BRIMOPRESS® PF

BRIMONIDINE TARTRATE 0.2%

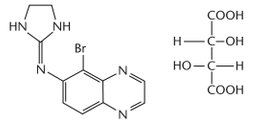
Poen

STERILE OPHTHALMIC SOLUTION

Made in Argentina - Rx ONLY

Formula:
Each 100 mL of ophthalmic solution contains:
Brimonidine tartrate 200 mg
Polyvinyl alcohol 1400 mg; Sodium chloride 700 mg; Sodium citrate dihydrate 450 mg; Citric acid monohydrate 50 mg; Sodium hydroxide 10 N q.s. pH 6.4; Purified water q.s. 100 ml.

Chemical structure:



Brimonidine Tartrate

Chemical formula: $C_{11}H_{10}BrN_5 . C_4H_6O_6$
Molecular weight: 442.2 g/ mol

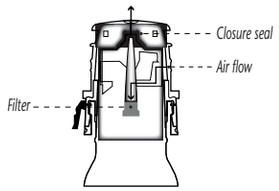
Therapeutical action:
Brimonidine tartrate 0.2% reduces intraocular pressure (IOP) with minimal effect on cardiovascular and pulmonary parameters.
ATC classification: S01EA05.

Indications:
It is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.
BRIMOPRESS® PF differs from standard multidose eye drops in that it is preservative-free (PF). Preservatives can cause serious allergic and inflammatory reactions in the eyes with long-term use in chronic conditions such as ocular hypertension and glaucoma. Preservative-free eye drops, on the other hand, preserve the integrity of the ocular surface. For this reason, BRIMOPRESS® PF is recommended for patients with sensitive eyes.

Pharmacological characteristics / Properties:
Pharmacological action
Brimonidine tartrate is an alpha-2 adrenergic receptor agonist. 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. The maximum hypotensive effect occurs two hours after the application of the dose.
Pharmacokinetics
After ocular administration of 0.2% solution, plasma concentration peaks occurred within the first to fourth hour and declined with a systemic half-life of approximately 3 hours. In humans, the systemic metabolism of Brimonidine tartrate is extensive. It is primarily metabolized in the liver. Urinary excretion is the main route of elimination of the drug and its metabolites. Approximately 87% of an orally administered radioactive dose was eliminated within 120 hours, 74% being found in the urine.

PRESERVATIVE-FREE - NEW OPHTHALMIC PF VIAL

BRIMOPRESS® PF is supplied in an OSD (Ophthalmic Squeeze Dispenser, Preservative-Free Multidose System) dropper bottle, specially designed for Preservative-Free (PF) ophthalmic formulations, which consists of a filtration system that prevents contamination of the bottle contents by filtering the air that enters the bottle during use. When the container is squeezed, the pressure forces the closure seal to open, allowing the drop to form. At the same time, the air flow used to balance pressures within the system is forced through a sterile filter (0.2 µm), stopping the entry of particles and microorganisms, thus preventing product contamination and prolonging the shelf-life of the product once the container is opened.



This novel system allows the dosing of preservative-free ophthalmic formulations, avoiding the irritation and cytotoxicity that can be produced by the prolonged use of traditional preservatives, and represents significant benefits for patients with pathologies that require chronic treatment, such as ocular hypertension and glaucoma.
Several controlled short and long-term studies on healthy volunteers and patients have shown that preservative-free eye drops are better tolerated by the corneoconjunctival surface than preservative-containing eye drops, less cytotoxic to the corneal epithelium, less damaging to the tear film, as well as they reduce the symptoms reported by patients significantly and provide greater comfort of use.

Dosage and administration:
Solution for topical ophthalmic administration.
The recommended dose is one drop of Brimonidine tartrate 0.2% ophthalmic solution, two or three times daily, at regular intervals apart.
If other topical ophthalmic products are used, BRIMOPRESS® PF and the other products should be instilled at least 10 minutes apart.

Contraindications:
General:
Known hypersensitivity to any component of the product.
Related to alpha-2 adrenergic receptor agonists:
Patients receiving therapy with monoamine oxidase (MAO) inhibitors.
BRIMOPRESS® PF is contraindicated in infants under the age of 2 years.

Warnings:
Do not inject. Do not ingest. Product intended for ophthalmic use only.
Do not use the drug product after the expiration date indicated on the package.
Use the product only if the container is intact.
Keep the dropper bottle carefully closed.
In case of pain in the treated eye(s), irritation or changes in vision, if the condition worsens or persists for more than 72 hours, discontinue use of the product and consult your doctor.
Contamination of topical ophthalmic products
The product is packaged under sterile conditions. To prevent contamination of the dropper bottle tip, avoid touching eyelids, eyelashes and adjacent areas of the eye, or any other surface with the container. Improper handling of the dropper bottle can contaminate it; and then cause serious eye damage, with subsequent decrease in vision. The bottle should be closed immediately after each instillation.
Use of contact lenses
For a correct absorption of the drug, it is recommended to remove the lenses before the instillation of the product and wait 15 minutes before putting your them back.

Precautions:
Patients prescribed IOP-lowering medication should have their intraocular pressure checked frequently.
General
Although Brimonidine tartrate 0.2% had minimal effect on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.
Brimonidine tartrate has not been studied in individuals with hepatic or renal disorders; therefore, extreme caution should be exercised in the treatment of these patients.
BRIMOPRESS® PF should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.
During the studies, a loss of effect was observed in some patients. The IOP lowering efficacy observed with Brimonidine tartrate during the first month of therapy does not always reflect long-term lowering levels. Patients prescribed an IOP-lowering medication should have their intraocular pressure monitored frequently.
Carcinogenesis, Mutagenesis, Impairment of Fertility
No effects have been observed with Brimonidine tartrate in 21-month and 2-year studies in mice and rats administered oral doses of 2.5 mg/kg/day (as free base) and 1.0 mg/kg/day, respectively (77 and 118 times, respectively, the drug concentration in human plasma at the recommended ophthalmic dose).
Brimonidine tartrate 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, and cytogenetic studies in mice, and dominant lethal assay.
Pregnancy
Teratogenic effects:
Reproduction studies in rats with oral doses of Brimonidine tartrate 0.66 mg base/kg revealed no evidence of impairment of fertility or harm to the fetus resulting from use of the product. Dosing at this level produced 100 times the plasma concentration seen in humans with multiple ophthalmic doses.
Because adequate studies have not been performed with BRIMOPRESS® PF in humans, it should be used during pregnancy only if the potential benefit to the mother justifies a possible risk to the fetus.
Lactation
It is not known whether Brimonidine tartrate is excreted in human milk, although in animal studies, Brimonidine tartrate has been shown to be excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants, 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
In clinical studies conducted in pediatric glaucoma patients (2 to 7 years of age) the most commonly observed adverse reactions with Brimonidine tartrate ophthalmic solution 0.2% dosed three times daily were somnolence (50-83% in patients 2 to 6 years of age). In pediatric patients older than 7 years of age, somnolence appears to occur less frequently (25%). Approximately 16% of patients discontinued treatment with Brimonidine tartrate 0.2% ophthalmic solution due to this adverse event.
BRIMOPRESS® PF is not recommended for use in pediatric patients under 12 years of age and is contraindicated in neonates and infants (under 2 years of age). No clinical studies have been performed in adolescents (between 12 and 17 years of age). The safety and effectiveness in children have not been established.
Interactions
Although specific drug interaction studies have not been conducted with BRIMOPRESS® PF, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.
In clinical studies, Brimonidine tartrate had no significant effects on pulse or blood pressure. However, since alpha agonists are a class of medications that can reduce pulse and blood pressure, caution should be exercised in the concomitant use of drugs such as (ophthalmic or systemic) beta-blockers, antihypertensives and/or cardiotonic glycosides.
Tricyclic antidepressants have been reported to blunt the hypotensive effect of clonidine. It is not known whether the concurrent use of these agents with Brimonidine tartrate can lead to resulting interference with the IOP lowering effect.
No data are available regarding the level of circulating catecholamines after instillation of BRIMOPRESS® PF. However, caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Adverse reactions:
The following adverse reactions were reported with an incidence of 10 to 30%: dry mouth, ocular hyperemia, burning and stinging, headache, blurred vision, foreign body sensation, fatigue/somnolence, conjunctival follicles, ocular allergic reactions, and ocular pruritus.
Reactions that occurred in approximately 3 to 9% of patients, in descending order include: corneal erosion, photophobia, palpebral erythema, ocular pain, ocular dryness, lacrimation, upper respiratory tract symptoms, palpebral edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival pallor, abnormal vision, and muscle pain.
The following adverse reactions were reported in less than 3% of patients: palpebral crusting, conjunctival hemorrhage, dysgeusia, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.
Adverse reactions reported in infants receiving Brimonidine tartrate ophthalmic solutions during postmarketing studies were: apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence.
Postmarketing studies have been conducted and the most commonly reported reactions were: bradycardia, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, pruritus palpebrae, rash and vasodilation) and tachycardia.
Reporting of serious adverse reactions in pediatric patients: Serious adverse reactions associated with the administration of Brimonidine tartrate 0.2% ophthalmic solution in pediatric patients (between 28 days and 3 months of age) have been reported.
These reactions included: bradycardia, coma, pallor, respiratory depression and somnolence, hypotension, hypothermia, hypotonia, apnea, dyspnea, hypoventilation, cyanosis and lethargy, which resulted in hospitalization. After discontinuation of Brimonidine tartrate 0.2%, the pediatric patients recovered without sequelae.

Symptoms and treatment of an overdosage:
No information is available regarding overdosage of BRIMOPRESS® PF (Brimonidine tartrate 0.2%) ophthalmic solution in humans.
If an overdosage occurs, go to the nearest hospital or toxicology centers.

How supplied:
Dropper bottle containing 5 ml of sterile ophthalmic solution, with its corresponding package insert.

PATIENT INFORMATION

"Read this information carefully before using this medicine. Keep this leaflet as you may need to read it again. If you have any questions, ask your doctor or pharmacist. This medicine has been prescribed only for you; do not give (or recommend) it to others, even if they have the same symptoms, as it may harm them. This information is not a substitute for talking to your doctor about your condition or treatment. This medicine must be indicated and prescribed by your doctor. If you think that any of the side effects you are experiencing are serious or if any undesirable effects not mentioned in this leaflet occur, please tell your doctor or pharmacist."

WHAT IS BRIMOPRESS® PF AND WHAT IS IT USED FOR?
It is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.
BRIMOPRESS® PF differs from standard multidose eye drops in that it is preservative free (PF). Preservatives can cause serious allergic and inflammatory reactions in the eyes with long-term use in chronic conditions, such as ocular hypertension and glaucoma. Preservative-free eye drops, on the other hand, preserve the integrity of the surface of the eye. For this reason, BRIMOPRESS® PF is recommended for patients with sensitive eyes.

CONSULT YOUR DOCTOR BEFORE USING BRIMOPRESS® PF:
- If you are pregnant or breastfeeding, since adequate and well-controlled studies on the efficacy and safety of BRIMOPRESS® PF in pregnant and nursing women have not been carried out.
- If you are allergic to any of the components of the formula.
- If you are taking any other medication.
- If you have any physical or psychological pathology.

WHO SHOULD NOT USE BRIMOPRESS® PF?
Patients who are allergic to any of the components of the formula. Patients receiving therapy with monoamine oxidase (MAO) inhibitors. The use of BRIMOPRESS® PF is contraindicated in children under 2 years of age.

APPROPRIATE USE OF THE MEDICINE:
For topical ophthalmic use only.

HOW MUCH, WHEN AND HOW IS BRIMOPRESS® PF USED?
The recommended dose is one drop of BRIMOPRESS® PF, two or three times daily, at regular intervals apart.
If other topical ophthalmic products are used, BRIMOPRESS® PF and the other products should be instilled at least 10 minutes apart.
Method of administration: Tilt the dropper bottle downwards, press it, and administer the dose in the conjunctiva.
Do not inject. Do not ingest.
Do not use the product after the expiration date indicated on the package.
Use the product only if the container is intact.
Keep the dropper bottle carefully closed.
In case of pain in the treated eye(s), irritation or changes in vision, if the condition worsens or persists for more than 72 hours, discontinue use of the product and consult your doctor.

CONTAMINATION PREVENTION
The product is packaged under sterile conditions. The dropper bottle tip should be handled correctly, avoiding contact with the eye, eyelashes and adjacent areas or any other surface, in order to avoid contamination with bacteria that commonly cause eye infections. Contaminated product use can cause serious eye damage, with subsequent decrease in vision.
The dropper bottle should be closed immediately after each instillation.

ADDITIONAL INFORMATION
It is recommended to remove the lenses before instillation of the product and wait 15 minutes before putting them back.

POSSIBLE ADVERSE EFFECTS
The following adverse reactions were reported: dry mouth, red eye, burning and itching, headache, blurred vision, foreign body sensation, tiredness/sleep disturbance, conjunctival disturbances, ocular allergic reactions, corneal disturbances, light intolerance, eyelid disturbances, ocular pain, dry eye, tearing, upper respiratory tract symptoms, dizziness, eye irritation, gastrointestinal symptoms, muscle pain, taste disturbance, difficulty sleeping, depression, increased blood pressure, anxiety, palpitations/pulse disturbance, nasal dryness and decreased cerebral blood supply.
Other adverse effects observed: cessation of breathing, coma, decreased blood pressure and body temperature. Decreased muscle tone, pallor, increased immune reactions, iris alterations, nausea, skin reactions and increased heart rate.
Reporting of serious adverse reactions in pediatric patients: decreased pulse, coma, pallor, slow or stopped breathing, drowsiness, decreased blood pressure, decreased body temperature and muscle tone, bluish coloration of the skin and mucous membranes, sleep disturbances. After discontinuation of BRIMOPRESS® PF administration, pediatric patients recovered without sequalae.

REMINDER
This medicine has been prescribed only for your current medical problem. Do not recommend it to others.

Storage conditions:
Store below 30°C.

Discard the product after three months of being opened.

Keep drugs out of reach of children.

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

Manufactured by:
LABORATORIOS POEN S.A.U.
Bermúdez 1004 - C1407BDR Buenos Aires, Argentina

Technical Director:
Victor D. Colombari, Pharmacist

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DIRECCIÓN TÉCNICA
ASUNTOS REGULATORIOS
DESARROLLO
Nombre y Firma/ Name and Signature
Día/ Day Mes/ Month Año/ Year

CCA N°: _____

surcan	**SURCAN S.R.L.** Alvarez Thomas 198 3°A Buenos Aires - C1427CCO Tel/Fax: 4553-2422 disenografico@surcan.com.ar www.surcan.com.ar	Laboratorio/Laboratory: **LABORATORIOS POEN** Producto/Product: **BRIMOPRESS PF** Contenido/Content: **SOLUCION** País/Country: **EXPORTACIÓN INGLÉS** Elemento/Item: **PROSPECTO (DORSO Y FRENTE)**	**Tamaño/Size:** **ancho/wide:** 150 mm **alto/high:** 240 mm N° Material: **4209529840** Pharmacode N°: **697** Código visual/Visual code: **1 - 37**	Fecha/Date: **23/JUN/25** Versión N°: **1** **Guía de colores/Colours Guide** Pantone Black C Colores/Colours: **1**