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DorvistaTM T

Preservative Free Eye Drops 5 mL

(Dorzolamide Hydrochloride with Timolol Maleate Eye Drops IP)

COMPOSITION:

Dorzolamide Hydrochloride IP equivalent to Dorzolamide	2% w/v
Timolol Maleate IP equivalent to Timolol	0.5% w/v
Aqueous Vehicle	q.s.

Dorvista T is supplied as a sterile, isotonic, buffered, slightly viscous, aqueous solution.

Indications:

Dorvista T is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to beta-blockers (failed to achieve target IOP determined after multiple measurements over time).

Pharmacodynamic properties:

Dorvista T is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decreases elevated intraocular pressure, whether or not associated with glaucoma, by reducing aqueous humor secretion. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. The higher the level of intraocular pressure, the greater the likelihood of glaucomatous field loss and optic nerve damage.

Dorzolamide hydrochloride is an inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a beta 1 and beta 2 (non-selective) adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anesthetic (membrane-stabilizing) activity. The combined effect of these two agents administered as a fixed dose combination b.i.d. results in additional intraocular pressure reduction compared to either component administered alone, but the reduction is not as much as when dorzolamide t.i.d. and timolol b.i.d. are administered concomitantly.

Pharmacokinetics:

Dorzolamide hydrochloride:

When topically applied, dorzolamide reaches the systemic circulation. To assess the potential for systemic carbonic anhydrase inhibition following topical administration, drug and metabolite concentrations in RBCs and plasma and carbonic anhydrase inhibition in RBCs were measured. Dorzolamide accumulates in RBCs during chronic dosing as a result of binding to CA-II. The parent drug forms a single N-desethyl metabolite, which inhibits CA-II less potently than the parent drug but also inhibits CA-I. The metabolite also accumulates in RBCs where it binds primarily to CA-I. Plasma concentrations of dorzolamide and metabolite are generally below the assay limit of quantitation. Dorzolamide binds moderately to plasma proteins (approximately 33%).

Dorzolamide is primarily excreted unchanged in the urine; the metabolite also is excreted in urine. After dosing is stopped, dorzolamide washes out of RBCs nonlinearly, resulting in a rapid decline of drug concentration initially, followed by a slower elimination phase with a half-life of about four months.

Timolol Maleate:

In a study of plasma drug concentrations in six subjects, the systemic exposure to timolol was determined following twice daily topical administration of timolol maleate ophthalmic solution 0.5%. The mean peak plasma concentration following morning dosing was 0.46 ng/mL.

Dosage And Administration:

The dose is one drop of Dorvista T in the affected eye(s) two times daily.

If more than one topical ophthalmic drug is being used, the drugs should be administered at least ten minutes apart.

Use in special populations (such as pregnant women, lactating women, pediatric patients, geriatric patients etc.): See precautions, warnings and contraindications.

Contraindications:

Dorvista T is contraindicated in patients with

Bronchial asthma;

A history of bronchial asthma;

Severe chronic obstructive pulmonary disease ;

Sinus bradycardia;

Second or third degree atrioventricular block;

Overt cardiac failure;

Cardiogenic shock; or

Hypersensitivity to any component of this product.

Warnings and Precautions:**Systemic Exposure:**

Dorvista T contains dorzolamide, a sulfonamide, and timolol maleate, a beta-adrenergic blocking agent; and although administered topically, is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides and/or systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate . Fatalities have occurred, although rarely, due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sensitization may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

General:

Dorzolamide has not been studied in patients with severe renal impairment ($\text{CrCl} < 30 \text{ mL/min}$). Because dorzolamide and its metabolite are excreted predominantly by the kidney, Dorvista T is not recommended in such patients.

Dorzolamide has not been studied in patients with hepatic impairment and should therefore be used with caution in such patients.

While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

In clinical studies, local ocular adverse effects, primarily conjunctivitis and lid reactions, were reported with chronic administration of Dorvista T. Many of these reactions had the clinical appearance and course of an allergic-type reaction that resolved upon discontinuation of drug therapy. If such reactions are observed, Dorvista T should be discontinued and the patient evaluated before considering restarting the drug.

The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. Dorvista T has not been studied in patients with acute angle-closure glaucoma.

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

Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness).

Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

There have been reports of bacterial keratitis associated with the use of multiple dose 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.

Information for Patients:

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product.

Dorvista T contains dorzolamide (which is a sulfonamide) and although administered topically is absorbed systemically. Therefore the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration. Patients should be advised that if serious or unusual reactions or signs of hypersensitivity occur, they should discontinue the use of the product.

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

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 or if the tip of the dispensing container contacts the eye or surrounding structures, 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 contaminated solutions.

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

If more than one topical ophthalmic drug is being used, the drugs should be administered at least ten minutes apart.

Pregnancy:

Teratogenic Effects .Pregnancy Category C.

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

Lactating women:

It is not known whether dorzolamide is excreted in human milk. Timolol maleate has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from Dorvista T in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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.

Side effects:

Dorzolamide –timolol fixed dose combination was evaluated for safety in 1035 patients with elevated intraocular pressure treated for open-angle-glaucoma or ocular hypertension. Approximately 5% of all patients discontinued therapy with Dorzolamide –timolol fixed dose combination because of undesirable effects. The most frequently reported undesirable effects were taste perversion (bitter, sour, or unusual taste) or ocular burning and/or stinging in up to 30% of patients. Conjunctival hyperemia, blurred vision, superficial punctate keratitis or eye itching were reported between 5-15% of patients. The following

undesirable effects were reported in 1-5% of patients: abdominal pain, back pain, blepharitis, bronchitis, cloudy vision, conjunctival discharge, conjunctival edema, conjunctival follicles, conjunctival injection, conjunctivitis, corneal erosion, corneal staining, cortical lens opacity, cough, dizziness, dryness of eyes, dyspepsia, eye debris, eye discharge, eye pain, eye tearing, eyelid edema, eyelid erythema, eyelid exudate/scales, eyelid pain or discomfort, foreign body sensation, glaucomatous cupping, headache, hypertension, influenza, lens nucleus coloration, lens opacity, nausea, nuclear lens opacity, pharyngitis, post-subcapsular cataract, sinusitis, upper respiratory infection, urinary tract infection, visual field defect, vitreous detachment.

Overdosage:

There are no human data available on overdosage with Dorzolamide-timolol fixed dose combination.

Symptoms consistent with systemic administration of beta-blockers or carbonic anhydrase inhibitors may occur, including electrolyte imbalance, development of an acidotic state, dizziness, headache, shortness of breath, bradycardia, bronchospasm, cardiac arrest and possible central nervous system effects. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored

A study of patients with renal failure showed that timolol did not dialyze readily.

Shelf-life: 24 months from the date of manufacturing

Storage and handling instructions:

Store below 30°C. Do Not Freeze. Use the solution within one month after opening the container.

Do not touch the tip of the container to any surface. Replace cap after using. Protect from light.

KEEP OUT OF REACH OF CHILDREN

NOT FOR INJECTION

FOR EXTERNAL USE ONLY

Presentation:

Dorvita T preservative free eye drops: 5 mL of clear, colourless solution in a white opaque preservative free bottle.

Directions for use :



Turn the cap anti-clockwise to open the bottle.

Tilt your head backwards and gently pull down the lower eyelid to form a pocket.



Hold the bottle above the eye & gently squeeze one drop into the pocket.

Shake the bottle once to get rid of any remaining solution from the tip.



Recap the bottle after every use.

Manufactured in INDIA by :

Senses Pharmaceuticals Pvt. Ltd.,

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TM: Trademark for Registration

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