POENTIMOL®
0.25% / 0.50%

TIMOLOL 0.25% AND 0.50%

STERILE OPHTHALMIC SOLUTION
Made in Argentina - Rx ONLY

Qualitative-quantitative formula:
POENTIMOL 0.25%
Each ml contains:
Timolol (as maleate) 2.50 mg
Disodium phosphate anhydrous 11.58 mg; Monosodium phosphate dihydrate 7.21 mg; Preservative: Benzalkonium chloride 0.10 mg; Purified water, q.s.

POENTIMOL 0.50%
Each ml contains:
Timolol (as maleate) 5.00 mg
Disodium phosphate anhydrous 12.06 mg; Monosodium phosphate dihydrate 5.40 mg; Preservative: Benzalkonium chloride 0.10 mg; Purified water, q.s.

Therapeutical action:
It is indicated for the reduction of elevated intraocular pressure, either associated or not associated to glaucoma.
ATC Classification: S01ED01

Indications:
POENTIMOL® Ophthalmic Solution is indicated for the treatment of high ocular pressure in patients with ocular hypertension or open-angle glaucoma.

Pharmacological characteristics / Properties:
Timolol is a beta-1 and beta-2 (non selective) adrenergic receptor blocking agent, which does not have significant intrinsic sympathomimetic, direct myocardial depressant or local anesthetic activity (membrane stabilizing activity).
The reduction in intraocular pressure following POENTIMOL® administration may be usually detected within one-half hour after a single dose.
The maximum effect usually occurs from 1 to 2 hours following the application, and a lowering of IOP may be maintained for 24-hour periods with a single dose.

Dosage and Administration:
POENTIMOL® Ophthalmic Solution: at 0.25 and 0.50% concentrations.
The usual initial dose is 1 drop of POENTIMOL® 0.25% b.i.d. into the affected eye(s).
If the clinical response is not adequate, the dosage may be changed to 1 drop of POENTIMOL® 0.50% b.i.d. into the affected eye(s).
Since in some patients the pressure treated with POENTIMOL® may require a few weeks to stabilize, the evaluation should include a determination of intraocular pressure after 4 week-treatment with POENTIMOL®.

Contraindications:
POENTIMOL® is contraindicated in patients having:
Bronchial asthma; History of bronchial asthma; Severe chronic obstructive pulmonary diseases; Sinus bradycardia; Sick sinus syndrome sino-atrial block; Second or third degree atrioventricular block; overt heart failure; cardiogenic shock; Severe peripheral circulatory disturbance (Raynaud disease); known hypersensitivity to any components of the product.

Warnings:
For ophthalmic topical use only.
DO NOT INJECT. POENTIMOL® is intended exclusively for ophthalmic topical use.
Do not use the medicine after the indicated expiration date.
Use the product only if the package is intact.
If the condition worsens and persists more than 72 hours, pain or alterations of the vision appear and/or the eye irritation is worsen, suspend the use of the product and consult with a professional.
The preservative of POENTIMOL®, benzalkonium chloride, may be deposited or absorbed by soft contact lenses. The lenses should be removed prior to the administration of POENTIMOL® and they should not be reinserted for 15 minute period after the administration. Inform your doctor if you are allergic or if you have any problems following this drug administration.
There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the corneal epithelial surface. POENTIMOL® ophthalmic solution is packed under sterile conditions. In order to prevent contamination, care should be taken not to touch the eyelids, eyelashes and adjacent zones or any other surface with the dropper-bottle sprout. Serious damage to the eye and subsequent loss of vision may result from using contaminated ophthalmic solutions. Keep the dropper-bottle carefully closed.

Precautions:
The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patient with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of Timolol maleate.
Cardiac failure: Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition of beta-adrenergic receptor blockade may precipitate more severe failure.
In patients without a history of cardiac failure continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, POENTIMOL® should be discontinued.
In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina, and cardiac failure) and hypotension therapy with beta-blockers, signs of cardiac failure and heart rate should be watch. Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block. Heart failure should be well-controlled before starting the treatment.
Obstructive pulmonary disease: Patient with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma, in which POENTIMOL® is contraindicated), should, in general, not receive beta-blockers, including POENTIMOL®.
Major Surgery: The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents. If necessary during surgery, the effects of beta-adrenergic receptor blocking agents may be reversed by sufficient doses of adrenergic agonist.
Diabetes mellitus: Beta-adrenergic blocking should be administered with caution in patients subject to spontaneous hypoglycemia or diabetic patients (especially those with labile diabetes) who are receiving insulin or hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.
Tyrotoxicosis: Beta-adrenergic blocking agents may mask certain clinical signs (e.g. tachycardia) of hyperthyroidism. Patients suspected of developing thyroxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents which might precipitate a "thyroid storm".
Cerebrovascular disease: Due to the beta-adrenergic blocking agents effects on pressure and pulse, these agents should be cautiously used in patients with cerebrovascular failure. If symptoms and signs suggesting reduced cerebral blood flow develop following initiation of therapy with POENTIMOL® an alternative treatment should be considered.
Closed-angle glaucoma: In patients with close angle glaucoma the immediate objective of treatment is to reopen the angle. This requires constricting the pupil. Timolol maleate has little or no effect on the pupil. POENTIMOL® should not be used alone in the closed-angle glaucoma treatment.
Corneal diseases: Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.
Choroidal detachment: Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g. Timolol).
Anaphylaxis: 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 patients may be unresponsive to the usual dose of epinephrine used to treat anaphylactic reactions.
Muscle weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with either certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.
Prolonged therapy: A reduction in ocular hypotensive response has been reported in some patients following prolonged therapy with Timolol maleate eye drops.

Drug interactions:
Beta-adrenergic blocking agents: Patients who are receiving a beta-adrenergic blocking agent orally and POENTIMOL® should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure. Usually, two topical ophthalmic beta-adrenergic blocking agents should not be simultaneously administered.
Calcium antagonists: Caution should be used in the coadministration of beta-adrenergic blocking agents, such as POENTIMOL®, and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, coadministration should be avoided.
Catecholamine-depleting drugs: Close observation of the patients is recommended when a beta blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.
Digitalis and calcium antagonist: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.
Quinidine: Potentiated systemic beta-blockage (e.g., decreased hert rate) has been reported during combined treatment with quinidine and Timolol, possibly because quinidine inhibits the metabolism of Timolol via P-450 enzyme, CYP2D6.
CYP2D6 inhibitors: Potentiated systemic beta-blockage (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. fluoxetine, paroxetine) and Timolol.
Clonidine: Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. There have been no reports of exacerbation of rebound hypertension with ophthalmic Timolol maleate.
Epinephrine: Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.
Anesthetic drugs: Increased risk of myocardial depression and hypotension due to blockage of cardiac response to reflex sympathetic stimuli.
Cimetidine, hydralazine, phenothiazines and alcohol: may increase plasma level of Timolol.
There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administrated concomitantly with antiarrhythmics (including amiodarone), parasympathomimetics, guanethidine.
Fertility and mutagenesis
Timolol maleate was devoid of mutagenic potential when evaluated in vivo in the micronucleus test and cytogenic assay in mice (doses higher than 800 mg/kg); and in vitro in a neoplastic cell transformation assay (up to 100 µ/ml).
Reproduction and fertility studies in rats showed no adverse effects on male or female fertility at doses higher than 21,000 times the systemic exposure following the maximum recommended human ophthalmic dose.
Pregnancy
There are no adequate and well-controlled studies in pregnant women. POENTIMOL® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nursing mothers
Timolol maleate has been detected in human milk, following ophthalmic and oral drug administration. Because of the potential for serious adverse reactions from POENTIMOL® in children, a critical decision should be made whether to discontinue nursing or to discontinue the product administration, taking into account the importance of the drug to the mother.
Pediatric use
Safety and effectiveness of this product in children have not been established.
Geriatric use
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Adverse reactions:
Occasionally, it may cause burning, lacrimation, blurred vision or headaches, which disappear immediately.
The most frequently reported adverse reactions have been burning and stinging upon instillation (about 1 out of 8 patients).
The following additional adverse experiences have been reported less frequently with ocular administration or this or other Timolol maleate formulations:
Ocular: Irritation, conjunctivitis, blepharitis, keratitis, ocular pain, discharge, foreign body sensation, dry eye, ptosis, decreased corneal sensitivity, corneal erosion, cystoid macular edema, visual disturbances including refractive changes and diplopia, pseudopemphigoid, choroidal detachment following filtration surgery, eyelid erythema, cataract and retinal vascular disorder.
General: Asthenia/fatigue, headache and fever combined with general muscle aches.
Auditive: Tinnitus, otitis.
Cardiovascular: Bradycardia, arrhythmia, hypotension, hypertension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema, chest pain, vasodilation, signs of worsening arterial insuffiency including claudication, Raynaud´s phenomenon and cold hands and feet.
Digestive: Nausea, diarrhea, dyspepsia, anorexia, dry mouth and abdominal pain.
Immunologic: Systemic lupus erythematosus.
Nervous system: Dizziness, increased signs and symptoms of myasthenia gravis, paraesthesia, somnolence, insomnia, nightmares, behavioral changes, psychic disturbances, depression, confusion, hallucinations, anxiety, disorientation, nervousness, memory loss, vertigo, decreased ability to concentrate, emotional lability and catatonia.
Skin: Alopecia and psoriasiform rash or exacerbation of psoriasis and pemphigoid.
Hypersensitivity: Signs and symptoms of systemic allergic reactions, including angioedema, urticaria, and localized and generalized rash.
Respiratory: Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure, dyspnea, nasal congestion, cough, upper respiratory infections.
Endocrine: Masked symptoms of hypoglycemia in diabetic patients. Hyperglycemia.
Urogenital: Retroperitoneal fibrosis, decreased libido, impotence, Peyronie´s disease and dysuria.
Musculoskeletal and connective tissue: Pain, arthralgia.

Overdosage:
There is no specific information about the emergency treatment in overdosage cases.
The most common effects are: bradycardia, bronchos-pasm and hypotension.
If accidental ocular overdosage occurs, it is advisable to wash the area with water or saline solution.
If an overdosage eventually occurs, go to the nearest hospital or toxicology centers.

Patient information:
Patients should know that POENTIMOL® ophthalmic solution contains benzalkonium chloride which may be absorbed by contact lenses. Contact lenses should be removed from the eye before applying the product. Said lenses may be reinserted 15 minutes after POENTIMOL® administration. If more than one topical ophthalmic drug is used, such drugs should be administered with at least five minutes apart.

How supplied:
Dropper bottle containing 0.25% and 0.50% 5 ml- sterile ophthalmic solution.

Storage conditions:
Store below 30°C. Protect from light.

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.

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