodiesterase type-5 inhibitors (e.g. sildenafil).

Severe cerebrovascular insufficiency (e.g. trauma or haemorrhage) or hypotension are relative contraindications to the use of *Sormon*.

4.4 Special warnings and precautions for use

Sormon is indicated for the prophylaxis of angina and not for the treatment of acute angina attacks. In the event of an acute attack, oral or sublingual glyceryl trinitrate tablets should be used.

The actions of oral nitrate revolve around vascular smooth muscle relaxation which in turn causes a reduction in primarily preload but also afterload. As a result, cardiac workload is reduced. Such a response, however, may not be beneficial when treating angina associated with hypertrophic cardiomyopathy due to any cause, restrictive cardiomyopathy or low output states secondary to aortic or mitral stenosis, hypoxemia, hypovolaemia or cardiogenic shock. The use of oral nitrates in such conditions may precipitate acute syncope and possible vascular collapse.
Vascular dilatation may precipitate venous pooling with diminished cardiac return, hypotension and reflex tachycardia. For this reason, oral nitrates should not be used in patients susceptible to the effects of hypotension such as those with pre-existing hypotension, shock, vascular collapse or significant cerebrovascular disease, significant anaemia or hypothyroidism. Similarly, oral nitrates should be used with caution for patients with angina secondary to other causes or with pre-existing hyperdynamic states (e.g. malnutrition, hypothermia, severe hepatic or renal impairment). Because oral nitrates produce venous dilatation they should not be used for patients with raised intra-cranial pressure.

This medicine contains Lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interactions

Concurrent administration of drugs with blood pressure lowering properties; e.g. beta-blockers, calcium channel blockers, vasodilators (including neuroleptics and tricyclic antidepressants), alprostadil, aldesleukin, antihypertensives, diuretics, angiotensin II receptor antagonists etc and/or alcohol may potentiate the hypotensive effect of isosorbide mononitrate.
Any blood pressure lowering effect of isosorbide mononitrate will be increased if used together with phosphodiesterase type-5 inhibitors (e.g. sildenafil), which are used for erectile dysfunction. This might lead to life threatening cardiovascular complications. Patients who are on isosorbide mononitrate therapy therefore must not use phosphodiesterase type-5 inhibitors (see section 4.3).
Reports suggest that concomitant administration of isosorbide mononitrate may increase the blood level of dihydroergotamine and its hypertensive effect.
There is no evidence of interaction with food.

4.6 Fertility, pregnancy and lactation

The safety and efficacy of isosorbide mononitrate during pregnancy or lactation has not been established.

4.7 Effects on ability to drive and use machines

Isosorbide mononitrate can occasionally cause a drop in blood pressure, which may cause dizziness. This is especially true on initiation of treatment or dose increase. If affected, the patient should not drive or operate machinery.

4.8 Undesirable effects

The majority of side effects are pharmacologically mediated and dose dependent. Headache occurs in approximately 25% of patients at the start of treatment and can be attributed to the vasodilatation effect of the preparation and usually disappears within a week or so.
Hypotension (with dizziness, reflex tachycardia, fainting and nausea) has been reported but resolves with continued treatment.

The following adverse reactions are classified by system organ class and ranked under heading of frequency using the following convention:

- Very common (³1/10)
- Common (³1/100 to <1/10)
- Uncommon (³1/1,000 to <1/100)
- Rare (³1/10,000 to <1/1,000)
- Very rare (<1/10,000)
- Not known (cannot be estimated from the available data)

Nervous system disorders
Very common: headache
Common: dizziness
Rare: fainting
Not known: somnolence

Cardiac disorders
Common: tachycardia
Not known: (aggravation of) angina pectoris, bradyarrhythmia, orthostatic hypotension

Vascular disorders
Common: hypotension
Uncommon: flushing
Not known: circulatory collapse

Gastrointestinal disorders
Common: nausea
Uncommon: vomiting, diarrhoea.

Skin and subcutaneous tissue disorders
Rare: rash, pruritus
Not known: exfoliative dermatitis, allergic skin reactions

Musculoskeletal and connective tissue disorders
Very rare: myalgia

General disorders and administration site conditions
Common: fatigue

The frequency of headache may be reduced by starting treatment at 30 mg for the first 2-4 days and gradually titrating the dose upwards as required (see section 4.2).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971 FREE; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms of intoxication
(Orthostatic) hypotension, reflex tachycardia and headache, fatigue, dizziness, vertigo, flushing, nausea, vomiting, and diarrhoea may occur. After high doses methaemoglobinaemia, cyanosis, dyspnoea, and tachypnoea may occur based on the nitrite ion.

Treatment
If necessary induction of emesis, activated charcoal and stomach aspiration. In the presence of clinically significant hypotension administration of intravenous fluids should be considered. (In cases of cyanosis as a result of methaemoglobinaemia, methyl thionine 1-2 mg/Kg, slow intravenous delivery).
Treat symptomatically.
In case of pronounced hypotension, the patient should be placed in a reclining position with the legs elevated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vasodilators used in cardiac diseases, organic nitrates, ATC code: C01DA14

Mechanism of action
Vessel dilating agent for prophylaxis of angina pectoris.

This is a prolonged-release preparation of isosorbide-5-mononitrate, which is an active metabolite of isosorbide dinitrate. Nitro compounds cause dose-dependent relaxation of smooth muscle tissue. The therapeutic effect is dependent on the dose and individual sensitivity.

Low doses produce dilatation of the veins and reduced venous return to the heart (reduced preload). High doses also produce arterial dilatation and reduced vessel resistance (reduced afterload). Isosorbide mononitrate reduces the work load for the heart by venous and arterial dilatation and may have a direct dilatory effect on the coronary arteries. By reducing the end diastolic pressure and volume, it lowers intramural pressure, thus improving subendocardial blood flow. The net effect of Isosorbide mononitrate is a reduced workload for the heart and better oxygenation of the myocardium.

Sormon is intended for use in the prophylactic treatment of angina pectoris. The duration of effect measured by stress testing is at least 12 hours. At this point in time the plasma concentration is at the same level as 1-2 hours after taking the tablet (ca 1300 nmol/litre).

Continuous treatment with nitro compounds is associated with the development of tolerance which varies on an individual basis. For this reason, the tablets should be taken once a day to obtain an interval with low nitrate concentration.

Isosorbide mononitrate consists of an insoluble skeleton that most often decomposes due to/via intestinal peristalsis. The tablet can thus appear to be completely intact while the active substance is dissolved during passage through the gastrointestinal tract.

5.2 Pharmacokinetic properties

Absorption
The drug starts to take effect within one hour. The biological availability of prolonged-release tablets is approx. 90%. Absorption is not affected by simultaneous food intake. Isosorbide mononitrate prolonged-release tablets produce a gradual and pH-independent release of the active substance which ceases after approx. 10 hours. After repeated oral administration with 60 mg once daily, maximal plasma levels (approx. 3000 nmol/litre) are attained after about 4 hours.
The plasma concentration then diminishes and at the end of the dosage interval, it falls below 500 nmol/litre (24 hours after a dose).

Distribution
The distribution volume for Isosorbide mononitrate is approx. 0.6 litre/kg and the clearance is 115 ml/minute.

Biotransformation and elimination
Elimination mainly occurs by way of denitration and conjugation in the liver into inactive metabolites. The metabolites are mainly excreted by way of the kidneys. Only about 2% of an administered dose is excreted intact via the kidneys.

Hepatic and renal impairment
Impaired liver or kidney function will not affect the clinical effect.

5.3 Preclinical safety data

No information of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core
Cellulose, microcrystalline
Kaolin, heavy
Magnesium stearate
Silica, colloidal anhydrous
Paraffin wax, synthetic
Paraffin wax, hard
Coat
Hypromellose
Titanium dioxide (E171)
Lactose monohydrate
Macrogol
Iron oxide, yellow (E172)
Iron oxide, black (E172)
Iron oxide, red (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVdC, clear, aluminium foil blister.
Polypropylene containers with polyethylene caps (with optional polyethylene ullage filler).

Pack sizes: 7, 14, 28, 30, 60, 90, 98, 100, 250 tablets and 100 x 1 tablets (unit dose).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

McDermott Laboratories Ltd t/a Gerard Laboratories
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0577/202/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 23 October 2008

10 DATE OF REVISION OF THE TEXT

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