Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sustac Tablets 6.4mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains glyceryl trinitrate 6.4mg as Diluted Nitroglycerin.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Modified-release tablet.

Round, biconvex, pink tablets with surface speckling, embossed with a 'P' in a hexagon on one surface.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the prophylaxis of angina pectoris.

4.2 Posology and method of administration

Oral.

Adults and Elderly Patients:

Sustac Tablets must be swallowed whole, not chewed. Sustac Tablets are not for sublingual administration. Dosage should be tailored to the requirements of the individual patient. The usual dose is 1 or 2 tablets of either strength (2.6 or 6.4mg) taken two or three times daily.

Suggested initial doses are:

Mild angina:	One 2.6mg tablet three times daily.
Moderate angina:	One 6.4mg tablet two or three times daily.
Severe angina:	One or two 6.4mg tablets three times daily.

Children:

Not recommended.

4.3 Contraindications

1. Use in patients with a known sensitivity to the nitrates.

2. Use in patients with severe anaemia, head trauma, cerebral haemorrhage or incipient glaucoma.

Inhibitors of cGMP specific phosphodiesterase type 5 (PDE5), such as sildenafil, vardenafil and tadalafil have been shown to potentiate the hypotensive effects of nitrates, and their co-administration with nitrates or nitric oxide donors is therefore contrainidicated.

4.4 Special warnings and precautions for use

This product should be used with caution in patients who are predisposed to closed-angle glaucoma.

As with other drugs for the treatment of angina pectoris, abrupt discontinuation of therapy may lead to exacerbation of symptoms. When discontinuing long term treatment, the dosage should be reduced gradually over several days, and the patient carefully monitored.

4.5 Interaction with other medicinal products and other forms of interaction

Sustac dilates peripheral blood vessels and may increase the antihypertensive properties of vasodilators, calcium antagonists, tricyclic antidepressants and alcohol.

In common with other nitric oxide donors, Sustac should not be co-administered with inhibitors of cGMP specific phosphodiesterase type 5 (PDE5), such as sildenafil, vardenafil and tadalafil, as a significant fall in blood pressure may result.

4.6 Pregnancy and lactation

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

4.7 Effects on ability to drive and use machines

Side effects such as headache may affect the ability to drive and use machines. Patients should not drive if severely affected.

4.8 Undesirable effects

Headache may occur at the onset of treatment but will usually subside after a few days. If the headache persists dosage should be decreased. Other side effects include tachycardia, postural hypotension and syncope, cyanosis and methaemoglobinaemia.

4.9 Overdose

In the event of accidental or deliberate overdosage toxic effects of glyceryl trinitrate include vomiting, restlessness, cyanosis, methaemoglobinaemia, tachycardia and syncope. Patients should receive gastric aspiration and lavage and be given respiratory and circulatory support. The physician should be aware that tablets in the intestine will release their content over several hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Glyceryl trinitrate relaxes smooth muscle including vascular muscle. In its action on vascular muscle vasodilation predominates over dilatation of the arterioles resulting in a reduction in preload and a smaller or less important reduction in afterload with a consequent reduction in the primary determinants of myocardial oxygen demand. Glyceryl trinitrate also improves regional coronary blood flow to ischaemic areas and this may contribute to the pain relief obtained on an acute attack (Martindale).

5.2 Pharmacokinetic properties

Following oral administration glyceryl trinitrate is well absorbed and rapidly metabolised to glyceryl 1,2 dinitrate and glyceryl 1,3 dinitrate. Although less potent the metabolites probably provide the predominant pharmacological effect. Sustac is formulated as a sustained release tablet and studies with Sustac 2.6mg and 6.4mg demonstrate a T_{max} for both metabolites of approx. 1 hr and an apparent $T_{½}$ of approx 2 hrs. There is evidence of activity extending over 6 hours or more.

5.3 Preclinical safety data

Glyceryl trinitrate is virtually free of toxicological effects unrelated to its action on the cardiovascular system. There are no reports of teratogenic or mutagenic effects. Carcinogenicity tests have demonstrated increased hepatocellular carcinoma and interstitial cell tumours in a 2-year study at a dose of 388 mg/kg/day. These effects were absent at 38 mg/kg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Compressible Sugar – contains invert sugar
Erythrosine (E127)
Magnesium Stearate
Ethylcellulose
Castor Oil
Shellac
Lactose
Sucrose
Corn Starch
Talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

White or grey polypropylene Securitainers with white or grey polythene caps containing 30, 60, 90, 120 or 180 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 1161/006/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last authorisation: 01 April 2005

10 DATE OF REVISION OF THE TEXT

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