Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Slomon SR

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sustained release capsule contains 60 mg isosorbide mononitrate.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Sustained Release Capsules.

Each size 1 capsule contains spherical off-white microgranules.
The capsule shell has an opaque white cap and body.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the prophylaxis of angina pectoris and as an adjunct for the treatment of chronic heart failure.

4.2 Posology and method of adminstration

Dosage Recommendations:

Capsules may be taken with or without food, and should be swallowed whole and not chewed.

Prophylaxis of Angina

Adults: One capsule per day.

Children: Safety and efficacy in children has not been established.

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

Congestive Heart Failure

Adults: 60 mg every twelve hours. Slomon SR capsules can be used in addition to first-line diuretic therapy.

Children: Safety and efficacy in children has not been established.

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

4.3 Contraindications

This product should not be given to patients with a known sensitivity to nitrates.

Isosorbide mononitrate should not be used in patients with acute myocardial infarction with low filling pressure, marked anaemia, head trauma, cerebral haemorrhage, severe hypotension or hypovolaemia.

The co-administration of isosorbide mononitrate with sildenafil is contra-indicated; it has been shown that the hypotensive effects of nitrates are potentiated by sildenafil, which is consistent with the known effects of sildenafil on the nitric oxide / cyclic guanosine monophosphate pathway.

4.4 Special warnings and precautions for use

Isosorbide mononitrate should be used with caution in patients who are predisposed to closed angle glaucoma.

Isosorbide mononitrate should be used with caution in patients suffering from hypothyroidism, hypothermia, malnutrition, severe liver or renal disease.

Slomon SR capsules are not indicated for relief of acute angina attacks; in the event of an acute attack, sublingual or buccal glyceryl trinitrate tablets / sprays should be used.

Isosorbide mononitrate should not be co-administered with sildenafil. As a result of its vasodilator properties, sildenafil can potentiate the hypotensive effects of nitrates.

4.5 Interaction with other medicinal products and other forms of interaction

Some of the effects of alcohol may be potentiated by this agent.

Vasodilators, antihypertensives and diuretics may potentiate the hypotension caused by nitrates particularly in the elderly.

Sildenafil has been shown to potentiate the hypotensive effects of nitrates and therefore, it should not be administered in combination with isosorbide mononitrate.

There is no evidence of interaction with food.

4.6 Pregnancy and lactation

This product should not be used during pregnancy or lactation unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

Since postural hypotension with symptoms such as dizziness has been reported, patients should be advised to be careful when driving or operating machinery if they suffer from these symptoms.

4.8 Undesirable effects

Side effects including cutaneous vasodilation, postural hypotension and dry skin rashes may occur occasionally. Headache may occur at the onset of treatment but may be minimised by commencing with low doses and gradually increasing the dose.

Using the recommended dosage schedules there is no evidence of development of nitrate tolerance.

4.9 Overdose

Treatment should be symptomatic. The main symptom is likely to be hypotension.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Nitrate compounds relax smooth muscle causing dilatation of the veins and arteries, and to a lesser extent of the arterioles. The result is a very marked reduction of preload, accompanied by lowering of right heart pressures and left ventricular and diastolic pressure.

The dimensions of the right and left ventricles and ejection volumes are reduced but the reflex increase of heart rate prevents any reductions of cardiac output. Myocardial oxygen consumption may thus fall by more than 50 % in parallel with the reduction of left ventricular preload. At higher doses, afterload is also decreased by arterial and arteriolar dilation; this also helps to improve cardiac function.

Nitrate compounds exert a dilatory and antispasmodic effect on the coronary vessels; they are effective against both spontaneous and induced spasms.

5.2 Pharmacokinetic properties

In man, isosorbide mononitrate is absorbed completely and rapidly following oral administration.

Isosorbide mononitrate is not subject to the "hepatic first-pass" effect, and provides a low degree of inter-individual variation of blood levels.

Slomon SR capsules have all the pharmacokinetic characteristics of a true sustained-release dosage form. Compared with an immediate-release dosage form, the peak plasma concentration obtained is lower and occurs later, while the apparent elimination half-life is unchanged; there is less fluctuation between C_{max} and C_{min}, whereas, bioavailability is equivalent to an immediate-release formulation.

The slow continuous diffusion of the active ingredient from the sustained-release microgranules makes it possible, at steady state, to maintain plasma concentrations above the putative effective level of 100 ng/ml for a period of 20 hours for the 60 mg capsules.

5.3 Preclinical safety data

Isosorbide mononitrate produces very few toxic effects and is less toxic than isosorbide dinitrate. After chronic administration at high doses (60 mg/kg), signs of toxicity have been detected in canine liver and kidneys. Tests conducted have shown no evidence of a teratogenic or mutagenic potential. The sustained-release microgranules in Slomon SR capsules have proven to be less toxic after single doses than isosorbide mononitrate alone.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Sucrose

<u>For Microgranule Coating:</u>
Lactose monohydrate
Eudragit L100
Eudragit RS 100
Shellac (E 904)

Talc

For Capsule Shell:
Gelatin
Titanium dioxide (E 171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The capsules are enclosed in blisters composed of 250µm PVC film / 20µm aluminium foil.

The blisters are packed into folded printed cardboard cartons with a patient information leaflet.
Packs contain 8 (sample packs only), 28, 30, 56, 0r 60 sustained release capsules.

6.6 Instructions for use and handling

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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Highfield
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8 MARKETING AUTHORISATION NUMBER

PA 743/4/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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