110 x 80 mm

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

℞ Brimonidine Tartrate & Timolol Maleate Ophthalmic Solution

BRIMOSAFE – PF™

Eye Drops

COMPOSITION:

Brimonidine Tartrate	IP	0.2% w/v
Timolol Maleate	IP	
Equivalent to Timolol		0.5% w/v
Sterile Aqueous Vehicle		q.s.
Preserved with Ionic Solvent		

CLINICAL PHARMACOLOGY

BRIMOSAFE - PF is comprised of two components: brimonidine tartrate and timolol. Each of these two components decreases elevated intraocular pressure, whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. The higher the level of intraocular pressure, the greater the likelihood of glaucomatous field loss and optic nerve damage. BRIMOSAFE - PF is a selective alpha-2 adrenergic agonist with a non-selective beta-adrenergic receptor blocking agent. Both brimonidine and timolol have a rapid onset of action, with peak ocular hypotensive effect seen at two hours post-dosing for brimonidine and one to two hours for timolol. Fluor photometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action by reducing aqueous humour production and increasing non-pressure dependent uvoscleral outflow.

Timolol decreases aqueous humour production with little or no significant effect on episcleral venous pressure, outflow facility or uvoscleral outflow. Because timolol and brimonidine have different sites of action and different mechanisms by which they lower IOP. It is reasonable to expect that there will be an added IOP-lowering effect when the two are used adjunctively.

Timolol is a beta 1 and beta 25 (non-selective) adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anaesthetic (membrane-stabilizing) activity.

INDICATIONS AND USAGE

BRIMOSAFE - PF (brimonidine tartrate/timolol ophthalmic solution) 0.2%/0.5% is indicated for the reduction of intraocular pressure in patients with chronic open angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta blockers.

CONTRAINDICATIONS

BRIMOSAFE - PF is contraindicated in patients with (1) reactive airway disease including bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease **(see WARNINGS)**; (4) Sinus bradycardia; (5) sick sinus syndrome, (6) sino-atrial nodal block (7) second and third atrioventricular block not controlled with a pace maker; (8) overt cardiac failure (see WARNINGS); (9) CARDIOGENIC SHOCK; (10) In patient receiving monoamine oxidase (MAO) inhibitor therapy; (11) hypersensitivity to any component of this medication; or (12) Neonates and Infants (children under the age of 2 years)

WARNINGS

As with many topically applied ophthalmic drugs, the active substances (brimonidine tartrate and timolol) in BRIMOSAFE - PF may be absorbed systematically. No enhancement of the systemic absorption of the individual active substances has been observed. Due to the beta-adrenergic component, timolol, adverse reactions typical of systemic beta – adreno receptor blocking agents may occur. The same types of adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration of BRIMOSAFE - PF For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol. **(see CONTRAINDICATIONS**

Liver and renal function: BRIMOSAFE - PF has not been studied in patient with hepatic or renal impairment; caution should be used in treating such patients.

PRECAUTIONS

While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patient may be unresponsive to the usual doses to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patient may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

INFORMATION FOR PATIENT

Patient should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures. Patient should also be instructed that ocular solutions, if handled improperly or if the tip of the dispensing container contact the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

DRUG INTERACTIONS

Antihypertensive/cardiac glycosides: Because BRIMOSAFE - PF may reduce blood pressure, caution in using drugs such as antihypertensive and/or cardiac glycosides is advised. There is the potential for additive effects resulting in hypotension, and/or cardiac glycosides is advised. There is the potential for additive effects resulting in hypotension, and/or marked bradycardia when beta-blocker eye drops are administered concomitantly with oral calcium channel blockers, anti-arrhythmic (including amiodarone), digitalis glycosides, para-sympathomimetic, guanethidine, and other anti-hypertensive.

PREGNANCY: Pregnancy Category C : Teratogenicity studies have been performed in animals. There are no adequate and well-controlled studies in pregnant women; however, in animal studies, brimonidine crossed the placenta and entered into the fatal circulation to a limited extend. Because animal reproduction studies are not always predictive of human responsive

NURSING MOTHERS: Timolol has been detected in human milk following oral and ophthalmic drug administration. 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 adverse reactions from timolol or brimonidine tartrate 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.

OVERDOSAGE

There is limited data available of over-dosage in humans with the use of BRIMOSAFE - PF. There have been reports of inadvertent over-dosage with timolol ophthalmic solution resulting in systemic effect similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained. An in vitro hemodialysis study, using 14 C timolol added to human plasma or whole blood showed that timolol was readily dialyzed from these fluids; however, a study of patients with Renal failure showed that timolol did not dialyze readily.

Ophthalmic overdose of brimonidine tartrate ophthalmic solution 0.2% : In those cases received, the events reported have generally been already listed adverse reactions.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of BRIMOSAFE - PF in the affected eye(s) twice daily approximately 12 hours apart. As with any eye drops, to reduce possible systemic absorption, it is recommended that lacrimal sac be compressed at the medial canthus (punctual occlusion) for at least 1 minute. This should be performed immediately the instillation of each drop. If more than one topical ophthalmic product is to be used, the different products should be instilled at least 10 minutes apart.

PRECAUTIONS:

Do not swallow the eye drop solution.
Close the bottle immediately after the use.
Do not use after the expiry date marked on the product.
Do not use the bottle if the tamper proof seal on the bottle neck is broken before your first use.
Avoid contamination, do not touch the bottle tip to any surface and avoid direct contact with the eye.
Do not use the product allergic to any of its ingredients.
Retain the carton with the bottle for future reference.
Allow 5 minutes between the admiration of other ophthalmic products.

HOW SUPPLIED

BRIMOSAFE - PF is supplied sterile in 5 ml bottle.

STORAGE: Store below 30°C. Protect from light & moisture. Do not freeze.

NOT FOR INJECTION
FOR EXTERNAL USE ONLY

Keep out of reach of children.

Manufactured by:
SION HEALTHCARE (SHL) LIMITED

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