BRIMOPRESS® T PF

BRIMONIDINE TARTRATE 0.2%
TIMOLOL 0.5%

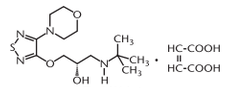
STERILE OPHTHALMIC SOLUTION

Made in Argentina - Rx ONLY

Poen

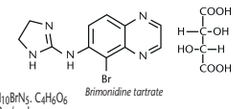
Formula:
Each 100 mL of ophthalmic solution contains:
Brimonidine tartrate 200.0 mg
Timolol (as maleate) 500.0 mg
Sodium chloride 320.0 mg; Monosodium phosphate dihydrate 210.0 mg; Anhydrous disodium phosphate 758.0 mg; Disodium edetate dihydrate 10.0 mg; Purified water q.s. 100 ml.

Chemical structure:



Timolol Maleate

Chemical formula: $C_{13}H_{24}N_4O_3S.C_4H_4O_4$
Molecular weight: 432.5 g/mol



Brimonidine tartrate

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

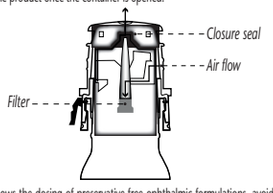
Therapeutical action:
A topical ophthalmic combination of a beta-adrenergic receptor blocking agent (Timolol) and an alpha-2 adrenergic receptor agonist agent (Brimonidine), which reduces intraocular pressure (IOP).
ATC classification: S01ED51.

Indications:
Treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension and/or open-angle glaucoma when local treatment with a combination of an alpha-2 adrenergic receptor agonist and a beta-adrenergic receptor blocker is indicated, and in patients with intolerance or inadequate response to other medications. BRIMOPRESS® T 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® T PF is recommended for patients with sensitive eyes.

Pharmacological characteristics / Properties:
Pharmacological action: BRIMOPRESS® T PF ophthalmic solution (Brimonidine tartrate 0.2% / Timolol 0.5%) reduces intraocular pressure (IOP) by decreasing aqueous humor production and increasing uveoscleral outflow. Each component of BRIMOPRESS® T PF is used individually for IOP control. Brimonidine 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.
Timolol is a (non-selective) beta-1 and beta-2 adrenergic receptor-blocking agent that lacks intrinsic sympathomimetic activity and does not exhibit significant membrane-stabilizing effects. Timolol reduces intraocular pressure by decreasing aqueous humor production.
The reduction in intraocular pressure after Timolol administration is usually detected within the first 30 minutes of dosing. The maximum effect generally occurs between 1 and 2 hours after application, and a significant reduction in IOP can be maintained for 24 hours with a single dose.
Pharmacokinetics: After ocular administration of Brimonidine tartrate 0.2%, 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.
When administered orally, Timolol is rapidly and completely absorbed (approximately 90%). Timolol can be detected in plasma within 30 minutes, with peak plasma concentration occurring 2 hours after ingestion. The plasma half-life is approximately 4 hours and remains largely unchanged in patients with moderate renal impairment. Timolol is partially metabolized in the liver and excreted along with its metabolites via the kidneys. Timolol does not extensively bind to plasma proteins.

PRESERVATIVE-FREE - NEW OPHTHALMIC PF VIAL

BRIMOPRESS® T 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.
Clinical Study: A clinical study evaluated intraocular pressure (IOP) in 861 patients with ocular hypertension and bilateral open-angle glaucoma after switching from traditional medication to a combination of Brimonidine 0.2% and Timolol 0.5%. Patients experienced a reduction in IOP from 20.8 ± 3.5 mmHg to 16.9 ± 2.6 mmHg after 4–6 weeks of treatment and to 16.5 ± 2.7 mmHg after 12 weeks of combination therapy. The target intraocular pressure was achieved in 79.5% of all eyes after 12 weeks. Tolerability was rated as excellent by 97.1% of healthcare professionals and by 93.4% of the patients themselves. Few adverse effects were reported. The results demonstrate that Brimonidine 0.2%-Timolol 0.5% is an effective, well-tolerated, and safe treatment for patients with primary open-angle 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:
The recommended dose is one drop of BRIMOPRESS® T PF in the affected eye(s) twice a day, approximately every 12 hours.
When replacing other topical ophthalmic antiglaucoma medication(s) with BRIMOPRESS® T PF, discontinue the previous medication(s) after the last scheduled dose of that day and start BRIMOPRESS® T PF the following day.
If other topical ophthalmic products are used, BRIMOPRESS® T PF and the other products should be instilled at least 10 minutes apart.
Method of administration: Tilt the dropper bottle downward, squeeze it, and instill the dose into the conjunctiva.

Contraindications:
General: Known hypersensitivity to any component of the product.
Related to beta-adrenergic blockers: As with many topically applied ophthalmic drugs, Timolol is systemically absorbed. The same adverse reactions observed with the systemic administration of beta-adrenergic blockers may occur with topical application.
- Bronchial asthma or a history of bronchial asthma.
- Severe chronic obstructive pulmonary diseases.
- Manifest heart failure.
- Cardiogenic shock.
- Second-or third-degree atrioventricular block.
- Prinzmetal's angina.
- Sinus bradycardia (< 45–50 beats per minute) or any sinoatrial node dysfunction.
- Raynaud's disease and other peripheral circulatory disorders.
- Manifest pheochromocytoma.
- Hypotension.
- Drug interaction with floctafenine or sultopride.

Related to alpha-2 adrenergic receptor agonists: Patients receiving therapy with monoamine oxidase (MAO) inhibitors.
Children under 7 years of age and/ or weighing ≤ 20 kg should be treated with caution and carefully monitored due to the high incidence and severity of adverse effects.

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: It is recommended to remove the lenses before the instillation of the product and wait 15 minutes before putting your them back.
Timolol: Choroidal detachment cases have been reported due to ocular hypotonia following glaucoma surgery with the administration of antiglaucoma agents that reduce aqueous humor secretion (Timolol, acetazolamide).
As with many topically applied ophthalmic drugs, Timolol is systemically absorbed. Topical application may cause the same adverse reactions observed with systemic administration of beta-adrenergic blockers.
Heart failure: Sympathetic stimulation may be essential for maintaining circulation in individuals with reduced myocardial contractility. In these patients, beta-adrenergic receptor inhibition by beta-blocking agents may precipitate more severe heart failure. In patients without a history of heart failure, prolonged myocardial depression with beta-blockers may, in certain cases, lead to heart failure. BRIMOPRESS® T PF should be discontinued at the first sign or symptom of heart failure.
Obstructive pulmonary diseases: Patients with mild to moderate chronic obstructive pulmonary diseases (e.g., chronic bronchitis, emphysema), bronchospastic diseases, or a history of bronchospastic diseases other than bronchial asthma -where BRIMOPRESS® T PF is explicitly contraindicated- should not receive beta-blocking agents.
Diabetes mellitus: Beta-adrenergic blockers should be used with caution in patients with spontaneous hypoglycemia or diabetic patients (particularly those with labile diabetes) undergoing treatment with insulin or hypoglycemic agents. Beta-blockers may mask the signs and symptoms of acute hypoglycemia.
Thyrotoxicosis: Beta-adrenergic blockers may mask certain clinical manifestations (e.g., tachycardia) of hyperthyroidism. In patients suspected of having thyrotoxicosis, treatment should be handled with great care, as abrupt discontinuation of beta-blockers may precipitate a "thyroid storm".
Pheochromocytoma: The use of beta-blockers in patients with treated pheochromocytoma requires close monitoring of blood pressure.
Renal and/or hepatic impairment: Dosage adjustments are typically required in at-risk cases when beta-blockers are administered systemically.
Psoriasis: Since cases of worsening psoriasis have been reported, the use of beta-blockers should be carefully evaluated in these patients.
Allergic reactions: In patients susceptible to severe anaphylactic reactions or undergoing desensitization treatments, beta-blockers may exacerbate reactions and cause resistance to adrenaline treatment.
General anesthesia: Beta-blockers attenuate sympathetic reflex responses, which may increase the risk associated with general anesthesia during surgical procedures. Beta-blocker therapy reduces the risk of arrhythmias, myocardial ischemia, and perioperative hypertensive processes. It is advisable to inform the anesthesiologist if the patient is undergoing beta-blocker treatment.
Treatment discontinuation: Beta-blocker therapy should not be abruptly discontinued, as sudden withdrawal may cause severe arrhythmias, myocardial infarction, or sudden death.
Bradycardia: If the resting heart rate falls below 50 to 55 beats per minute and is associated with bradycardia-related symptoms, the dosage should be reduced.
First-degree atrioventricular block: Due to the negative dromotropic effect of beta-blockers, they should be used with caution in these patients.
Brimonidine: *Ophthalmic reactions:* Ocular hypersensitivity reactions to Brimonidine tartrate 0.2% ophthalmic solution have been reported, some of which are associated with increased intraocular pressure.

Precautions:
Patients prescribed IOP-lowering medication should have their intraocular pressure checked frequently.
Timolol: Due to the effects of beta-adrenoceptor blockers on blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency. If symptoms or signs suggest a reduction in blood flow to the brain after initiating therapy with BRIMOPRESS® T PF, alternative treatment should be considered.
Cases of bacterial keratitis have been observed in association with the use of topical ophthalmic products in multidose packages. In these cases, the multidose packages were inadvertently contaminated by patients, most of whom had concurrent corneal disease or an epithelial corneal surface injury.
Beta-blockers can induce dry eyes. Patients with corneal diseases should be treated with caution.
Closed-angle glaucoma: In patients with closed-angle glaucoma, the immediate goal of treatment is to reopen the angle. This requires pupil constriction. Timolol has minimal or no effects on the pupil.
The use of BRIMOPRESS® T PF is not sufficient for the treatment of acute closed-angle glaucoma. Therefore, it is recommended not to be used as a single medication in these patients.
Muscle weakness: Beta-blockers have been reported to potentially exacerbate muscle weakness, including diplopia, ptosis, and generalized weakness.
Brimonidine: *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 has not been studied in individuals with hepatic or renal disorders; therefore, extreme caution should be exercised in the treatment of these patients. BRIMOPRESS® T 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 during the first month of therapy does not always reflect long-term lowering levels.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Timolol has been shown not to be mutagenic in vivo in the micronucleus test and in cytogenetic assays in mice (doses greater than 800 mg/kg) and in vitro in the neoplastic cell transformation assay (up to 100 µg/mL).
Fertility and reproduction studies in rats have not shown adverse effects on the fertility of both females and males at doses greater than 21,000 times the systemic exposure caused by the maximum recommended dose in human ophthalmology. No effects have been observed with Brimonidine 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 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: Teratogenicity studies with Timolol in mice, rats, and rabbits at oral doses greater than 80 mg/kg/day (7,000 times the systemic exposure caused by the maximum recommended dose in ophthalmology) did not show fetal malformations.
Reproduction studies in rats with oral doses of Brimonidine 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® T 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 is excreted in human milk. Timolol has been detected in breast milk after both oral and ophthalmic administration of the substance. 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: The safety and effectiveness in children have not been established.
Interactions: Ocular: Ophthalmologic monitoring is necessary when administering an eye drop containing epinephrine concomitantly (risk of mydriasis).
General
Timolol: *Beta-adrenergic blockers:* Patients treated concomitantly with oral beta-adrenergic blockers and BRIMOPRESS® T PF should be closely monitored due to the potential additive effects of beta-blockade on both intraocular and systemic pressure. Generally, two topical ophthalmic beta-adrenergic blockers should not be administered simultaneously.
Calcium antagonists: Caution is required when co-administering beta-adrenergic blockers, such as Timolol, with oral or intravenous calcium antagonists due to potential atrioventricular conduction disorders, left ventricular insufficiency, and arterial hypotension. In patients with heart failure, the concomitant use of these drugs should be avoided.
Drugs that reduce catecholamine levels: Beta-blockers should be used with caution in patients receiving drugs that lower catecholamine levels -such as reserpine- due to possible additive effects leading to marked hypotension and/or bradycardia, which may present as dizziness, syncope, or postural hypotension.
Digitalis glycosides and calcium antagonists: Concomitant use of beta-adrenergic blockers with digitalis glycosides and calcium antagonists may cause additive effects, prolonging atrioventricular conduction time.
Quinidine: An enhancement of the beta-blocking effect has been reported with the combined use of Timolol and quinidine, possibly due to quinidine's inhibition of Timolol metabolism via the cytochrome P450 system.
Floctafenine: In cases of shock or hypotension associated with floctafenine, beta-blockers reduce the cardiovascular compensatory response.
Sultopride: Additive bradycardic effect.
Amiodarone: Contractility disorders, automaticity dysfunction, and conduction disturbances (suppression of compensatory sympathetic mechanisms).
Halogenated volatile anesthetics: Reduced cardiovascular compensatory responses due to the beta-blocking effect.
Class I antiarrhythmic agents: Contractility disorders, automaticity dysfunction, and conduction disturbances (additive effect).
Baclofen: Enhanced hypotensive effect.
Clonidine: Beta-adrenergic blockers may exacerbate rebound hypertension following clonidine withdrawal. No cases of rebound hypertension have been reported with ophthalmic Timolol.
Insulin and oral hypoglycemic agents: Beta-blockers may mask symptoms of hypoglycemia.
Lidocaine: Some beta-blockers have been reported to decrease the metabolism of lidocaine, increasing its plasma concentrations.
Iodinated contrast media: In cases of shock or hypotension caused by iodinated contrast agents, beta-blockers reduce cardiovascular compensatory responses.
NSAIDs: Reduced hypotensive effect.
Tricyclic antidepressants, neuroleptics: Increased risk of orthostatic hypotension.
Corticosteroids: Reduced hypotensive effect.
Mefloquine: Risk of bradycardia (additive bradycardic effect).
Brimonidine: Although specific drug interaction studies have not been conducted with BRIMOPRESS® T 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 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 can lead to resulting interference with the IOP lowering effect.
No data are available regarding the level of circulating catecholamines after instillation of BRIMOPRESS® T PF. However, caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Adverse reactions:
Clinical studies demonstrated that BRIMOPRESS® T PF ophthalmic solution (Brimonidine tartrate 0.2% and Timolol 0.5% as maleate) was safe and well tolerated, with an acceptable safety profile. No adverse reactions were observed specifically due to the combination of the product.
All adverse reactions had been previously reported, with different incidences, after the use of Brimonidine tartrate 0.2% or Timolol 0.5%.
In two clinical studies conducted in 385 patients treated with BRIMOPRESS® T PF over a period of up to 12 months, adverse reactions manifested in approximately 15% - 10% of individuals, including, in descending order of frequency: conjunctival hyperemia and burning sensation.
Adverse events manifested in approximately 9% - 4% of patients, including, in descending order of incidence: stinging, ocular pruritus, allergic conjunctivitis, and conjunctival folliculosis.
The following adverse reactions were reported in less than 4% of patients: blurred vision, epiphora, ocular dryness, superficial punctate keratitis, eyelid erythema, blepharitis, ocular discharge, eyelid edema, corneal erosion, ocular pain, foreign body sensation, conjunctival edema, follicular conjunctivitis, asthenia, depression, ocular irritation, headache, hypertension, dry mouth, drowsiness.
New adverse effects identified in post-marketing evaluation were: iritis, keratoconjunctivitis sicca, miosis, and tachycardia.
Adverse reactions that were reported during the use of any of the components and could potentially cause adverse effects during the use of BRIMOPRESS® T PF include:
Brimonidine: *Adverse events that occurred in ≥ 1% < 8% of patients who received Brimonidine tartrate 0.2% included:* dizziness, upper respiratory symptoms, gastrointestinal symptoms, abnormal taste, nasal dryness, photophobia, tearing, conjunctival edema, conjunctival discoloration, conjunctival papillae, abnormal vision, allergic reaction, blepharoconjunctivitis, blurred vision, bronchitis, cataracts, conjunctival blanching, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspepsia, dyspnea, fatigue, flu syndrome, follicular conjunctivitis, hypercholesterolemia, hypotension, infections (primary colds and respiratory infections), stye, insomnia, keratitis, crusting and eyelid disorders, muscle pain, pharyngitis, rash, rhinitis, sinus infection, sinusitis, superficial punctate keratopathy, visual field defects, vitreous detachment, vitreous disorders, floaters, decreased visual acuity.
Timolol: *Adverse reactions reported during the use of Timolol were:*
Cardiovascular: worsening or precipitation of certain cardiovascular disorders, pulmonary and others, presumably related to systemic beta-blockers: bradycardia, arrhythmia, hypotension, syncope, heart block, stroke, cerebral ischemia, palpitations, cardiac arrest, edema, claudication, Raynaud's phenomenon, cold sensation in hands and feet, congestive heart failure, pulmonary edema, worsening of angina pectoris.
Endocrine: masking of hypoglycemia symptoms in insulin-dependent diabetic patients.
Respiratory: bronchospasm (predominantly in patients with pre-existing bronchospastic diseases), respiratory failure, dyspnea, cough.
General: chest pain, fatigue.
Psychiatric/nervous system: increased myasthenia gravis symptoms, paresthesia, insomnia, nightmares, memory loss.
Dermatological: alopecia, psoriasis-like rash or exacerbation of psoriasis.
Hypersensitivity: signs and symptoms of allergic reactions, including angioedema, urticaria, localized and generalized rash.
Immunological: systemic lupus erythematosus.
Digestive: nausea, diarrhea, dyspepsia.
Special senses: decreased corneal sensitivity, visual disturbances including refractive changes (due to interruption of miotic therapies in some cases), diplopia, ptosis, post-filtration surgery choroidal detachment, tinnitus.
Urogenital: decreased libido, peyronie's disease.
Adverse reactions of unknown causal relationship: *The following adverse reactions were reported, but their causal relationship with Timolol therapy has not been established:* aphakic cystoid macular edema, nasal congestion, anorexia, effects on the central nervous system (e.g., behavioral changes, including confusion, hallucinations, anxiety, disorientation, nervousness, drowsiness, and other mental disturbances), hypertension, retroperitoneal fibrosis, and pseudopemphigoid.
Laboratory clinical tests: Clinically significant changes in standard laboratory parameters were rarely associated with systemic administration of Timolol. Recorded changes included: mild increase in urea nitrogen levels, potassium and uric acid in blood, and triglycerides; and mild decrease in hemoglobin, hematocrit, and HDL cholesterol; but these were neither progressive nor associated with clinical manifestations.
Timolol (systemic formulation): The adverse reactions reported following Timolol administration orally could be considered potential adverse effects for its ophthalmic administration.
Report 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, drowsiness, hypotension, hypothermia, hypotonia, apnea, dyspnea, hypoventilation, cyanosis, and lethargy, leading to hospitalization. After discontinuation of Brimonidine tartrate 0.2%, pediatric patients recovered without sequelae.
Symptoms and treatment of an overdosage: No information is available regarding overdosage of BRIMOPRESS® T PF (Brimonidine tartrate 0.2% and Timolol 0.5%) ophthalmic solution in humans.
Cases of overdose with Timolol ophthalmic solution have been reported, with manifestations similar to those observed with systemic beta-blocking agents, such as: dizziness, headache, dyspnea, bradycardia, bronchospasm, and cardiac arrest.
Treatment for oral overdose includes supportive and symptomatic therapy. The airway should be kept clear. Gastric evacuation should be considered within the first few hours following the overdose.
A study conducted in patients with renal insufficiency demonstrated that Timolol is not easily dialyzed.
Therapeutic measures for Timolol overdose:
- ***Gastric lavage:*** If ingested.
- ***Symptomatic bradycardia:*** Administer intravenous atropine sulfate at a dose of 0.25 to 2 mg to induce vagal blockage. If bradycardia persists, intravenous isoproterenol hydrochloride should be administered with caution. In refractory cases, the use of a transvenous cardiac pacemaker should be considered.
- ***Hypotension:*** Administer a sympathomimetic hypertensive drug such as dopamine, dobutamine, or levarterenol. In refractory cases, glucagon hydrochloride may be used.
- ***Bronchospasm:*** Use isoproterenol hydrochloride. Additional treatment with aminophylline may be considered.
- ***Acute heart failure:*** Conventional therapy with digitalis, diuretics, and oxygen should be administered. In refractory cases, intravenous aminophylline is recommended. Subsequently, if necessary, glucagon hydrochloride may be administered.
- ***Cardiac blockage (second or third degree):*** Use isoproterenol hydrochloride or a transvenous cardiac pacemaker.

If an overdosage occurs, go to the nearest hospital or toxicology centers.

How supplied:
Dropper bottle containing 5 ml of sterile ophthalmic solution.

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® T PF AND WHAT IS IT USED FOR?
It is an antiglaucoma agent for topical ophthalmic use, composed of a beta-adrenergic receptor-blocking agent (Timolol) and an alpha-2 adrenergic receptor agonist (Brimonidine).
It is used for the treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension and/ or open-angle glaucoma when local treatment with a combination of an alpha-2 adrenergic receptor agonist and a beta-adrenergic receptor blocker is indicated, and in patients who have intolerance or an insufficient response to other medications.
BRIMOPRESS® T 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® T PF is recommended for patients with sensitive eyes.

CONSULT YOUR DOCTOR BEFORE USING BRIMOPRESS® T PF:
- If you are pregnant or breastfeeding, since adequate and well-controlled studies on the efficacy and safety of BRIMOPRESS® T PF in pregnant and nursing women have not been carried out.
- If a child will receive BRIMOPRESS® T PF
- If you are allergic to any of the components of the formula.
- If you are taking any other medication.
- If you have heart, circulatory, respiratory, kidney, liver, cerebrovascular, thyroid, or adrenal problems, if you are going to undergo surgery, if you are a diabetic or suffer from depression, if you have psoriasis, corneal dryness, or muscle weakness.
- If you have undergone glaucoma surgery.

WHO SHOULD NOT USE BRIMOPRESS® T PF?
Patients allergic to any of the components of the formula. Patients with heart, respiratory, circulatory, adrenal problems, or hypotension. Patients treated with floctafenine or sultopride. Children under 7 years of age and/ or weighing ≤ 20 kg.

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

HOW MUCH, WHEN AND HOW IS BRIMOPRESS® T PF USED?
The recommended dose is one drop of BRIMOPRESS® T PF in the affected eye(s), twice daily, approximately every 12 hours.
When replacing another topical ophthalmic antiglaucoma medication with BRIMOPRESS® T PF, discontinue the previous medication after its last scheduled administration and start BRIMOPRESS® T PF the following day.
If other topical ophthalmic products are being used, BRIMOPRESS® T PF and the other products should be administered 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
Treatment with beta-blockers should not be abruptly discontinued; sudden withdrawal may lead to severe cardiac consequences, including sudden death.
It is recommended to remove the lenses before instillation of the product and wait 15 minutes before putting them back.

POSSIBLE ADVERSE EFFECTS
Clinical studies have shown that the most common adverse events were eye redness and burning. Less frequent adverse effects included allergic conjunctivitis, itching, stinging sensation, and ocular follicles.
The following adverse reactions were rarely reported: vision disturbances, excessive tearing, dry eye, superficial punctate keratitis, eyelid and conjunctival swelling, blepharitis, increased ocular secretions, corneal disorders, eye pain and irritation, foreign body sensation, follicular conjunctivitis, cataracts, increased sensitivity to light, double vision, changes in conjunctival color or bleeding, stye or crusting, eyelid and conjunctival disorders, vitreous disorders, and floaters.
Other reported reactions included respiratory and digestive disorders such as nasal dryness, difficulty breathing, respiratory infections, abnormal taste, dry mouth, tinnitus, and muscle pain. Cardiovascular disturbances such as decreases or increases in blood pressure, changes in heart rate, temporary cessation of heart and respiratory movements, stroke, cerebral ischemia, cardiac arrest, and a sensation of cold in hands and feet were also reported. Endocrine disturbances: masking of hypoglycemia symptoms in insulin-dependent diabetic patients. Nervous system disturbances: tingling, cold or hot sensations in the body, fatigue, depression, headache, sleep disturbances, dizziness, and memory loss. Dermatological disturbances: hair loss, skin rash, psoriasis, urticaria, allergic reactions, lupus erythematosus, and urogenital disturbances.
Aphakic cystoid macular edema, retroperitoneal fibrosis, pseudopemphigoid, and laboratory test abnormalities were reported, including mild increase in blood urea nitrogen, potassium, uric acid, and triglycerides, as well as slight decreases in hemoglobin, hematocrit, and HDL cholesterol levels.
The most recently identified adverse effects were iris inflammation, keratoconjunctivitis sicca, pupil size reduction, and cardiac rhythm disturbances.
Reported adverse reactions in pediatric patients included decreased heart rate and respiratory rate, coma, pallor, inability to breathe, difficulty breathing, sleep disturbances, decreased blood pressure, reduced body temperature, decreased muscle tone, bluish discoloration of the skin and mucous membranes, and drowsiness, leading to hospitalization.

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

4281129840
698
C.V. 1 - 38

869

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DIRECCIÓN TÉCNICA
ASUNTOS REGULATORIOS
DESARROLLO
Nombre y Firma/ Nome 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 T 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: **4281129840**
Pharmacode N°: **698**
Código visual/Visual code: **1 - 38**

Fecha/Date: **23/JUN/25**
Versión N°: **1**
Guía de colores/Colours Guide
Pantone Black C
Colores/Colours: **1**