BRINZOTEN®

BRINZOLAMIDE 1%

STERILE OPHTHALMIC SUSPENSION
Made in Argentina - Rx ONLY

Formula:
Each 100 ml of ophthalmic suspension contains:
Brinzolamide 1000 mg
Mannitol 3300 mg; Carbopol 974 P 400 mg; Tyloxapol 250 mg; Sodium chloride 250 mg; Disodium edetate dihydrate 10 mg; Benzalkonium chloride 10 mg; 1N Hydrochloric acid / 10N Sodium hydroxide q.s. pH 7.5; Purified water q.s. 100 ml.

Therapeutic action:
Antiglaucoma agent.

Indications:
BRINZOTEN® is indicated for the treatment of elevated intraocular pressure in patients with ocular hypertension or open angle glaucoma.

Pharmacological action:
Pharmacodynamics
Brinzolamide is a sulfonamide and inhibits the carbonic anhydrase. This is an enzyme present in many tissues including the eye. Carbonic anhydrase catalyzes the hydration reversible reaction of the carbon dioxide and the dehydration of carbonic acid. In human beings, the carbonic anhydrase is present as isoenzymes, of which the carbonic anhydrase II is the most active enzyme. Inhibition of the carbonic anhydrase in the eye ciliary processes reduces secretion of the aqueous humor, likely by less formation of bicarbonate ions and the consequent reduction in sodium and eye fluids transportation. As a result, the intraocular pressure decreases as well as the optic nerve damage risk. In clinical studies of up to 3 months duration in patients with glaucoma or ocular hypertension, brinzolamide reduced the intraocular pressure in about 4 or 5 mmHg.
Pharmacokinetics
When topically applied into the eye, brinzolamide is systemically absorbed. In a study designed for pretending systemic absorption during prolonged topical administration into the eyes, healthy subjects were treated with 1 mg of oral brinzolamide twice a day for 32 weeks (the oral dose of 1 mg twice a day is very similar to the amount of active ingredient systemically released via the ophthalmic application of 1% brinzolamide in both eyes three times a day). Saturation of the carbonic anhydrase II in erythrocytes caused by brinzolamide (approximate concentrations of 20 µmol) was reached after 4 weeks, while the accumulation during equilibrium of the metabolite N-desethyl brinzolamide in erythrocytes (6 to 30 µmol) was observed from 20 to 28 weeks.
During chronic administration, brinzolamide is accumulated in erythrocytes by binding to the carbonic anhydrase II. The metabolite N-desethyl gets also accumulated in the erythrocytes by binding mainly to the carbonic anhydrase I in the presence of brinzolamide. Plasma concentrations of brinzolamide and the metabolite N-desethyl brinzolamide are generally below the minimum limit of 10 ng/ml.
Brinzolamide moderately binds to plasma proteins inn about 60%).
Biotransformation affects the metabolite N-desethyl which mainly binds to the carbonic anhydrase I in the presence of brinzolamide.
The half-life of brinzolamide in whole blood, after ocular topical administration, is about 111 days.
Brinzolamide is eliminated mainly intact by renal way. In urine, the metabolite N-desethyl brinzolamide and, in less proportion, the metabolites N-desmetoxypropil and O-desmethyl are also detected.

Posology and Way of administration:
1 drop in the affected eye(s), three times a day. BRINZOTEN® can be used concomitantly with other ocular topical anti-hypertensive agents. If more than one medication is used, they should be applied within 10 minute time interval.
Shake well before use.

Contraindications:
BRINZOTEN® is contraindicated in patients with known hypersensitivity to any of its components.

Warnings:
Brinzolamide is a sulfonamide and when it is administered by ocular topical way, it is systematically absorbed. Therefore, the same adverse reactions observed with the administration of sulfonamides can occur after topical administration of BRINZOTEN®.
If serious hypersensitive reactions occur, immediately stop the administration of the medication.

Precautions:
Patients sensitive to sulfonamides can also be sensitive to brinzolamide.
Vision can be temporarily blurred after the medication application; therefore, caution should be taken when driving vehicles or operating machinery.
Patients should be careful to avoid the drop vial from being in contact with the eye or with any other surfaces since the medication can get contaminated by bacteria causing ocular infections. Using contaminated solutions can cause serious eye damage and consequently, vision loss.
Patients will be instructed to immediately see a doctor or an eye specialist to determine if they will continue using the multiple dose drop vial if patients undergo surgery or if an intercurrent eye infection occurs (i.e., trauma or infection).
If more than one topical eye medication is used, medications should be applied within a 10 minute time period.
The preservative of BRINZOTEN® (benzalkonium chloride) can be absorbed by soft contact lenses. Contact lenses should be removed before instilling BRINZOTEN® and then they can be placed again 15 minutes after product application.
Interactions
Concomitant use of BRINZOTEN® with an oral inhibitor of the carbonic anhydrase is not recommended since there is a probability of a synergistic effect of the known systemic effects of the inhibition of the carbonic anhydrase in patients simultaneously treated with oral inhibitors of the carbonic anhydrase.
Even though clinical studies on brinzolamide showed no alterations of either the acid-basic relationship or the electrolyte relationship in patients treated with oral inhibitors of the carbonic anhydrase, patients treated with oral inhibitors of the carbonic anhydrase have exhibited infrequent cases of interactions with salicylates at high doses. Therefore, the possibility of such interaction should be considered in patients treated with BRINZOTEN®.
Carcinogenesis - Mutagenesis - Fertility disorders
No brinzolamide carcinogenicity data are available. The following tests on potential mutagenic effects resulted negative: in vivo murine micronucleous test; sister chromatid exchange assay, and the Ames test with E. coli. The in vitro murine lymphoma anticipated mutation assay was negative in the absence of microsomal activation, but it was positive in the presence of activation.
In reproduction tests conducted in rats treated with brinzolamide, no adverse effects were observed either on fertility or on the reproductive capacity of males and females with doses of up to 18 mg/kg/day (375 times the recommended ophthalmic dose in human beings).
Pregnancy
No studies with brinzolamide were conducted in pregnant women. BRINZOTEN® should be used during pregnancy only when the potential benefit justifies the risk for the fetus.
Lactation
It is not known whether brinzolamide is excreted into human milk. Due to the possibility of serious adverse reactions for the infant, the interruption of either the lactation or the treatment should be considered based on the importance of the treatment for the mother.
Pediatric use
Safety and effectivity of brinzolamide have not been determined in children.
Geriatric use
No data relating the age and effects of brinzolamide in geriatric patients are available.
Use with liver and renal failure
The topical use of brinzolamide has not been studied in patients with liver failure; therefore, BRINZOTEN® should be used with caution in those patients.
The topical use of brinzolamide has not been studied in patients with severe renal failure (clearance of creatinine < 30 ml/min). Since brinzolamide and its metabolite are mainly excreted by renal way, the use of BRINZOTEN® is not recommended in those patients.

Adverse reactions:
In clinical studies with 1% brinzolamide, the most common adverse reactions were blurred vision and bitter, sour or unusual taste. These reactions occurred in about 5% to 10% of patients.
With an incidence of 1 to 5% the following events were informed: blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular secretion, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus, and rhinitis.
With an incidence below 1%, the following adverse reactions were informed: allergic reactions, alopecia, thoracic pain, conjunctivitis, diarrhea, diplopia, dizziness, dry mouth, dyspnea, dyspepsia, eyestrain, hypertonia, keratoconjunctivitis, keratopathy, renal pain, sticky sensation or sensation of having scabs on the eyelids, nausea, pharyngitis, tearing, and hives.

Overdosage:
Even though data from human beings are not available, after an oral administration of an overdose, the following events can occur: electrolyte imbalance, development of an acidotic state and possible effects on the nervous system. Sera level of electrolytes, particularly potassium, should be monitored as well as blood pH.
If an overdosage occurs, go to the nearest Hospital or Toxicology center.

How supplied:
Dropper vial containing 5 ml of sterile ophthalmic suspension.

Storage conditions:
Store below 30° C.

Once the container is opened for the first time, it should be used within 4 weeks.

Keep drugs out of reach of children.

Delicate use product. To be administered under prescription and medical surveillance.

Manufactured by:
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Technical Director:
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