GLAUCOPROST®

TRAVOPROST 0.004%

STERILE OPHTHALMIC SOLUTION
Made in Argentina - Rx ONLY

Quali-Quantitative formula:
Each 100 ml of ophthalmic solution contains:
Travoprost 4.0 mg
Polyoxyl 40 hydrogenated castor oil 0.50 g; Tromethamine 0.12 g; Boric acid 0.30 g; Edetate disodium dihydrate 10.0 mg; Mannitol 4.60 g; Benzalkonium chloride 15.0 mg; Hydrochloric acid or sodium hydroxide q.s. pH; Purified water q.s.

Therapeutical action:
It reduces the elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension by increasing uveoscleral outflow of the aqueous humor.

Indications:
It is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are intolerant of other intraocular pressure lowering medications or insufficiently responsive to another intraocular pressure lowering medication (i.e., failed to achieve the desirable or ideal IOP, as determined after multiple measurements performed along a determined study period).

Pharmacological characteristics/Properties:
Pharmacological action
Travoprost free acid is a selective FP prostanoid receptor agonist. Based on researches, it is believed that Travoprost reduces intraocular pressure by increasing uveoscleral outflow of the aqueous humor.
Pharmacokinetics
Absorption: Travoprost is an isopropyl ester prodrug. Travoprost is absorbed through the cornea.
Distribution: In humans, peak plasma concentrations of Travoprost free acid (25 pg/mL or less) were reached within 30 minutes following topical ocular administration and was rapidly eliminated.
Biotransformation: Travoprost, an isopropyl ester prodrug, is hydrolyzed by esterases in the cornea to Travoprost free acid, which is its biologically active compound.
Travoprost free acid percentage reaching the systemic circulation, is transformed into inactive analog metabolites 1,2- dinor and 1,2,3,4-tetranor via beta-oxidation of the α-carboxylic acid chain, via oxidation of the 15-hydroxyl moiety, as well as via reduction of the 13,14 double bond.
Excretion: Elimination of travoprost free acid from human plasma is rapid. Plasma levels are below the limit of quantitation (< 10 pg/mL) within one hour following topical ophthalmic administration.

Dosage and administration:
The recommended dosage is one drop of Travoprost in the affected eye(s) once-daily in the evening.
The dosage should not exceed once-daily since it has been shown that the increased daily dose, decreases the intraocular pressure lowering effect. Travoprost may be used concomitantly with other topical ophthalmic antiglaucomatous drug products. Other topical ophthalmic drops should be instilled at least five (5) minutes apart after Travoprost administration.
Patients wearing contact lenses should remove them prior to the administration of Travoprost, and then wait for 15 minutes before reinserting them.
Reduction of intraocular pressure starts approximately 2 hours after administration of Travoprost, and the maximum effect is reached after 12 hours.

Contraindications:
Known hypersensitivity to some ingredients of GLAUCOPROST®.
Travoprost may be abortive, and therefore it should not be used by women during pregnancy or by women with suspected pregnancy.

Warnings:
Travoprost has been reported to cause changes to pigmented tissues. The most frequently reported changes have been:
- ***increased pigmentation of the iris and eyelid***
- ***increased pigmentation and growth of eyelashes.***

Travoprost may gradually change iris color, increasing the amount of brown pigmentation in the iris by increasing the number of melanosomes (pigment granules) in melanocytes.
This effect was more frequently observed in patients with mixed colored irides, i.e., blue-brown, grey-brown, green-brown or yellow-brown; however, it has also been observed in patients with brown irides. This change is believed to be due to increased melanin content in the stromal melanocytes of the iris.
The long term effects on the melanocytes and the consequences of potential injury to the melanocytes and/or deposition of pigment granules to other areas of the eye are currently unknown.
The change in iris color occurs slowly and may not be noticeable for months to years.
Patients should be informed of the possibility of iris color change, before prescribing a treatment with GLAUCOPROST®.
Eyelid skin darkening has been reported in association with the use of Travoprost.
Travoprost may gradually change eyelashes; these changes include increased length, thickness, pigmentation, and/or number of eyelashes.
The unilateral treatment could result in a permanent heterochromia (iris change color, periorbital tissue, and eyelashes between the eyes) and in a potential disparity between the eyes in length, thickness, and number of eyelashes.

Precautions:
Patients may slowly develop an increased brown pigmentation of the iris. This change may not be noticeable for months or years. The exact mechanism of action is unknown at this time. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become brownish. Until more information about increased brown pigmentation is available, patients should be examined regularly and, depending on the situation, treatment may be stopped if increased pigmentation ensues. During clinical researches, the increased iris brownish pigmentation does not continue progressing after treatment discontinuation, but the resulting color change may be permanent. The iris nevus or freckles were not affected by the treatment.
Travoprost should be used with caution in patients with active intraocular inflammation (iritis/uveitis).
Macular edema, including cystoid macular edema, has been reported during treatment with Travoprost ophthalmic solution. Travoprost should be used with caution in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.
There is no experience with the Travoprost use in angle closure, inflammatory or neovascular glaucoma.
Travoprost has not been studied in patients with renal or hepatic failure and should be used with caution in such patients.
Since prostaglandins are biologically active and may be absorbed through the skin, women who are pregnant or attempting to become pregnant should exercise appropriate precautions to avoid direct exposure to the contents of the bottle. In case of accidental contact with the contents of the bottle, thoroughly cleanse the exposed area with soap and water immediately.
Information for patients
Patients should be advised about the possibility of a gradual color change in the iris, darkening and increased growth of eyelashes, eyelid skin darkening and the possible resulting cosmetic difference when only one eye is treated. These changes may be permanent.
Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, the surrounding structures, the fingers or any other surface, 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 should also 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 multi-dose 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 be advised that GLAUCOPROST® ophthalmic solution contains benzalkonium chloride which may be absorbed by contact lenses. Contact lenses should be removed prior to the administration of the solution. Lenses may be reinserted 15 minutes following administration of Travoprost. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.
Carcinogenesis, Mutagenesis, Impairment of fertility
Travoprost was not mutagenic in the Ames test, murine micronucleus test and rat chromosome aberration assay. A slight increase in the mutant frequency was observed in one of two murine lymphoma assays in the presence of rat S-9 activation enzymes.
Travoprost did not affect mating or fertility rates in male or female rats at subcutaneous doses up to 10 µg/kg/day (about 250 times the maximum recommended human ocular dose). At 10 µg/kg/day, the mean number of corpora lutea was reduced, and the post-implantation losses were increased. These effects were not observed at 3 µg/kg/day (75 times the maximum recommended human ocular dose).
Pregnancy
Travoprost was teratogenic in rats, at intravenous (IV) doses up to 10 µg/kg/day (about 250 times the maximum recommended human ocular dose), evidenced by an increase in the incidence of skeletal malformations as well as external and visceral malformations, such as fused sternebrae and hydrocephaly. Travoprost was not teratogenic in rats at IV doses up to 3 µg/kg/day (75 times the maximum recommended human ocular dose), and in mice at subcutaneous doses up to 1.0 µg/kg/day (25 times the maximum recommended human ocular dose).
No adequate and well-controlled studies have been performed in pregnant women, since that animal reproduction studies, not always are predictive of human response. Travoprost may interfere with the maintenance of pregnancy and should not be used by women during pregnancy or by women with suspected pregnancy.
Nursing mothers
It is not known whether Travoprost is excreted in human milk; caution should be exercised when Travoprost is administered to a nursing woman.
Pediatric use
Safety and effectiveness in pediatric patients have not been established.
Geriatric use
No clinical differences in safety and effectiveness have been observed between elderly and other adult patients.

Adverse reactions:
The most common ocular adverse event observed in controlled clinical studies with Travoprost was ocular hyperemia which was reported in 35 to 50% of patients. Approximately 3% of patients discontinued therapy due to conjunctival hyperemia.
Ocular adverse events reported in 5 to 10% of patients included decreased visual acuity, eye discomfort, foreign body sensation, eye pain, and pruritus.
Ocular adverse events reported in a lower proportion, in 1 to 4% of treated patients included, abnormal vision, blepharitis, blurred vision, conjunctivitis, dry eye, eye disorder, flare, iris discoloration, keratitis, lid margin crusting, photophobia, subconjunctival hemorrhage, and tearing. Systemic adverse events more frequently observed with Travoprost, reported at a rate of 1 to 5% were accidental injury, angina pectoris, anxiety, arthritis, back pain, bradycardia, bronchitis, chest pain, cold syndrome, depression, dyspepsia, gastrointestinal disorder, headache, hypercholesterolemia, hypertension, hypotension, infection, pain, prostate disorder, sinusitis, urinary incontinence, and urinary tract infection.

Overdosage:
There is no available information about overdosage in humans. In case of overdosage with Travoprost ophthalmic solution 0.004%, a symptomatic treatment should be instituted.
In case of accidental overdosage or administration, go to the nearest hospital or toxicology centers.

How supplied:
Container with 1 dropper bottle, containing 3 ml sterile ophthalmic solution, including its corresponding package insert.

Storage conditions:
Store between 2°C and 25°C.

Once the container is opened, it should be used within 6 weeks.

Keep drugs out of reach of children.

Delicate use product. To be administered under prescription and medical surveillance.

Manufactured by:
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