PACKAGE INSERT FOR LOXOPTIC® OPHTHALMIC SOLUTION

SCHEDULING STATUS **S3**

PROPRIETARY NAME AND DOSAGE FORM
Loxoptic® Ophthalmic Solution

COMPOSITION
Each ml contains betaxolol hydrochloride equivalent to 5 mg (0,5 % *m/v*) betaxolol and 0,01% *m/v* benzalkonium chloride as the preservative.
The other ingredients are disodium edetate, sodium chloride and water for injection.

PHARMACOLOGICAL CLASSIFICATION
A.15. 4 Ophthalmic Preparations, other

PHARMACOLOGICAL ACTION
Pharmacodynamic properties:
Betaxolol hydrochloride is a cardio-selective (beta-1-adrenergic) receptor blocking agent.
When administered to the eye, betaxolol reduces elevated and normal intraocular pressure.
The mechanism of ocular hypotensive action appears to be a reduction of aqueous production.

Pharmacokinetic properties:
The onset of action of betaxolol is observed within 30 minutes with a duration of 12 to 24 hours.
The maximal effect is usually detected 2 hours after topical administration to the eye. A single dose results in a 12 hour reduction in intraocular pressure. No negative effect on the blood supply to the optic nerve has been observed while on treatment with betaxolol ophthalmic solution. Betaxolol ophthalmic solution does not produce miosis and accommodative spasm**.**

INDICATIONS
LOXOPTIC has been shown to be effective in lowering intraocular pressure and is indicated in the treatment of:

- Patients with chronic open-angle glaucoma
- Patients with elevated intraocular pressure (ocular hypertensive patients).

CONTRA-INDICATIONS

- Hypersensitivity to betaxolol hydrochloride or to any of the excipients.
- Cardiac shock and overt cardiac failure.
- Sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third degree atrioventricular (AV) block not controlled with a pace maker.
- Reactive airway disease including bronchial asthma or a history of severe bronchial asthma, severe chronic obstructive pulmonary disease.
- Patients with damaged cornea.

WARNINGS AND SPECIAL PRECAUTIONS

- LOXOPTIC is absorbed systemically and the same adverse reactions observed with systemic beta-blocker therapy may occur (see SIDE EFFECTS).
- Due to its negative effect on conduction time, caution should be used in treating patients with a history of cardiac failure or first degree heart block (see CONTRA-INDICATIONS). Treatment with LOXOPTIC should be discontinued at the first signs of cardiac failure.
- Cardiac disorders: Therapy with LOXOPTIC should be assessed in patients with cardiovascular disease (e.g. coronary heart disease, Prinz Metal's angina, cardiac failures) and hypotension.

Patients should be observed for signs of deterioration of the disease state and exacerbation of adverse reactions.

- Anaphylactic reactions: While using LOXOPTIC, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dosage of epinephrine (adrenaline) used to treat anaphylactic reactions.
- Respiratory disorders: LOXOPTIC should be used with extreme caution in patients with bronchospasm, bronchial asthma or patients with a history of asthma or chronic obstructive pulmonary disease (COPD) when there is no alternative treatment as bronchoconstriction, shortness of breath may be precipitated (see SIDE EFFECTS).
- Death due to bronchospasm in patients with bronchospasm has been reported following the administration of an ophthalmic beta-blocker such as LOXOPTIC.
- 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. LOXOPTIC has no effect on the pupil; therefore LOXOPTIC should be used with a miotic to decrease elevated intraocular pressure in angle-closure glaucoma.
- LOXOPTIC may induce dryness of eyes. Caution should be exercised in the use of LOXOPTIC in patients with corneal diseases, sicca syndrome or similar tear film abnormalities.
- As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations may occur, regular ophthalmological examination is required.
- Caution should be exercised in the use of benzalkonium chloride preserved topical medication such as LOXOPTIC over an extended period.
- LOXOPTIC should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes as LOXOPTIC may mask the signs and symptoms of acute hypoglycaemia. LOXOPTIC may also mask the signs of hyperthyroidism. LOXOPTIC should therefore be used with caution in patients with diabetes or in patients with thyrotoxicosis.
- LOXOPTIC used alone has little or no effect on pupil size; however concurrent therapy of LOXOPTIC and epinephrine (adrenaline) has resulted in mydriasis.
- Other beta-blocking agents: Patients on treatment with an oral beta-adrenergic blocking agent and LOXOPTIC should be monitored for a potential additive effect either on the intraocular pressure or on the known systemic effects of beta blockade.
- LOXOPTIC contains benzalkonium chloride. Diminished responsiveness to LOXOPTIC following long term therapy may occur.
- Beta blockers such as LOXOPTIC may reduce tear flow, resulting in irritation of the eye in wearers of contact lenses possibly due to the dehydration of soft lenses.
- Clinical studies to establish the safety and efficacy in children have not been performed.

Effects on ability to drive and use machines:
LOXOPTIC may cause dizziness, fatigue, transient ocular irritation, blurred vision and lacrimation.
Patients should be advised to exercise caution until they know how LOXOPTIC affects them.

INTERACTIONS

- LOXOPTIC used alone has little or no effect on pupil size; however concurrent therapy of LOXOPTIC and epinephrine (adrenaline) has resulted in mydriasis.
- There is a potential for additive effects resulting in hypotension and/or marked bradycardia when LOXOPTIC is administered concomitantly with oral calcium channel blockers, beta adrenergic blocking agents, anti-dysrhythmics (including amiodarone, digoxin), parasympathomimetics and catecholamine-depleting agents such as reserpines (see WARNINGS AND SPECIAL PRECAUTIONS).
- Caution should be exercised in patients using LOXOPTIC, hypoglycaemic agents and phenothiazines concurrently.

- Caution should be exercised in patients using concomitant adrenergic psychotropic medicines.

PREGNANCY AND LACTATION

Pregnancy:

Safety in pregnancy has not yet been established. Infants of mothers administered beta-blockers shortly before giving birth, or during labour may be born hypotonic, collapsed and hypoglycaemic.

Lactation:

LOXOPTIC is secreted in human milk therefore caution should be exercised when administering LOXOPTIC to mothers breastfeeding their babies.

DOSAGE AND DIRECTIONS FOR USE

The usual dose is one drop of LOXOPTIC in the affected eye(s) twice daily.

In some patients, the intraocular pressure lowering response to LOXOPTIC may require a few weeks to stabilise.

A clinical follow up should include a determination of the intraocular pressure during the first month of treatment with LOXOPTIC. Thereafter, intraocular pressure readings should be determined on an individual basis at the judgement of the medical practitioner.

When substituting LOXOPTIC for another ophthalmic anti-glaucoma agent, continue the agent already used and add one drop of LOXOPTIC in the affected eye(s) twice a day. On the following day, discontinue the previous anti-glaucoma agent completely and continue with LOXOPTIC.

Due to diurnal variations of intraocular pressure in individual patients, a satisfactory response to twice a day therapy is best determined by measuring intraocular pressure at different times during the day.

Therapy with LOXOPTIC should be individualised. If the intraocular pressure of the patient is poorly controlled on this regimen, concurrent therapy with pilocarpine, other miotics, epinephrine (adrenaline) or systemically administered carbonic anhydrase inhibitors can be initiated.

If more than one eye drop is being used, the eye drops should be administered at least 10 minutes apart.

When a patient is transferred from several concomitantly administered anti-glaucoma agents individualisation is needed. The adjustment should involve one agent at a time made at intervals of not less than one week. A recommended approach is to continue the agents being used and add one drop of LOXOPTIC in the affected eye(s) twice a day. On the following day, discontinue one of the other anti-glaucoma agents. The remaining anti-glaucoma agents may be decreased or discontinued according to the patient's response to treatment.

Method of administration:

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced.

SIDE EFFECTS

LOXOPTIC is absorbed into the systemic circulation and may cause similar undesirable effects as seen with systemic beta-blockers.

Immune system disorders:

Frequency unknown: Systemic allergic reactions including angioedema, urticaria, localised and generalised rash, pruritus.

Eye disorders:

Frequent: Discomfort on instillation.

Less frequent: Tearing, instances of decreased corneal sensitivity, itching sensation, corneal punctuate staining, keratitis, anisocoria, photophobia, erythema.

Frequency unknown: Blepharitis, decreased tear production and dry eyes, blurred vision, conjunctivitis, soreness, ocular irritation (burning, stinging, redness), diplopia, ptosis, corneal erosion.

Psychiatric disorders:
Frequency unknown: Depressive neurosis, malaise, vivid dreams and nightmares, overt psychosis, hallucinations.

Nervous system disorders:
Frequent: Headache.
Less frequent: Depression.
Frequency unknown: Insomnia, confusion, memory loss, syncope, cerebrovascular accident, cerebral ischaemia, increase in signs and symptoms of myasthenia gravis, dizziness, paraesthesia.

Metabolism and nutrition disorders:
Frequency unknown: Hypoglycaemia.

Cardiac disorders:
Less frequent: Marked bradycardia.
Frequency unknown: Congestive cardiac failure, chest pain, palpitations, dysrhythmia, cardiac failure, atrioventricular block, cardiac arrest, a slowed AV-conduction or increase of an existing AV-block.

Vascular disorders:
Frequency unknown: Exacerbation of peripheral vascular disease, Raynaud's phenomenon (due to unopposed arteriolar sympathetic activation), severe peripheral vascular disease, peripheral gangrene, hypotension, cold and cyanotic hands and feet, oedema, exacerbation of intermittent claudication.

Respiratory, thoracic and mediastinal disorders:
Less frequent: Dyspnoea, asthma.
Frequency unknown: Bronchospasm, cough.

Gastro-intestinal disorders:
Frequency unknown: Nausea, vomiting, diarrhoea, constipation, abdominal cramping, dysgeusia, dyspepsia, dry mouth.

Skin and subcutaneous tissue disorders:
Less frequent: Alopecia.
Frequency unknown: Erythema, psoriasiform rash or exacerbation of psoriasis.

Musculoskeletal, connective tissue and bone disorders:
Frequency unknown: Skeletal muscle weakness, myalgia.

Reproductive system and breast disorders:
Frequency unknown: Sexual dysfunction, impotence, decreased libido.

Side-effects are frequent in patients with renal decomposition.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
(see SIDE EFFECTS and WARNINGS AND SPECIAL PRECAUTIONS)
The symptoms which might be expected in an overdosage of a systemically administered beta-1-adrenergic receptor blocking agent are hypotension, bradycardia, and acute cardiac failure.
A topical overdose of LOXOPTIC may be flushed from the eye(s) with warm tap water.

IDENTIFICATION
LOXOPTIC ophthalmic solution is a clear, colourless solution free from visible particulate matter.

PRESENTATION
Carton containing a colourless, translucent, LDPE bottle with a white to off-white polystyrene cap.
Each bottle contains 5 ml of LOXOPTIC ophthalmic solution.

STORAGE INSTRUCTIONS
Store at or below 30 °C. Protect from light.
Do not use more than 28 days after opening.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
47/15.4/0526

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
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