IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA1117/001/001
Case No: 2028206

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

EGIS UK Ltd

Regulatory Assistant, **127 Shirland Road**, **W9 2EP**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

NITROMIN 400 Microgram/dose Sublingual Spray

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **09/10/2006** until **13/05/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nitromin 400 microgram /dose Sublingual Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose contains 400 microgram Glyceryl trinitrate.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Sublingual Spray
Colourless or almost colourless clear oromucosal spray solution free from sediments.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment and prophylaxis of angina pectoris.

4.2 Posology and method of administration

Adult:
At the onset of an attack: 1 or 2 sprays (400-800 micrograms). Dose should not exceed more than 3 sprays at any one time.

For prophylaxis: 1-2 sprays (400-800 micrograms) immediately prior to an angina inducing event.

The patient should be in the sitting position. The spray should be held upright and should not be inhaled. After spraying under the tongue the mouth should be closed immediately after each dose.

Elderly:
As adult.

Children:
Not recommended.

4.3 Contraindications

Hypersensitivity to nitrates. Hypotensive shock. Severe anaemia. Cerebral haemorrhage and brain trauma. Mitral stenosis. Angina caused by hypertrophic obstructive cardiomyopathy.

Sildenafil has been shown to potentiate the hypotensive effects of nitrates, and its coadministration with nitric oxide donors or nitrates in any form is therefore contra-indicated.

4.4 Special warnings and precautions for use

Tolerance and cross-tolerance to other nitrates may occur.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol may potentiate the hypotensive effects.
Nitromin may be employed in conjunction with other nitrate containing products, but care should be taken to avoid excessive total intake. In practical terms this means that sublingual GTN tablets should not be taken in addition to Nitromin for the same anginal attack unless under close medical supervision (this does not apply to long acting nitrate preparations used for attack prevention).

Sildenafil has been shown to potentiate the hypotensive effects of nitrates (See Section 4.3 Contra-indications).

4.6 Pregnancy and lactation

There are no specific data available on the use of Nitromin in human pregnancy. Since angina is uncommon in pregnancy it is unlikely that the need for Nitromin would arise. In all cases, the benefit of treatment to the patient must be balanced against any possible hazard to the foetus. There is no information regarding excretion of glyceryl trinitrate in breast milk.

4.7 Effects on ability to drive and use machines

Nitromin should not impair ability to drive or use machines; however, patients should be advised not to drive etc. if they feel unwell or faint after using the spray.

4.8 Undesirable effects

The following side effects occur in approximately 30-40% of patients: taste disturbance (metallic taste), headache, postural hypotension, flushing, and palpitations. These are usually mild and disappear within a few minutes.

4.9 Overdose

Symptoms - flushing, severe headache, a feeling of suffocation, hypotension, fainting. Rarely cyanosis and methaemoglobinaemia. In a few patients a reaction comparable to shock with nausea, vomiting, weakness, sweating and syncope.

Emergency procedures - recovery often occurs without special treatment.
Elevate legs to promote venous return.

Antidote - treat methaemoglobinaemia with intravenous methylene blue. Treat symptomatically for serious respiratory and circulatory effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Glyceryl trinitrate relaxes smooth muscle and reduces blood pressure. Its anti-anginal effects are believed to depend on reducing myocardial oxygen demand by means of peripheral vasodilation.

5.2 Pharmacokinetic properties

The onset of action following sublingual administration is within 2 minutes. Duration of action is about 30 minutes.

5.3 Preclinical safety data

No animal toxicological studies have been performed using Nitromin. Animal studies using inorganic nitrates have shown toxic effects due to excessive pharmacodynamic action (e.g. hypovolaemia, shock, and circulatory collapse) or

due to the effects of methaemoglobinaemia. These effects have always occurred at doses proportional to doses in the toxic range in humans.
Studies in pregnant animals have shown similar toxic effects but no evidence of a direct teratogenic effect.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
Ethanol

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Store in the original packaging. Do not expose to temperature above 50^{o}C.

Do not pierce or burn after use. Do not spray onto a naked flame or any incandescent material.

6.5 Nature and contents of container

Aluminium canister with metered dosing valve and nozzle. Plastic protective cap. Each canister contains 10 grams (180 doses) of solution.

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

EGIS UK Ltd.
127 Shirland Road
London
W9 2EP
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 1117/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 May 1999

Date of last renewal: 14 May 2004

10 DATE OF REVISION OF THE TEXT

October 2006