Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Betagan 0.5% w/v Eye Drops, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Levobunolol hydrochloride 0.5% w/v

Product imported from Spain:
Clear, viscous, sterile, colourless to light yellow eye drops solution

Excipients: Benzalkonium chloride.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.

Clear, viscous, sterile, colourless to light yellow eye drops solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the control of intraocular pressure in chronic open angle glaucoma and ocular hypertension.

4.2 Posology and method of administration

Adults (including the elderly): the recommended dosage of Betagan is one drop in the affected eye(s) once or twice daily.

Betagan is not recommended for use in children due to lack of safety and efficacy data (see section 5.1.).

Method of administration: topical into the conjunctival sac.

Concurrant therapy may be used where necessary.
As with any eye drops, to reduce possible systemic absorption, it is recommended that the lachrymal sac be compressed at the medial canthus (punctual occlusion) for one minute. This should be performed immediately following the instillation of each drop.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.
Bronchial asthma (or a history of bronchial asthma) or chronic obstructive pulmonary disease.
Uncontrolled cardiac failure.
History of sinus bradycardia, second and third-degree atrioventricular block, overt cardiac failure or cardiogenic shock.

4.4 Special warnings and precautions for use

As with other topically applied ophthalmic drugs, Betagan may be absorbed systemically and adverse reactions typical of oral beta-adrenoceptor agents may occur.

Respiratory and cardiac reactions have been reported including, rarely, death due to bronchospasm or associated with cardiac failure.

Congestive heart failure should be adequately controlled before beginning therapy with Betagan. In patients with a history of significant cardiac disease, pulse rates should be monitored.

Because these agents may block the systemic effects of hypoglycaemia they should be used with caution in diabetic patients who use insulin or oral hypoglycaemic drugs.

Stevens-Johnson syndrome has been reported following the use of levobunolol; however a causal relationship has not been established.

Beta-blockers have been associated with alopecia; however, a causal relationship between levobunolol and alopecia has not been established.

The preservative in Betagan, bensalkonium chloride, may cause eye irritation. Avoid contact with soft contact lenses. Remove contact lenses prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

Additive effects may be noted if the product is used in patients taking systemic antihypertensive drugs. These possible additive effects may include hypotension, including orthostatic hypotension, bradycardia, dizziness, and/or syncope. Conversely, systemic beta-adrenoceptor blocking agents may potentiate the ocular hypotensive effect of Betagan.

4.6 Fertility, pregnancy and lactation

For levobunolol hydrochloride no clinical data on exposed pregnancies are available.

Betagan should not be used during pregnancy unless clearly necessary.

If treatment with levobunolol hydrochloride during lactation is considered necessary for the benefit of the mother, consideration should be given to the cessation of breast feeding.

4.7 Effects on ability to drive and use machines

Betagan may cause fatigue and/or drowsiness, which may impair the ability to drive or operate machinery.
Betagan may cause blurred and/or abnormal vision, which may also impair the ability to drive or to use machinery, especially at night or in reduced lighting. The patient should wait until these symptoms have cleared before driving or using machinery.

4.8 Undesirable effects

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The following terminologies have been used in order to classify the occurrence of undesirable effects: **Very Common (≥ 1/10); Common (≥ 1/100 to < 1/10); Uncommon (≥ 1/1,000 to < 1/100); Rare (≥ 1/10,000 to < 1/1,000); Very rare (<1/10,000), not known (cannot be estimated from the available data).**

Immune System Disorders

Not Known: Hypersensitivity

Psychiatric Disorders
Not known: Depression

Nervous System Disorders
Not known: Ataxia, Confusion, Dizziness, Somnolence, Lethargy, Headache

Eye Disorders
Very Common: Eye irriataion, Conjunctival irritation
Common: Blepharitis, Conjunctivitis
Not known: Corneal reflex decreased, Iridocyclitis, Keratitis, Visual disturbance, Eye/Eyelids pruritus, Eye/Eyelid oedema, Eye discharge, Lacrimation increased, Ocular hyperaemia.

Cardiac Disorders
Not known: Syncope, Bradycardia, Atrioventricular block, Palpitations

Vascular Disorders
Not known: Hypotension

Respiratory, Thoracic, and Mediastinal Disorders
Not known: Asthma, Dyspnoea, Throat irritation, Nasal discomfort

Gastrointestinal Disorders
Not known: Nausea

Skin and Subcutaneous Tissue Disorders
Not known: Urticaria, Dermatitis, Rash, Erythema, Skin exfoliation, Lichenoid keratosis, Pruritus

General Disorders and Administration Site Conditions
Not known: Face oedema, Asthenia

The following additional adverse reactions have been reported with ophthalmic use of $beta_1$ and $beta_2$ (non-selective) blocking agents.
Cardiovascular: cerebrovascular accident, cerebral ischaemia, congestive heart failure, cardiac arrest.
Respiratory: respiratory failure.

4.9 Overdose

There are no data available on human overdosage with Betagan, which is unlikely to occur via the ocular route. Should accidental ocular overdosage occur, flush the eye(s) with water or normal saline. If accidentally ingested systemic symptoms may result. The symptoms associated with systemic overdosage are most likely to be bradycardia, hypotension, bronchospasm and cardiac failure. Therapy for overdosage of a beta-adrenergic agent should be instituted, such as intravenous administration of atropine sulphate 0.25 to 2 mg to induce vagal blockade. Conventional therapy for hypotension, bronchospasm, heart block and cardiac failure may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Safety and effectiveness of Betagan in paediatric patients have not been established.

Levobunolol is a non-cardioselective beta-adrenoceptor blocking agent, equipotent at both beta1 and beta2 receptors. Levobunolol is greater than 60 times more potent than its dextro isomer in its beta-blocking activity. In order to obtain the highest degree of beta-blocking potential without increasing the potential for direct myocardial depression, the levo isomer, levobunolol, is used. Levobunolol does not have significant local anaesthetic (membrane-stabilising) or intrinsic sympathomimetic activity. Betagan has shown to be as effective as Timolol in lowering intraocular pressure.

Betagan when instilled in the eye will lower elevated intraocular pressure as well as normal intraocular pressure, whether or not accompanied by glaucoma. Elevated intraocular pressure presents a major risk factor in the pathogenesis of glaucomatous field loss. The higher the level of intraocular pressure, the likelihood of optic nerve damage and visual field loss.

The primary mechanism of action of levobunolol in reducing intraocular pressure is most likely a decrease in aqueous humour production. Betagan reduces intraocular pressure with little or no effect on pupil size in contrast to the miosis which cholinergic agents are known to produce. The blurred vision and night blindness often associated with miotics would not be expected with the use of Betagan. Patients with cataracts avoid the inability to see around lenticular opacities caused by pupil constriction.

5.2 Pharmacokinetic properties

The onset of action with one drop of Betagan can be detected within one hour after instillation, with maximum effect seen between two and six hours. A significant decrease can be maintained for up to 24 hours following a single dose.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyvinyl alcohol
Benzalkonium chloride
Sodium metabisulphite (E223)
Sodium chloride
Disodium edetate
Sodium phosphate, dibasic, heptahydrate
Potassium dihydrogen phosphate
Sodium hydroxide
Hydrochloric acid
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.
After first opening: discard after 1 month.

6.4 Special precautions for storage

Do not store above 25°C. Store the bottle in the original package in order to protect from light.

6.5 Nature and contents of container

10ml white plastic bottle with dropper tip and safety seal. The bottle is filled with 5ml of Betagan.

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 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co. Meath

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 465/210/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisastion : 18th January 2008

10 DATE OF REVISION OF THE TEXT

April 2011