Droptim

Sterile Ophthalmic Solution

(Dorzolamide HCl + Timolol Maleate)

ڈروپٹم

جراثیم سے پاک آنکھوں کے قطرے

(ڈورزولامائیڈ ایچ سی ایل + ٹمولول میلیٹ)

COMPOSITION

Each ml contains:

Dorzolamide (as hydrochloride)..... 20mg

Timolol (as maleate).....5mg

(USP Specifications)

DESCRIPTION

Droptim is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decrease 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.

MECHANISM OF ACTION

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.

INDICATIONS AND USAGE

Droptim 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).

DOSAGE AND ADMINISTRATION

The dose is one drop of Droptim 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.

PHARMACOKINETICS & PHARMACODYNAMICS

- **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 (15nM).

- **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.

WARNINGS

- **Systemic Exposure**

Droptim 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.

- **Cardiac Failure**

Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition by beta- adrenergic receptor blockade may precipitate more severe failure.

- **Obstructive Pulmonary Disease**

Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma, in which Droptim is contraindicated.

- **Major Surgery**

The necessity or desirability of withdrawal of beta- adrenergic blocking agents prior to major surgery is controversial.

- **Diabetes Mellitus**

Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.

- **Thyrotoxicosis**

Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to. avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.

PRECAUTIONS

General

Dorzolamide has not been studied in patients with severe renal impairment (CrCl <30 ml/min). Because dorzolamide and its metabolite are excreted predominantly by the kidney, Droptim 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.

- **Pregnancy**

Teratogenic Effects. Pregnancy Category C. Droptim should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

- **Nursing Mothers**

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 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**

The safety and effectiveness of dorzolamide hydrochloride ophthalmic solution and timolol Maleate ophthalmic solution has been established when administered individually in pediatric patients aged 2 years and older. Use of these drug products in these children is supported by evidence from adequate and well-controlled studies in children and adults. Safety and efficacy in pediatric patients below the age of 2 years have not been established.

- **Geriatric Use**

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

ADVERSE REACTIONS

The most frequently reported adverse events 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 adverse events 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-sub-capsular cataract, sinusitis, upper respiratory infection, urinary tract infection, visual field defect, vitreous detachment.

General, depression, diarrhea, dry mouth, dyspnea, heart block, hypotension, iridocyclitis, myocardial infarction, nasal congestion, paresthesia, photophobia, respiratory failure, skin rashes, urolithiasis, and vomiting.

OVERDOSAGE

There are no human data available on overdosage with Dorzolamide / Timolol 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.

DRUG INTERACTIONS

- **Carbonic anhydrase inhibitors:**

There is a potential for an additive effect on the known systemic effects of carbonic.anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor.

- **Beta-adrenergic blocking agents:**

Patients who are receiving a beta-adrenergic blocking agent orally and Droptim should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure.

- **Calcium antagonists:**

Caution should be used in the co-administration of beta-adrenergic blocking agents, such as Droptim, and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension.

- **Catecholamine-depleting drugs:**

Close observation of the patient is recommended when a beta blocker is administered to patients receiving catecholamine- depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.

- **Digitalis and calcium antagonists:**

The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

CONTRAINDICATIONS

Droptim 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.

HOW SUPPLIED

5ml sterile ophthalmic solution in plastic dropper bottle.

STORAGE & INSTRUCTIONS:

Store between 15-25°C. Protect from heat, sunlight, moisture and do not freeze. Keep away from the reach of children. Use within one month after first opening the bottle and discard the remaining portion.

Do not touch the dropper tip to any surface as this may contaminate the solution.

To be sold on the prescription of a registered medical practitioner only.

For ophthalmic use only.

خوراک و ہدایات: ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔ دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔ دھوپ، گرمی، نمی، اور منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ پہلی دفعہ بوتل کھولنے کے بعد دوا کو ایک ماہ تک استعمال کریں۔ صرف مستند ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:

PHARMASOL

PRIVATE LIMITED

Plot # 549,Sundar Industrial Estate, Lahore, Pakistan.

PM-1197-00

120 x 170mm

* Sign. Client

* Sign. Marketing Deptt. Shannza

* Sign. Designer Shannza

* for Design, Text, Size, Color & Color Placement

* Sign. Head of Design Deptt. Shannza