Dorzolamide HCl/Timolol Maleate Ophthalmic Solution contains dorzolamide hydrochloride and timolol maleate as the active ingredients. Dorzolamide hydrochloride 20 mg/mL and timolol maleate 5 mg/mL (6.83 mg/mL). This fixed-dose combination is for topical ocular use.

**INDICATIONS AND USAGE**

1. **Elevated Intraocular Pressure (IOP)**

   Dorzolamide HCl/Timolol Maleate Ophthalmic Solution is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to other topical medications.

2. **Secondary Open-angle Glaucoma**

   This combination is also indicated for the treatment of secondary open-angle glaucoma associated with ocular hypertension or primary open-angle glaucoma due to pigment dispersion.

**CONTRAINDICATIONS**

1. **Beta-blocker hypersensitivity**

2. **Second or third-degree atrioventricular block**

3. **Severe bradycardia**

4. **Hypertrophic subaortic stenosis**

5. **Angioedema**

**WARNINGS AND PRECAUTIONS**

1. **Cardiovascular Effects**

   Beta-adrenergic blocking agents should be administered with caution to patients with heart failure. Many patients with heart failure do not demonstrate the usual rise in pulse rate that might lead to the diagnosis of coronary insufficiency. Non-cardiovascular agents are indicated. When using timolol in the treatment of hypertension, beta-blockers may prevent the diagnosis of coronary insufficiency.

2. **Great Adverse Reactions**

   Severe respiratory reactions, including death have been reported in conjunction with the use of topical beta-blockers. There have been reports of patients who have developed angioedema in the eye after exposure to timolol. These reactions have been reported in patients with a history of asthma or angioedema.

3. **Pigmentary Changes**

   The use of timolol ophthalmic drops has been associated with pigmented changes to the iris, which can occur in both adults and children. These changes do not appear to result in any loss in vision. The iris may appear blue gray to light gray. The incidence of this effect may be greater in patients with blue or brown irises.

4. **Diabetes Mellitus**

   In general, beta-adrenergic blocking agents should be administered with caution to patients with diabetes mellitus. Beta-adrenergic blocking agents may mask the early symptoms of hypoglycemia, such as tachycardia, by reducing the physical activity of the beta-adrenergic system.

5. **Renal and Hepatic Impairment**

   Dorzolamide has not been studied in patients with hepatic impairment and should therefore be used with caution in such patients. Timolol Maleate Ophthalmic Solution is not recommended in such patients.

6. **Reproductive System**

   Pregnancy: It is unknown if Dorzolamide HCl/Timolol Maleate Ophthalmic Solution can cause fetal harm when administered to pregnant women. Use in pregnant women only when clearly needed. It is also unknown if timolol crosses the placenta or is distributed in human breast milk.

   Lactation: It is unknown if timolol crosses the placenta or is distributed in human breast milk. Use Dorzolamide HCl/Timolol Maleate Ophthalmic Solution with caution if lactation is necessary.

7. **Hypersensitivity Reactivity**

   Increased Reactivity to allergens may be more reactive to repeated accidental, diagnostic, or therapeutic use of timolol. Timolol Maleate should not be used if the patient has any history of sensitivity to this drug. Reactivity to allergens may increase in patients receiving timolol for ocular application.

**ADVERSE REACTIONS**

1. **Local Reactions:**

   - Foreign body sensation
   - Burning
   - Stinging
   - Redness
   - Irritation

2. **Systemic Reactions:**

   - Headache
   - Dizziness
   - Fatigue
   - Muscle weakness
   - Dryness of mouth
   - Nausea
   - Vomiting
   - Urinary retention

**OVERDOSAGE**

1. **Acute Overdose:**

   There is limited evidence on the treatment of patients who have consumed excessive doses of dorzolamide hydrochloride or timolol maleate. However, the management should be similar to the management of patients who have consumed excessive doses of other ophthalmic agents. Theophylline, if present, should be treated with supportive measures. Supports include intubation and mechanical ventilation. Supportive measures should be continued until the patient is stable.

2. **Management of Overdose:**

   The management of overdose should be supportive. No specific treatment is available for overdose of dorzolamide hydrochloride or timolol maleate. Supportive measures include intubation and mechanical ventilation. Treatment should be continued until the patient is stable.

**PATIENT INFORMATION**

1. **Dorzolamide HCl/Timolol Maleate Ophthalmic Solution**

   - To open the bottle, remove the shrink neck band and unscrew the cap to avoid contamination.
   - After each use, rinse out the tip of the bottle and cap with saline solution.
   - Place 1 drop into the eye of the affected eye(s) twice daily. The usual dose is one drop in the morning and one drop in the evening.
   - If you have diabetes, thyroid disease, or muscle weakness, consult your doctor before using this product.
   - Avoid touching the tip of the bottle to your eye, eyelid, fingers, or other surfaces.
   - Do not refrigerate the medication.
   - Use this medication for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to other topical medications.

2. **Dorzolamide HCl/Timolol Maleate Ophthalmic Solution**

   - Do not use if you have eye infections, red or swollen eyes, or if you develop an eye infection.
   - Do not use if you plan on having any type of surgery.
   - Do not use if you have a history of bronchial asthma, severe chronic obstructive pulmonary disease, or a history of bronchospastic disease (other than bronchial asthma).
   - Do not use if you have a history of heart disease, including heart failure.
   - Do not use if you have a history of MI, angina, or a history of hypertension.

**DOSAGE AND ADMINISTRATION**

1. **The usual dose is one drop in the morning and one drop in the evening.**

2. **How should I use Dorzolamide HCl/Timolol Maleate Ophthalmic Solution?**

   - Place 1 drop into the eye of the affected eye(s) twice daily.
   - If you have diabetes, thyroid disease, or muscle weakness, consult your doctor before using this product.
   - Avoid touching the tip of the bottle to your eye, eyelid, fingers, or other surfaces.
   - Do not refrigerate the medication.
   - Use this medication for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to other topical medications.

3. **How long should I use it?**

   - Treatment lasting more than 1 year has not been studied in patients with open-angle glaucoma or ocular hypertension. Your doctor will determine the length of your treatment.

4. **Possible side effects**

   - Burning, stinging, irritation, redness, foreign body sensation
   - Headache, dizziness, fatigue, muscle weakness, dryness of mouth, nausea, vomiting, urinary retention
Clonidine (for example, Catapres)
Injectable epinephrine (for example, EpiPen)
Oral beta-blockers (for example, propranolol, Inderal)
Severe skin reactions

Tell your doctor or pharmacist about all drugs that you are using or

7. Replace the cap on bottle and turn until closed.

When topically applied, dorzolamide reaches the systemic circulation.

12.3 Pharmacokinetics

Intraocular pressure reduction compared to either component

of the eye decreases aqueous humor secretion, presumably by

anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes

pressure, the greater the likelihood of glaucomatous field loss and

12.1 Mechanism of Action

Benzalkonium chloride 0.0075% is added as a preservative.

mg of dorzolamide hydrochloride) and 5 mg timolol (6.83 mg Timolol

Maleate USP is described chemically as: (-)-1-(4-(ethylamino)-5,6-dihydro-6-methyl-4

Dorzolamide Hydrochloride USP is optically active. The specific

11 DESCRIPTION

Symptoms consistent with systemic administration of beta-blockers

importance of the drug to the mother.

8.3 Nursing Mothers

It is not known whether dorzolamide is excreted in human milk.

8.2 Lactation

Fetal ossification was observed at this dose in rats, there were no

demonstrated no evidence of fetal malformations. Although delayed

vertebral bodies. These malformations occurred at doses that caused

hydrochloride in rabbits at oral doses of ≥2.5 mg/kg/day (37 times the

Teratogenic Effects.

13.1 Human Reproduction

Adverse reactions that are attributable to sulfonamides may occur with

topically, is absorbed systemically. Therefore the same types of

effects of carbonic anhydrase inhibition in patients receiving an oral

13.2 Animal Reproduction

because of possible atrioventricular conduction disturbances, left

blocking agents, such as Dorzolamide HCl/Timolol Maleate

Caution should be used in the coadministration of beta-adrenergic

7.3 Beta-Adrenergic Blocking Agents

these disturbances have been reported with oral carbonic anhydrase

Clinical trials with dorzolamide hydrochloride ophthalmic solution,

inhibitors is not recommended.

Ophthalmic Solution. The concomitant administration of Dorzolamide

effects of carbonic anhydrase inhibition in patients receiving an oral

13 NONCLINICAL TOXICOLOGY

mean peak plasma concentration following morning dosing was

Dorzolamide is primarily excreted unchanged in the urine; the

proteins (approximately 33%). Dorzolamide binds moderately to plasma

15.7.2 Schistosomiasis Neutrogena

17.2 Potential for Exacerbation of Asthma and COPD

17.1 Potential for Exacerbation of Asthma and COPD

15.7.1 Ocular Effects

15.1.4 Ocular Pharmacology

aqueous humor and the iridal sphincter muscles, that may lead to a decrease in

inclusion of 15 mg/kg/day (90 times the recommended human ophthalmic dose) in rats,

bovine, and monkey. The dose of 15 mg/kg/day was selected to provide 40 mg/kg/day

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats,

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats,

inclusion of 15 mg/kg/day (90 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (60 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (90 times the recommended human ophthalmic dose) in rats.

inclusion of 15 mg/kg/day (90 times the recommended human ophthalmic dose) in rats.