BRIMOPRESS®

BRIMONIDINE TARTRATE 0.2%

STERILE OPHTHALMIC SOLUTION
Made in Argentina - Rx ONLY

Qualitative-quantitative formula:
Each ml of solution contains:
Brimonidine tartrate 2.00 mg
Preservative: Benzalkonium chloride 0.05 mg; Polyvinyl alcohol 14.00 mg; Sodium chloride 7.00 mg; Sodium citrate dihydrate 4.50 mg; Citric acid monohydrate 0.50 mg; Hydrochloride acid or Sodium hydroxide, q.s. to adjust pH 6.4.; Purified water, q.s. 1.00 ml.

Therapeutical action:
Brimonidine tartrate 0.2% has the action of lowering intraocular pressure (IOP) with minimal effect on cardiovascular and pulmonary parameters.

Indications:
It is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Pharmacological characteristics/ Properties:
It is an alpha-adrenergic receptor agonist. It has a peak hypotensive effect occurring at two hours post-dosing. Fluorophotometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action by reducing aqueous humor production and increasing uveoscleral outflow.
Pharmacokinetics:
After ocular administration of a 0.2% solution, plasma concentrations peaked within 1 to 4 hours and declined with a systemic half-life of approximately 3 hours.
In humans, systemic metabolism of brimonidine tartrate is extensive. It is metabolized primarily by the liver. Urinary excretion is the major route of elimination of the drug and its metabolites. Approximately 87% of an orally-administered radioactive dose was eliminated within 120 hours, with 74% found in the urine.

Dosage and Administration:
Solution for topical ophthalmic administration.
The recommended dose is one drop of Brimonidine tartrate 0.2% ophthalmic solution b.i.d or t.id., which should be separated by regular intervals.

Contraindications:
Brimonidine tartrate is contraindicated in patients with hypersensitivity to brimonidine tartrate or any component of this medication. It is also contraindicated in patients receiving monoamine oxidase (MAO) inhibitor therapy.

Precautions:
General
Although Brimonidine tartrate 0.2% had minimal effect on blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.
BRIMOPRESS® has not been studied in patients with hepatic or renal disorder; therefore caution should be used in treating such patients.
BRIMOPRESS® should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangeitis obliterans.
During the studies there was a loss of effect in some patients. The IOP-lowering efficacy with BRIMOPRESS® during the first month of therapy may not always reflect the long-term level of IOP reduction. Patients prescribed IOP-lowering medication should be routinely monitored for IOP.
Patient Information:
BRIMOPRESS® contains benzalkonium chloride as preservative which may be absorbed by soft contact lenses. Patients wearing soft contact lenses should be instructed to wait at least 15 minutes after instilling BRIMOPRESS® to reinsert soft contact lenses.
As with other drugs in this class, BRIMOPRESS® may cause fatigue and/or drowsiness in some patients. Patients who engage in hazardous activities should be cautioned of the potential for a decrease in mental alertness.
Drugs Interactions
Although specific drug interaction studies have not been conducted with BRIMOPRESS®, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.
BRIMOPRESS® did not have significant effects on pulse or blood pressure in clinical studies. However, since alpha-agonists, as a class, may reduce pulse and blood pressure, caution in using concomitant drugs such as beta-blockers (ophthalmic and systemic), antihypertensives, and/or cardiac glycosides is advised.
Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with BRIMOPRESS® can lead to an interference in IOP-lowering effect.
No data on the level of circulating catecholamines after BRIMOPRESS® is instilled are available. Caution, however, is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.
Carcinogenesis - Mutagenesis - Impairment of fertility
No compound-related effects were observed in 21 month and 2 year studies in mice and rats given oral doses of 2.5 mg/kg/day (as the free base) and 1.0 mg/kg/day, respectively (77 and 118 times, respectively, the human plasma drug concentration following the recommended ophthalmic dose).
BRIMOPRESS® was not mutagenic or cytogenic in a series of in vitro and in vivo studies including the Ames test, host-mediated assay, chromosomal aberration assay in Chinese Hamster Ovary (CHO) cells, cytogenic studies in mice and dominant lethal assay.
Pregnancy
Teratogenic effects: Pregnancy Category B.
Reproduction studies performed in rats with oral doses of 0.66 mg base/kg revealed no evidence of impaired fertility or harm to the fetus due to product use. Dosing at this level produced 100 times the plasma drug concentration level seen in humans following multiple ophthalmic doses.
There are no studies of BRIMOPRESS® in pregnant women, however in animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. BRIMOPRESS® should be used during pregnancy only if the potential benefit to the mother outweighs the potential risk to the fetus.
Pediatric use
Safety and efficacy of this product in children have not been established.

Adverse reactions:
Adverse events occurring in approximately 10-30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus.
Events occurring in approximately 3-9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular pain, ocular dryness, lacrimation, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.
The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitation, nasal dryness, and syncope.

Overdosage:
No information is available on overdosage in humans. Treatment of an oral overdose includes supportive and symptomatic therapy. A patent airway should be maintained.
If an overdosage occurs, go to the nearest hospital or toxicology centers.

How supplied:
Dropper bottle, containing 5 ml-ophthalmic solution.

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:
LABORATORIOS POEN S.A.C.I.F.I.
Bermúdez 1004 - C1407BDR Buenos Aires, Argentina
www.poen.net.ar

Technical Director:
Victor D. Colombari, Pharmacist