PRODUCT CIRCULAR
Sterile Ophthalmic Solution
TRUSOPT®†
(dorzolamide hydrochloride ophthalmic solution, MSD)

I. THERAPEUTIC CLASS

TRUSOPT (dorzolamide hydrochloride ophthalmic solution, MSD) is a novel carbonic anhydrase inhibitor formulated for topical ophthalmic use. Unlike oral carbonic anhydrase inhibitors, TRUSOPT, which is administered topically, exerts its effects directly in the eye.

II. INDICATIONS

TRUSOPT Ophthalmic Solution is indicated in the treatment of elevated intraocular pressure in patients with:

- ocular hypertension
- open-angle glaucoma
- pseudoexfoliative glaucoma and other secondary open-angle glaucomas
- in the short-term treatment of pediatric glaucomas as adjunctive therapy to beta-blockers and for monotherapy.

III. DOSAGE AND ADMINISTRATION

When used as monotherapy, the dose is one drop of TRUSOPT Ophthalmic Solution in the affected eye(s) three times daily.

When used as adjunctive therapy with an ophthalmic beta-blocker, the dose is one drop of TRUSOPT in the affected eye(s) two times daily.

When substituting TRUSOPT for another ophthalmic antiglaucoma agent, discontinue the other agent after proper dosing on one day, and start TRUSOPT on the next day.

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

IV. CONTRAINDICATIONS

TRUSOPT is contraindicated in patients who are hypersensitive to any component of this product.

V. PRECAUTIONS

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TRUSOPT has not been studied in patients with severe renal impairment (CrCl < 30 mL/min). Because TRUSOPT and its metabolite are excreted predominantly by the kidney, TRUSOPT is not recommended in such patients.

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

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

TRUSOPT 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, including severe reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

In clinical studies, local ocular adverse effects, primarily conjunctivitis and lid reactions, were reported with chronic administration of TRUSOPT. Some 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, discontinuation of treatment with TRUSOPT should be considered.

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 TRUSOPT. The concomitant administration of TRUSOPT and oral carbonic anhydrase inhibitors has not been studied and is not recommended.

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

TRUSOPT Ophthalmic Solution contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses. Therefore, TRUSOPT should not be administered while wearing soft contact lenses. The contact lenses should be removed before application of the drops and not be reinserted earlier than 15 minutes after use.

There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Precautions should be used when prescribing TRUSOPT to this group of patients.

VI. PREGNANCY

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

VII. NURSING MOTHERS

It is not known whether this drug is excreted in human milk. 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.

VIII. PEDIATRIC USE

Safety and effectiveness in children have not been established.Safety and IOP-lowering effects of TRUSOPT have been evaluated in pediatric patients <6 years of age with glaucoma or elevated intraocular pressure (baseline IOP ≥22 mmHg). Use of TRUSOPT in this age group is supported by evidence from a 3-month, double-masked, active-treatment controlled study. (See XXIc1. Clinical Studies – Monotherapy)

IX. DRUG INTERACTIONS

Specific drug interaction studies have not been performed with TRUSOPT Ophthalmic Solution. In clinical studies, TRUSOPT was used concomitantly with the following medications without evidence of adverse interactions: timolol ophthalmic solution, betaxolol ophthalmic solution and systemic medications, including ACE-inhibitors, calcium channel blockers, diuretics, non-steroidal anti-inflammatory drugs including aspirin, and hormones (e.g. estrogen, insulin, thyroxine).

TRUSOPT is a carbonic anhydrase inhibitor and although administered topically, is absorbed systemically. In clinical studies, TRUSOPT was not associated with acid-base disturbances. However, 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 TRUSOPT.

X. SIDE EFFECTS

Adult Patients
In the previous long-term clinical studies of 1108 patients treated with TRUSOPT Ophthalmic Solution alone or as adjunctive therapy with ophthalmic beta-blockers, the most frequently reported drug-related adverse effects and local symptoms were: bitter taste, burning and stinging, blurred vision, eye itching, tearing, headache, conjunctivitis, eyelid inflammation, nausea, eyelid irritation and asthenia/fatigue. The most frequent cause of discontinuation (approximately 3%) from treatment with TRUSOPT was drug-related ocular adverse effects, primarily conjunctivitis and lid reactions. Iridocyclitis and rash were each reported rarely. There was one report of urolithiasis.

Pediatric Patients
In a 3-month, double-masked, active-treatment-controlled, multicenter study in 184 patients <6 years of age, the adverse experience profile of TRUSOPT was comparable to that seen in adult patients.

The most frequent adverse events associated with TRUSOPT in patients <2 years of age were ocular injection (5.4%) and eye discharge (3.6%). In patients ≥2 years but <6 years of age, the most frequent adverse events associated with TRUSOPT were burning/stinging in the eye (12.1%), ocular injection (7.6%), eye pain (3%), and eyelid inflammation (3%).

The following adverse reactions have been reported in post-marketing experience:

Hypersensitivity: signs and symptoms of local reactions including palpebral reactions and systemic allergic reactions including angioedema, bronchospasm, urticaria and pruritus

Nervous System: dizziness, paresthesia

Ocular: pain, redness, superficial punctate keratitis, transient myopia (which resolved upon discontinuation of therapy), eyelid crusting, choroidal detachment following filtration surgery

Skin/Mucous Membranes: contact dermatitis, epistaxis, throat irritation, dry mouth, Stevens-Johnson syndrome, toxic epidermal necrolysis

Urogenital: urolithiasis.

Xa. Laboratory Findings

TRUSOPT was not associated with clinically meaningful electrolyte disturbances.

XI. OVERDOSAGE

Treatment should be symptomatic and supportive. Electrolyte imbalance, development of an acidotic state, and possible central nervous system effects may occur. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

XII. AVAILABILITY

TRUSOPT® 2% (dorzolamide hydrochloride ophthalmic solution, MSD) is available in 5ml dispenser.

TRUSOPT Ophthalmic Solution is a clear, colorless to nearly colorless, slightly viscous solution.

XIIa. Storage

TRUSOPT Ophthalmic Solution:
Store at 15-30°C (59-86°F). Protect from light.