**PACKAGE INSERT TEMPLATE FOR LATANOPROST 0.005% EYE DROPS**

**Brand or Product Name**
*[Product name]* Eye Drops 0.005% w/v

**Name and Strength of Active Substance(s)**

Latanoprost …..0.005 % w/v

**Product Description**
*[Visual description of the appearance of the product (eg colour, viscosity etc)*
*eg Sterile, clear, colourless, odourless, free from visible particles ophthalmic solution*

**Pharmacodynamics**
Latanoprost is a prostaglandin F 2-alpha analogue and a selective FP prostanoid receptor agonist. It reduces intraocular pressure by increasing the outflow of aqueous humor. Studies suggest that the main mechanism of action is increased uveoscleral outflow.

**Pharmacokinetics**
*Absorption*
Latanoprost is absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active.
The peak concentration in the aqueous humor is reached about two hours after topical administration.

*Distribution*
Latanoprost is highly lipophilic and rapidly partitions into the cornea where it undergoes hydrolysis to hydrophilic free acids; these acids diffuse from the cornea preferentially through its more permeable endothelial surface toward the aqueous humor.

Free acids of latanoprost serve as substrates for the prostaglandin transport systems, preventing their accumulation in the retina or brain.

The distribution volume in humans is 0.16 ± 0.02 L/kg. The acid of latanoprost can be measured in aqueous humor during the first four hours, and in plasma only during the first hour after local administration.

*Metabolism*
Latanoprost, an isopropyl ester prodrug, is hydrolyzed by esterases in the cornea to the biologically active acid. The active acid of latanoprost reaching the systemic circulation is primarily metabolized by the liver to the 1,2-dinor and 1,2,3,4-tetranor metabolites via fatty acid β-oxidation.

*Elimination*
Following hepatic β-oxidation, the metabolites are mainly eliminated via the kidneys. Approximately 88% and 98% of the administered dose is recovered in the urine after topical and intravenous dosing, respectively.
The elimination half life , t1/2 =17 min

**Indication**

- Reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma, chronic angle closure glaucoma, and ocular hypertension.

- Reduction of elevated intraocular pressure in paediatric patients with elevated intraocular pressure and paediatric glaucoma

**Recommended Dosage**

*Use in adults (including the elderly):*
One drop in the affected eye(s) once daily. Optimal effect is obtained if latanoprost is administered in the evening.

The dosage of latanoprost should not exceed once daily since it has been shown that more frequent administration decreases the intraocular pressure lowering effect.
If one dose is missed, treatment should continue with the next dose as normal.

Latanoprost may be used concomitantly with other classes of topical ophthalmic drug products to lower IOP. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart.

Contact lenses should be removed before instillation of the eye drops and may be reinserted after fifteen minutes (if contains benzalkonium chloride)

*Pediatric Population*

Latanoprost eye drops may be used in paediatric patients at the same posology as in adults. No data are available for preterm infants (less than 36 weeks gestational age). Data in the age group < 1 year are limited.

**Mode of Administration**
Topical ophtalmic

**Contraindications**
Known hypersensitivity to latanoprost or any other component of the product

**Warnings and Precautions**

**General:**

This product contains benzalkonium chloride, which may be absorbed by contact lenses. (if product contains benzalkonium chloride)

**Ocular:**

Latanoprost eye drops may produce a gradual increase in the amount of brown pigment in the iris, due to increased melanin content of melanocytes. This change in eye colour is most evident in patients with mixed colour irises, and may be permanent in some patients. The onset of iris pigmentation is usually within the first 8 months of treatment, rarely during the second or third year, and has not been seen after the fourth year of treatment.

Treatment with latanoprost can be continued in patients who develop increased iris pigmentation. These patients should be examined regularly and, depending on the clinical situation, treatment may be stopped.

Increase in brown iris pigment has not been shown to progress further upon discontinuation of treatment, but the resultant color change may be permanent.

Darkening of the palpebral skin (eyelid skin) has been reported in association with the use of latanoprost.

Darkening, thickening, and lengthening of eyelashes may occur and are reversible upon stopping treatment.

The potential for heterochromia exists for patients receiving unilateral treatment.

Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost. These have mainly occurred in aphakic patients, in pseudophakic patients with torn posterior lens capsule, or in patients with known risk factors for macular edema. Caution is recommended when using latanoprost in these patients.

Concomitant use with other prostaglandins or prostaglandin analogues not recommended.

Use not recommended in those who have active inflammation; intraocular inflammation (iritis/uveitis).

Use with caution in those who have history of intraocular inflammation (iritis/uveitis)

There is limited experience with latanoprost in the treatment of inflammatory neovascular glaucoma. Therefore, it is recommended that latanoprost should be used with caution in these conditions until more experience is obtained.

Latanoprost should be used with caution in patients with a history of herpetic keratitis, and should be avoided in cases of active herpes simplex keratitis and in patients with a history of recurrent herpetic keratitis specifically associated with prostaglandin analogues.

*Paediatric Population*

Efficacy and safety data in the age group < 1 year (4 patients) are very limited . No data are available for preterm infants (less than 36 weeks gestational age).

In children from 0 to < 3 years old that mainly suffers from PCG (Primary Congenital Glaucoma), surgery (e.g. trabeculotomy/goniotomy) remains the first line treatment.

Long-term safety in children has not yet been established.

*Effects on the ability to drive and use machines*
Instillation of eye drops may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines.

**Interactions with Other Medicaments**

- Paradoxical increases in intra-ocular pressure have been reported after the concomitant ophthalmic use of 2 prostaglandin analogues. Therefore, the use of two or more prostaglandins, prostaglandin analogs, or prostaglandin derivatives is not recommended.

*Updated September 2013*

- Concurrent use of latanoprost and pilocarpine may result in reduced latanoprost efficacy.

- Concurrent use of thimerosal and latanoprost may result in precipitation in the eye.

**Statement on Usage During Pregnancy and Lactation**

*Pregnancy*

There are no adequate and well-controlled studies of latanoprost administration in pregnant women. Therefore, latanoprost should be used during pregnancy only if the maternal benefit justifies the potential fetal risk.

*Lactation*

It is not known whether latanoprost or its metabolites are excreted into human breast milk and the potential for adverse effects in the nursing infant from exposure to the drug are unknown. Because many drugs are excreted in human milk, caution should be used when latanoprost is administered to a nursing mother

**Adverse Effects / Undesirable Effects**

*Ophthalmic Disorders:*

Ocular irritation(burning, grittiness, itching, stinging and foreign body sensation, blurred vision, redness, generalized discomfort and/or dryness,), conjunctival hyperaemia, transient punctate epithelial erosions, eyelid oedema, eyelid erythema, eyelid skin darkening iritis/uveitis,macular edema, including cystoid macular edema. corneal edema and erosions; conjunctivitis; eyelash and vellus hair changes (increased length, thickness, pigmentation, and number);keratitis;misdirected eyelashes sometimes resulting in eye irritation, photophobia, periorbital and lid changes resulting in deepening of the eyelid sulcus. blepharitis, discomfort or pain, increased pigmentation of the iris, herpes simplex keratitis,

*Nervous System Disorders:* Dizziness, headache

*Respiratory, Thoracic and Mediastinal Disorders*: Asthma, asthma aggravation, acute asthma attacks, and dyspnea

*Skin and Subcutaneous Tissue Disorders*: Darkening of the palpebral skin of the eyelids and localized skin reaction on the eyelids, skin rash.

*Musculoskeletal and Connective Tissue Disorders:* arthralgia, myalgia, back pain

*General Disorders and Administration Site Conditions*: Non-specific chest pain

**Overdose and Treatment**
Overdose data are limited. The risk of toxicity from inadvertent ingestion is low because the amount contained in the bottles of ophthalmic solution is small. There are no reports of ingestion or ocular administration of large doses of latanoprost in humans.

*Symptoms*
Apart from ocular irritation and conjunctival hyperemia, no other ocular adverse effects are known if latanoprost is overdosed.

*Treatment*
If overdosage with latanoprost occurs, treatment should be symptomatic.

**Storage Conditions**
*[eg Store below….°C , Storage after opening…]*

**Dosage Forms and Packaging Available**
*[Packaging type & pack size]*

**Name and Address of Manufacturer**
*[Name & full address of manufacturer]*

**Name and Address of Marketing Authorization Holder**
*[Name & full address of marketing authorization holder]*

**Date of Revision of Package Insert**
*[day/month/year ]*

*Updated September 2013*