I.O.P

Eye Drops

Composition

Dorzolamide (As Hydrochloride) 2%

Action

Carbonic anhydrase (CA) is an enzyme found in many tissues of the body including the eye. In humans, carbonic anhydrase exists as a number of isoenzymes, the most active being carbonic anhydrase II (CA-II) found primarily in red blood cells (RBCs) but also in other tissues. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion. The result is a reduction in intraocular pressure (IOP).

I.O.P Ophthalmic Solution contains dorzolamide hydrochloride, a potent inhibitor of human carbonic anhydrase II. Following topical ocular administration, I.O.P reduces elevated intraocular pressure, whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. Unlike miotics, I.O.P reduces intraocular pressure without the common adverse effects of miotics such as night blindness, accommodative spasm, and pupillary constriction. Unlike topical beta-blockers, I.O.P has minimal or no effect on pulse rate or blood pressure.

Topically applied beta-adrenergic blocking agents also reduce IOP by decreasing aqueous humor secretion but by a different mechanism of action. Studies have shown that when Dorzolamide added to a topical beta-blocker, additional reduction in IOP observed; this finding is consistent with the reported additive effects of beta-blockers and oral carbonic anhydrase inhibitors.

Pharmacodynamics

In patients with glaucoma or ocular hypertension, the efficacy of Dorzolamide given t.d.s. as monotherapy (baseline IOP >23 mm Hg) or given b.d. as adjunctive therapy while receiving ophthalmic beta-blockers (baseline IOP >22 mm Hg) was demonstrated in large-scale clinical studies of up to one-year duration. The IOP-lowering effect of Dorzolamide as monotherapy and as adjunctive therapy was demonstrated throughout the day and this effect was maintained during long-term administration. Efficacy during long-term monotherapy was similar to betaxolol and slightly less than timolol. When used as adjunctive therapy to ophthalmic beta-blockers, Dorzolamide demonstrated additional IOP lowering similar to pilocarpine 2% q.d.s.

Indications

I.O.P is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

Contraindications

I.O.P is contraindicated in-patients who are hypersensitive to any component of this product.

Warnings

I.O.P 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 with I.O.P

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 re-administered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

Adverse Reactions

The most frequent adverse events associated with Dorzolamide were ocular burning, stinging, or discomfort immediately following ocular administration (approximately one-third of patients). Approximately one- quarter of patients noted a bitter taste following administration. Superficial punctate keratitis occurred in 10-15% of patients and signs and symptoms of ocular allergic reaction in approximately 10%. Events occurring in approximately 1-5% of patients were blurred vision, tearing, dryness, and photophobia. Other ocular events and systemic events were reported infrequently, including headache, nausea, asthenia/fatigue; and, rarely, skin rashes, urolithiasis, and iridocyclitis.

Precautions

General

Carbonic anhydrase activity has been observed in both the cytoplasm and around the plasma membranes of the corneal endothelium. The effect of continued administration of I.O.P on the corneal endothelium has not been fully evaluated.

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

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

In clinical studies, local ocular adverse effects, primarily conjunctivitis and lid reactions, were reported with chronic administration of Dorzolamide. 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, Dorzolamide should be discontinued and the patient evaluated before considering restarting the drug.

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 and Dorzolamide. The concomitant administration of Dorzolamide and oral carbonic anhydrase inhibitors is not recommended.

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

The preservative in I.O.P, benzalkonium chloride, may be absorbed by soft contact lenses. I.O.P. should not be administered while wearing soft contact lenses.

Pregnancy

Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers

It is unknown whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Dorzolamide, 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 children have not been established.

Geriatric Use

No overall differences in effectiveness or safety were observed between patients and younger patients, but greater sensitivity of some older individuals to the product cannot be ruled out.

Drug Interactions

Although acid-base and electrolyte disturbances were not reported in the clinical trials with Dorzolamide, these disturbances have been reported with oral carbonic anhydrase inhibitors and have, in some instances, resulted in drug interactions (e.g., toxicity associated with high-dose salicylate therapy). Therefore, the potential for such drug interactions should be considered in patients receiving Dorzolamide.

Dosage and Administration

The dose is one drop of I.O.P in the affected eye(s) three times daily.

I.O.P 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 ten minutes apart.

Patient Information

Dorzolamide HCl is any eye drop used to treat increased pressure in the eye. or the drops to most effective, proper instillation into the eye is important. Your pharmacist or physician can instruct you. This drug may produce allergic reactions in those with sulfa allergies. Allergies can develop after several exposures and any signs of allergy (itchy watery eyes, rash, and difficulty breathing in severe cases) should be reported to a healthcare professional immediately.

This eye drop does contain a preservative (Benzalkonium chloride) to which some may be sensitive. It should not be used by those wearing contact lenses. With all eye drops, care should be taken to avoid touching the tip of the dropper to the eye or surrounding skin. This could cause contamination of the medication and result in a serious eye infection. Potentially contaminated solutions should be replaced. If you are using more than one eye drop medication, wait ten minutes between each medication.

Some patients will experience burning; itching or discomfort after instilling the eye drops, and fewer will experience a bitter taste in their mouth. Talk to your pharmacist or physician if you are concerned about eye discomfort.

Presentation

Bottle of 5 ml