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Latanoprost 0.005% ®

COMPOSITION

Each ml contains:
Latanoprost..... 50 mcg
Preservative
Benzalkonium Chloride NF 0.01%w/v
aqueous vehicle..... q.s.

Latanoprost Sterile Ophthalmic Solution is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma and ocular hypertension.

INDICATIONS

Latanoprost Sterile Ophthalmic Solution is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma and ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the affected eye(s) once daily in the evening. The dosage of Latanoprost Sterile Ophthalmic solution should not exceed once daily since it has been shown that more frequent administration may decrease the intraocular pressure lowering effect. Reduction of the intraocular pressure starts approximately 3 to 4 hours after administration and the maximum effect is reached after 8 to 12 hours. Latanoprost may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

CONTRAINDICATIONS

Known hypersensitivity to latanoprost, benzalkonium chloride or any other ingredients in this product.

PACKAGING INFORMATION

Latanoprost 0.005% Eye Drops..... Container of 2.5 ml

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DOSAGE FORM
Ophthalmic solution

DESCRIPTION
Latanoprost is a prostaglandin F2 (alpha) analogue. Latanoprost is a prostanoid selective FP receptor agonist which is believed to reduce the intraocular pressure by increasing the outflow of aqueous humor. Studies in animals and man suggest that the main mechanism of action is increased uveoscleral outflow.

PHARMACOLOGY: Pharmacodynamics

Mechanism of Action: Latanoprost is a prostanoid selective FP receptor agonist that is believed to reduce the intraocular pressure (IOP) by increasing the outflow of aqueous humor. Studies in animals and man suggest that the main mechanism of action is increased uveoscleral outflow. Elevated IOP represents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss.

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

Distribution: 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 4 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 (beta)-oxidation.

Excretion: The elimination of the acid of latanoprost from human plasma is rapid (t½ = 17 min) after both intravenous and topical administration. Systemic clearance is approximately 7 mL/min/kg. Following hepatic (beta)-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.

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WARNINGS AND PRECAUTIONS

Latanoprost has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris and periorbital tissue (eyelid) and increased pigmentation and growth of eyelashes. These changes may be permanent. Latanoprost may gradually change eyelashes; these changes include increased length, thickness, pigmentation, and number of lashes. Patients who are expected to receive treatment in only one eye should be informed about the potential for increased brown pigmentation of the iris, periorbital tissue, and eyelashes in the treated eye and thus, heterochromia between the eyes.

General

Latanoprost Sterile Ophthalmic Solution may gradually increase the pigmentation of the iris. The eye colour change is due to increased melanin content in the stromal melanocytes of the iris rather than to an increase in the number of melanocytes. This change may not be noticeable for several months to years .Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with Latanoprost can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

During clinical trials, the increase in brown iris pigment has not been shown to progress further upon discontinuation of treatment, but the resultant colour change may be permanent.

Eyelid skin darkening, which may be reversible, has been reported in association with the use of Latanoprost.

Latanoprost may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Latanoprost should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation.

Macular edema, including cystoid macular edema, has been reported during treatment with Latanoprost. These reports have mainly occurred in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for acular edema.

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There is limited experience with Latanoprost in the treatment of angle closure, inflammatory or neovascular glaucoma.

There have been reports of bacterial keratitis associated with the use of multipledose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface

(Contact lenses should be removed prior to the administration of Latanoprost, and may be reinserted 15 minutes after administration

Drug Interactions In vitro studies have shown that precipitation occurs when eye drops containing thimerosal are mixed with Latanoprost. If such drugs are used they should be administered with an interval of at least five (5) minutes between applications.

Pregnancy
Pregnancy Category C
There are no adequate and well-controlled studies in pregnant women.
Latanoprost should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation
It is not known whether this drug or its metabolites are excreted in human milk.
Because many drugs are excreted in human milk, caution should be exercised when latanoprost is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

UNDESIRABLE EFFECTS
Eyelash changes (increased length, thickness, pigmentation, and number of lashes); eyelid skin darkening; intraocular inflammation (iritis/uveitis); iris pigmentation changes; and macular edema, including cystoid macular edema.

A TAJ PHARMACEUTICALS QUALITY PRODUCT
LATANOPROST 0.005%
Latanoprost Eye Drops /2.5 ml

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INFORMATION FOR PATIENTS

Patients should be informed about the possibility of iris color change due to anincrease of the brown pigment and resultant cosmetically different eye colorationthat may occur when only one eye is treated. Iris pigmentation changes may be more noticeable in patients with green-brown, blue/gray-brown or yellow-brown irises.

Patients should also be informed of the possibility of eyelash changes in the treated eye, which may result in a disparity between eyes in lash length, thickness, pigmentation, and/or number.

Patients should also be informed about the possibility of eyelid skin darkening. The increased pigmentation to the iris and eyelid, as well as the changes to the eyelashes, may be permanent.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures because this could cause the tip to become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

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

Patients should be advised that if they develop any ocular reactions, particularly conjunctivitis and lid reactions, they should immediately seek their physician's advice.

Patients should also be advised that Latanoprost contains benzalkonium chloride which may be absorbed by contact lenses. Contact lenses should be removed.