SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Glyceryl Trinitrate Spray 400 micrograms/metered dose, sublingual spray.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient
Glyceryl Trinitrate: 400 micrograms/metered dose

Excipients with known effect:
This product contains small amounts of ethanol (alcohol) less than 100mg per spray.

For the full list of excipients, see Section 6.1

3 PHARMACEUTICAL FORM

Metered dose oromucosal (sublingual) spray solution
Small aerosol canister.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of acute angina pectoris.
Prevention of inducible angina (e.g. physical effort, emotional stress, exposure to cold).

Route of administration
Oromucosal (Sublingual)

4.2 Posology and method of administration
Oromucosal dosage.

Before using Glyceryl Trinitrate Spray for the first time, the patient should check that the spray is working by pressing the pump button a few times until it produces a fine mist of liquid. The patient should practice aiming the spray onto a tissue or similar item so that they will be able to aim it correctly under the tongue when they need to use it. If the patient does not need to use Glyceryl Trinitrate Spray very often, the spray should be checked regularly to see that it still works properly.

Adults including the Elderly
At the onset of an attack: one or two metered doses (400 to 800 micrograms glycercylic trinitrate) to be sprayed under the tongue for the relief of anginal pain while the breath is held. No more than three doses are recommended at any one time.

For the prevention of inducible angina (e.g. physical effort, emotional stress, exposure to cold) one or two 400 microgram metered doses sprayed under the tongue within 2-3 minutes of the event starting.

Children
Glyceryl Trinitrate Spray is not recommended for children. Administration
During application the patient should rest, ideally in the sitting position. The canister should be held vertically with the valve head uppermost and the spray orifice as close to the mouth as possible. The dose should be sprayed under the tongue and the mouth should be closed immediately after each dose. The spray should not be inhaled. Patients should be instructed to familiarise themselves with the position of the spray orifice, which can be identified by the finger rest on top of the valve, in order to facilitate orientation for the administration at night.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Severe hypotension (systolic blood pressure lower than 90mm Hg).

Hypotensive shock, severe anaemia, constrictive pericarditis, extreme bradycardia, Glucose-6-phosphate-Dehydrogenase-deficiency, cerebral haemorrhage and brain trauma, aortic and/or mitral stenosis and angina caused by hypertrophic obstructive cardiomyopathy.

Circulatory collapse, cardiogenic shock and toxic pulmonary oedema.

Concomitant use with phosphodiesterase inhibitors such as Sildenafil, Tadalafil or Vardenafil.
Concomitant use with the soluble guanylate cyclase stimulator riociguat (see section 4.5).

4.4 Special warnings and precautions for use

Tolerance to this drug and cross-tolerance to other nitrates may occur.

Glyceryl Trinitrate Spray should be administered with particular caution in:
- pericardial tamponade
- low filling pressures (e.g. acute myocardial infarction, left ventricular failure)
- tendency to dysregulation of orthostatic blood pressure
- diseases accompanied by an increase in intracranial pressure (so far further pressure increase has been observed solely in high doses of glycercyl trinitrate).

Alcohol should be avoided because of the hypotensive effect.

Medical controls of the intraocular pressure of glaucoma-patients are advisable. Particular caution should also be exercised when using Glyceryl Trinitrate Spray in patients with volume depletion from diuretic therapy, severe hepatic or renal impairment and hypothyroidism.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol may potentiate the hypotensive effect.

Vasodilators, antihypertensives, β-blockers, calcium antagonists, neuroleptics, tricyclic antidepressants and diuretics can increase nitrate induced hypotension.

The hypotensive effects of nitrates are potentiated by the concurrent administration of phosphodiesterase inhibitors, such as Sildenafil, Tadalafil or Vardenafil.

The use of a soluble guanylate cyclase stimulator such as riociguat is contraindicated (see section 4.3) since concomitant use can cause hypotension.

The bioavailability of dihydroergotamine may be increased by concomitant use of Glyceryl Trinitrate Spray, which can result in vasoconstriction since dihydroergotamine can antagonise the effects of glycercyl trinitrate.

The concomitant administration of Glyceryl Trinitrate Spray and heparin can reduce the antithrombotic effect of heparin. Regular monitoring of coagulation parameters and adjustments of the heparin dose may be necessary.

In patients pretreated with organic nitrates a higher dose of glycercyl trinitrate may be necessary to achieve the desired haemodynamic effect.
4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of glyceryl trinitrate in human pregnancy, especially during the first trimester has not been established.

Breastfeeding
It is not known whether glyceryl trinitrate is excreted into human breast milk. Glyceryl Trinitrate Spray should only be used after weighing the benefit for the mother against possible risks for the child. Nursing should be discontinued during treatment with this product.

4.7 Effects on Ability to Drive and Use Machines
The ability to react may be diminished because of the side effects or interactions due to the nitrates. This effect is potentiated by alcohol consumption. Therefore, driving and/or using machines should be avoided during treatment with Glyceryl Trinitrate Spray.

4.8 Undesirable effects
The following adverse reactions have been reported:

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Very Common (≥1/10)</th>
<th>Common (≥1/100 to &lt; 1/10)</th>
<th>Uncommon (≥ 1,000 to &lt; 1/100)</th>
<th>Rare (≥1/10,000 to &lt; 1,000)</th>
<th>Very Rare (&lt;1/10,000)</th>
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</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Headache</td>
<td>Vertigo Dizziness</td>
<td></td>
<td>Syncope</td>
<td></td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td></td>
<td></td>
<td></td>
<td>Allergic Dermatitis*</td>
<td>Exfoliative dermatitis</td>
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<tr>
<td>Vascular Disorders</td>
<td>Facial Flushing</td>
<td></td>
<td>Orthostatic hypotension Circulatory collapse</td>
<td></td>
<td></td>
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<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Asthenia</td>
<td>Application site discomfort including Burning Sensation And Stinging</td>
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<td></td>
<td></td>
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<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea</td>
<td>Tongue blistering</td>
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<tr>
<td>Cardiac Disorders</td>
<td></td>
<td>Tachycardia Bradycardia Angina pectoris aggravated</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Investigations</td>
<td></td>
<td>Blood pressure decreased</td>
<td></td>
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<td></td>
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</tbody>
</table>

*Symptoms which are known in conjunction with hypersensitivity reactions

Use of Glycerol Trinitrate Spray may give rise to transient hypoxaemia and, in patients with coronary heart disease, ischaemia as a result of a relative redistribution of the bloodstream, which is to hypoventilated alveolar areas.

Tolerance development and the occurrence of crossed tolerance of other nitro compounds have been found in chronic, continuous treatment using high doses. To avoid a decrease in efficacy or a loss of efficacy, high continuous doses should be avoided.

**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 the Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

### 4.9 Overdose

**Signs and Symptoms**

Flushing, severe headache, vertigo, tachycardia, a feeling of suffocation, hypotension, fainting and rarely cyanosis and methaemoglobinemia may
occur. In a few patients, there may be a reaction comparable to shock with nausea, vomiting, weakness, sweating and syncope.

**Treatment**

Recovery often occurs without special treatment. Hypotension may be corrected by elevation of the legs to promote venous return. Methaemoglobinaemia should be treated by intravenous methylthioninium chloride and/or toluidine blue. Symptomatic treatment should be given for respiratory and circulatory defects in more serious cases.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:** Vasodilators used in cardiac diseases, organic nitrates  
**ATC-Code:** C0IDA02

Glyceryl trinitrate acts on vascular smooth muscles to produce arterial and venous vasodilation. The vasodilation results in a reduction of venous return and an improvement in myocardial perfusion with the result of a reduction in the work performed by the heart and hence reduced oxygen demand.

### 5.2. Pharmacokinetic Properties

Glyceryl trinitrate is rapidly absorbed through the buccal and sublingual mucosa, and in man peak concentrations in plasma are observed within four minutes of sublingual administration.

The absolute bioavailability after sublingual administration is approximately 39%. After sublingual administration the plasma levels have shown a wide range of intra and inter-individual variability. The compound is extensively metabolised by liver enzymes and has a plasma half life of 1-3 minutes. The principle mechanism of metabolism involves denitration.

### 5.3 Preclinical safety data

Preclinical date reveal no special hazard for human based conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, or toxicity to reproduction.
6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

- Peppermint oil
- Propellant HFC 134A (1,1,1,2 Tetrafluoroethane)
- Ethanol

6.2. Incompatibilities

None known.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

6.5. Nature and contents of container

Internally lacquered monobloc Aluminium pressurised container sealed with a metered spray valve.

The product is presented in packs with one metered dose spray.

One metered dose spray (= one aluminium container) contains either 1760.0mg of solution (according to 11400.0mg of solution and propellant) providing 200 single metered doses, or 1584.0mg of solution (according to 10260.0mg of solution and propellant) providing 180 metered doses.

6.6. Special precautions for disposal

Glyceryl Trinitrate is an aerosol spray and contains a pressurised liquid. Do not expose to temperatures higher than 50 °C, and do not pierce the canister, even when empty. It should not be sprayed at a naked flame or any...
incandescent material. Patients, especially those who smoke should be warned not to use glyceryl trinitrate spray near a naked flame.

7  MARKETING AUTHORISATION HOLDER

Ayrton Saunders Ltd
9 Arkwright Road
Astmoor Industrial Estate
Runcorn
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WA7 1NU

8.  MARKETING AUTHORISATION NUMBER(S)

PL 16431/0018

9  Date of the first authorisation or renewal

15/09/2005

10  DATE OF REVISION OF THE TEXT

22/06/2017