Glytrin, 400 micrograms per metered dose, sublingual spray

Summary of Product Characteristics Updated 28-Jun-2016 | Aspire Pharma Ltd

1. Name of the medicinal product

Glytrin, 400 micrograms per metered dose, Sublingual Spray

2. Qualitative and quantitative composition

Active Ingredient

Glyceryl Trinitrate: 400 micrograms per metered dose

This product contains small amounts of ethanol (alcohol) less than 100mg per spray.

For 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 Glytrin 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 Glytrin 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 glyceryl trinitrate) to be sprayed under the tongue for the relief of anginal pain while 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

Glytrin 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 administration at night.

4.3 Contraindications

Hypersensitivity to nitrates or to any of the excipients. Severe hypotension (systolic blood pressure lower than 90mm Hg). Hypotensive shock, severe anaemia, constrictive pericarditis, extreme bradycardia, Glucose-6-phosphatedehydrogenase- 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.

4.4 Special warnings and precautions for use

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

Glytrin should be administered with particular caution in:

• Pericardial tamponade

• Low filling pressures (e.g. acute myocardial infarction, left ventricular failure)

• Tendancy to dysregulation of orthostatic blood pressure

• Diseases accompanied by an increase in intracranial pressure (so far further pressure has been observed solely in high doses of glyceryl trinitrate). Alcohol should be avoided because of the hypotensive effect and medical controls of the intraocular pressure of glaucoma patients are advisable. Particular caution should also be exercised when using Glytrin 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 bioavailability of dihydroergotamine may be increased by concomitant use of Glytrin, which can result in vasoconstriction since dihydroergotamine can antagonise the effects of glyceryl trinitrate. The concomitant administration of Glytrin and heparin can reduce the antithrombotic effect of heparin. Regular monitoring of coagulation parameters and adjustment of the heparin dose may be necessary.

In patients pre-treated with organic nitrates a higher dose of glyceryl trinitrate may be necessary to achieve the desired haemodynamic effect.

4.6 Pregnancy and lactation

The safety of glyceryl trinitrate in human pregnancy, especially during the first trimester has not been established. It is not known whether glyceryl trinitrate is excreted into human breast milk. Glytrin should be used only 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 Glytrin.

4.8 Undesirable effects

The following adverse reactions have been reported:

System Organ Class	Very Common (≥ 10%)	Common (≥ 1% < 10%)	Uncommon (≥ 0.1% < 1%)	Rare (≥ 0.01% <0.1%)	Very Rare (≥ 0.001% <0.01%)
Nervous System Disorders	Headache	Vertigo			
Skin and Subcutaneous Tissue Disorders		Facial Flushing			
Vascular Disorders		Dizziness		Postural Hypotension	
General Disorders and Administration Site Conditions		Weakness	Burning Sensation Stinging Sensation Tongue Blistering		
Gastrointestinal Disorders		Nausea			
Cardiac Disorders				Tachycardia Bradycardia	

Skin and Subcutaneous Tissue Disorders				Allergic Skin Reactions	Exfoliative Dermatitis

Rarely collapse states with bradycardia and syncope, a severe fall in blood pressure accompanied by an enhancement of the anginal symptoms may occur.

Use of Glytrin 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.

4.9 Overdose

Signs and symptoms

Flushing, severe headache, vertigo, tachycardia, a feeling of suffocation, hypotension, fainting and rarely cyanosis and methaemoglobinaemia 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

ATC-Code: COIDAO2

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 data reveal no special hazard for humans based on 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 BP

6.2 Incompatibilities

None.

6.3 Shelf life

Three 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 1760.0mg of solution (according to 11400.0mg of solution and propellant) providing 200 single metered doses.

6.6 Special precautions for disposal and other handling

Glytrin is an aerosol spray and contains a pressurised liquid. Do not expose to temperature 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 Glytrin near a naked flame.

7. Marketing authorisation holder

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8. Marketing authorisation number(s)

PL 16431/0017

9. Date of first authorisation/renewal of the authorisation

03/09/2006

10. Date of revision of the text

22/10/2015

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