1. NAME OF THE MEDICINAL PRODUCT

LUCOPTIC (BETAXOLOL OPHTHALMIC SOLUTION USP)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each ml contains:

Betaxolol Hydrochloride USP	0.56%W/V
Eq. to Betaxolol	0.5 % W/V
Benzalkonium Chloride (As Preservative)	0.01 % W/V
Sterile Aqueous Base	Q.S.

3. PHARMACEUTICAL FORM

Ophthalmic (Eye Drop)

4. Clinical particulars

4.1 Therapeutic indications

Reduction of elevated intraocular pressure in conditions such as ocular hypertension and chronic open-angle glaucoma.

4.2 Posology and method of administration

Adults (including the elderly): recommended therapy is one drop of Betaxolol 0.5% Eye Drops to be instilled into the affected eye(s) twice a day.

Children: No clinical studies have been performed to establish safety and efficacy in children. Therefore, this product is currently not recommended for use in children.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

Intraocular pressure should be reassessed approximately four weeks after starting treatment because response to Betaxolol 0.5% Eye Drops may take a few weeks to stabilise.

If necessary, concomitant treatment with miotics, adrenaline and/or carbonic anhydrase inhibitors can be instituted. In order to prevent the active substance(s) from being washed out when additional ophthalmic medication is used, an interval of at least 10 minutes between each application is recommended. The use of two topical beta-adrenergic agents is not recommended.

Transfer from a single antiglaucoma agent: Continue the agent and add one drop of Betaxolol 0.5% Eye Drops in each affected eye twice daily. On the following day, discontinue the previous agent completely, and continue with Betaxolol 0.5% Eye Drops.

When several antiglaucoma agents are being used, the patient should be assessed on an individual basis. Adjustment should involve one agent at a time at intervals of not less than one week.

Patients should be instructed to remove soft contact lenses before using betaxolol.

4.3 Contraindications

Betaxolol 0.5% Eye Drops are contraindicated in patients with:

- Sinus bradycardia, sick sinus syndrome, sino-atrial block;

- Cardiogenic shock;

- Overt cardiac failure;

- Second or third degree atrioventricular block not controlled with pace-maker;

- Hypersensitivity to the active substance (betaxolol), to any of the excipients listed in section 6.1 or other beta-blocking agents.

- Reactive airway disease including severe bronchial asthma or a history of severe bronchial asthma, severe chronic obstructive pulmonary disease.

4.4 Special warnings and precautions for use

For ocular use only.
General:

Like other topically applied ophthalmic drugs, betaxolol is absorbed systemically. Due to beta-adrenergic component, betaxolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.

Cardiac disorders:

In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

Vascular disorders:

Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.

Respiratory disorders:

Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers.

Patients with mild/moderate bronchial asthma, a history of mild/moderate bronchial asthma or, mild/moderate chronic obstructive pulmonary disease (COPD) should be treated with caution.

Hypoglycaemia/diabetes:

Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia. While Betaxolol has demonstrated a low potential for systemic effects, it should be used with caution in patients suspected of developing thyrotoxicosis.

Hyperthyroidism:

Beta-blockers may also mask the signs of hyperthyroidism.

Muscle weakness:

Beta adrenergic blocking agents have been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (eg. diplopia, ptosis and generalised weakness).

Corneal diseases:

In patients with angle-closure glaucoma, the immediate treatment objective is to re-open the angle by constriction of the pupil with a miotic agent, betaxolol has no effect on the pupil, therefore, Betaxolol should be used with a miotic to reduce elevated intraocular pressure in angle-closure glaucoma.

Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases, Sicca Syndrome or similar tear film abnormalities should be treated with caution.

Other beta-blocking agents:

The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when betaxolol is given to the patients already receiving a systemic beta- blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).

Anaphylactic reactions:

While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.

Choroidal detachment:

Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.

Surgical anaesthesia:

Beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving betaxolol. Consideration should be given to the gradual withdrawal of beta-adrenergic

blocking agents prior to general anaesthesia because of the reduced ability of the heart to respond to beta-adrenergically mediated sympathetic reflex stimuli.

Contact lenses:

This formulation of Betaxolol 0.5% Eye Drops contains 0.1 mg/ml benzalkonium chloride as a preservative which may be deposited in soft contact lenses. Hence, Betaxolol 0.5% Eye Drops should not be used while wearing these lenses. The lenses should be removed before instillation of the drops and not reinserted earlier than 15 minutes after use.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures.

Patients should also be instructed that ocular solutions, if handled improperly can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using.

Patients should also be advised that if they develop any intercurrent ocular condition (e.g. trauma, ocular surgery or infection), they should immediately seek their physician's advice concerning the continued use of present multi-dose container.

There have been reports of bacterial keratitis associated with the use of topical ophthalmic products.

4.5 Interaction with other medicinal products and other forms of interaction

No specific drug interaction studies have been performed with betaxolol.

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, anti-arrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics and guanethidine. Close observation of the patient is recommended.

Betablockers can decrease the response to adrenaline use to treat anaphylactic reactions. Special caution should be exercised in patients with a history of atophy or anaphylaxis.

Caution should be exercised in patients using concomitant adrenergic psychotropic drugs.

Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.6 Pregnancy and Lactation

Fertility

There are no data on the effects of Betaxolol eye drops on human fertility.

Pregnancy

There are no adequate data for the use of betaxolol in pregnant women. Betaxolol should not be used during pregnancy unless clearly necessary.

To reduce the systemic absorption, see 4.2.

Epidemiological studies have not revealed malformative effects but show a risk for intra-uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If Betaxolol Eye Drops is administered until delivery, the neonate should be carefully monitored during the first days of life.

Lactation

Beta-blockers are excreted in breast milk, having the potential to cause serious undesirable effects in the infant of nursing mother. However, at therapeutic doses of betaxolol in eye drops, it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2

4.7 Effects on ability to drive and use machines

Betaxolol 0.5% eye drops, solution has no or negligible influence on the ability to drive and use machines.

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

Like other topically applied ophthalmic drugs, betaxolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.

Summary of the safety profile

In clinical trials with Betaxolol eye drops the most common adverse reaction was ocular discomfort, occurring in 12.0% of patients.

The following undesirable effects have been observed and reported with the following frequencies:

Very common: may affect more than 1 in 10 people

Common: may affect up to 1 in 10 people

Uncommon: may affect up to 1 in 100 people

Rare: may affect up to 1 in 1,000 people

Very rare: may affect up to 1 in 10,000 people

Not known: frequency unknown/cannot be estimated from the available data

Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	**MedDRA Preferred Term**
Immune system disorders	Frequency unknown: hypersensitivity
Psychiatric disorders	Rare: anxiety, insomnia, depression
Nervous system disorders	Common: headache Rare: syncope Frequency unknown: dizziness
Eye disorders	Very common: ocular discomfort Common: vision blurred, lacrimation increased Uncommon: punctate keratitis, keratitis, conjunctivitis, blepharitis, visual impairment, photophobia, eye pain, dry eye, asthenopia, blepharospasm, eye pruritus, eye discharge, eyelid margin crusting, eye inflammation, eye irritation, conjunctival disorder, conjunctival oedema, ocular hyperaemia Rare: Cataract, decreased corneal sensitivity, erythema of eyelid
Cardiac disorders	Uncommon: bradycardia, tachycardia Frequency unknown: arrhythmia
Vascular disorders	Rare: hypotension
Respiratory, thoracic and mediastinal Disorders	Uncommon: asthma, dyspnoea, rhinitis Rare: cough, rhinorrhea
Gastrointestinal disorders	Uncommon: nausea Rare: dysgeusia
Skin and subcutaneous tissue disorders	Rare: dermatitis, rash, alopecia
Reproductive system and breast disorders	Rare: libido decreased
General disorders and administration site conditions	Frequency unknown: asthenia

Description of selected adverse reactions

Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with Betaxolol eye drops solution:

System Organ Classification	**MedDRA Preferred Term**
Immune system disorders:	Frequency unknown: Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.

Metabolism and nutrition disorders:	Frequency unknown: Hypoglycaemia.
Psychiatric disorders:	Frequency unknown: nightmares, memory loss, hallucinations, psychoses, confusion.
Nervous system disorders:	Frequency unknown: cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, paraesthesia
Eye disorders:	Frequency unknown: choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use), corneal erosion, ptosis, diplopia.
Cardiac disorders:	Frequency unknown: Chest pain, palpitations, oedema, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure. A slowed AV-conduction or increase of an existing AV-block
Vascular disorders:	Frequency unknown: Raynaud's phenomenon, cold and cyanotic hands and feet, Increase of an existing intermittent claudication.
Respiratory, thoracic, and mediastinal disorders:	Frequency unknown: Bronchospasm (predominantly in patients with pre-existing bronchspastic disease)
Gastrointestinal disorders:	Frequency unknown: dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.
Skin and subcutaneous tissue disorders:	Frequency unknown: Psoriasiform rash or exacerbation of psoriasis
Musculoskeletal and connective tissue disorders:	Frequency unknown: Myalgia.
Reproductive system and breast disorders:	Frequency unknown: Sexual dysfunction, impotence.
General disorders and administration site conditions:	Frequency unknown: fatigue.

4.9 Overdose

In case of accidental ingestion, symptoms of overdose from betablockade may include bradycardia, hypotension, cardiac failure and bronchospasm.

If overdose with Betaxolol eye drops occurs, treatment should be symptomatic and supportive.

A topical overdose of Betaxolol eye drops may be flushed from the eye(s) with warm tap water.

5. 1 Pharmacodynamics properties

Ophthalmologicals : Antiglaucoma Preparations & Miotics.

ATC Code: SO1E D02

Betaxolol is a cardioselective Beta1 receptor blocker which, when applied topically to the eye, lowers intraocular pressure. It is thought to produce this effect by reducing the rate of production of aqueous humour.

Clinical Pharmacology

Several studies have indicated that betaxolol may have a beneficial effect on visual function for up to 48 months in patients with chronic open-angle glaucoma and up to 60 months in patients with ocular hypertension. Moreover there is evidence that betaxolol maintains or increases ocular blood flow/perfusion.

5.2 Pharmacokinetic properties

Betaxolol is highly lipophilic which results in good permeation of the cornea, allowing high intraocular levels of the drug. Betaxolol is characterised by its good oral absorption, low first pass loss and a relatively long half-life of approx 16-22 hours. The elimination of betaxolol is primarily by the renal rather than faecal route. The major metabolic pathways yield two carboxylic acid forms plus unchanged betaxolol in the urine (approx. 16% of the administered dose).

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium Chloride Solution
Sodium chlor ide
Boric acid
Poloxamer 407
Sodium hydroxide pellets
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months for the date of manufacturing.

6.4 Special precautions forstorage

Store at a temperature not exceeding 30ºC in a dry place. Protect from light. Keep out of reach of children.

6.5 Natureandcontentsofcontainer<andspecialequipmentforuse, administration

or implantation>

1 x 5 ml

6.6 Special precautions for disposal <and other handling>

There are no special storage precautions. Any unused product or waste material should be disposed of in accordance with local requirements.

7 <APPLICANT/MANUFACTURER>

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