

BAUSCH + LOMB

Rimoflo™ Soft

(Brimonidine Tartrate Ophthalmic Solution 0.15% w/v)

GENERIC NAME

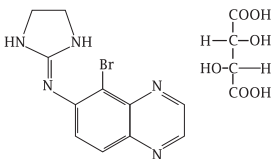
Brimonidine Tartrate Ophthalmic Solution 0.15% w/v

DOSAGE FORM

Ophthalmic Solution.

DESCRIPTION

Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) sterile, is a relatively selective alpha-2 adrenergic receptor agonist (topical intraocular pressure lowering agent). The structural formula of brimonidine tartrate is:



5-Bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate; MW=442.24

In solution, Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) has a clear, greenish-yellow color. It has an osmolality of 250-350 mOsmol/kg and a pH of 6.9-7.4 (0.15%).

Brimonidine tartrate appears as an off-white to pale-yellow powder and is soluble in both water (0.6 mg/mL) and in the product vehicle (1.4 mg/mL) at pH 7.7.

COMPOSITION

Active: Brimonidine Tartrate 0.15% w/v

Inactive Ingredients: Sodium CMC, Sodium Chlorite (Oxychloro Complex), Boric Acid, Borax, Potassium Chloride, Calcium Chloride Dihydrate, Magnesium Chloride (Hexahydrate), Sodium Hydroxide, Water for Injection IP

Preservative Added: Stabilised Oxychloro Complex 0.005% w/v

INDICATIONS

Rimoflo™ Soft is indicated for lowering of intraocular pressure in patients with open angle glaucoma or ocular hypertension

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) in the affected eye(s) three times daily, approximately 8 hours apart. Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic product is to be used, the different products should be instilled at least 5 minutes apart.

USE IN SPECIAL POPULATIONS

Teratogenic Effects

Pregnancy Category B: Teratogenicity studies have been performed in animals. Brimonidine tartrate was not teratogenic when given orally during gestation days 6 through 15 in rats and days 6 through 18 in rabbits. The highest doses of brimonidine tartrate in rats (2.5 mg/kg/day) and rabbits (5.0 mg/kg/day) achieved AUC exposure values 360- and 20-fold higher, or 260- and 15-fold higher, respectively, than similar values estimated in humans treated with Brimonidine Tartrate Ophthalmic Solution, 1 drop in both eyes three times daily.

There are no adequate and well-controlled studies in pregnant women; however, in animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. Because animal reproduction studies are not always predictive of human response, Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the foetus.

Nursing Mothers

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 from Brimonidine Tartrate Ophthalmic Solution 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

Brimonidine Tartrate Ophthalmic Solution is contraindicated in children under the age of 2 years. During postmarketing surveillance, apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine. The safety and effectiveness of brimonidine tartrate have not been studied in children below the age of 2 years.

In a well-controlled clinical study conducted in pediatric glaucoma patients (ages 2 to 7 years) the most commonly observed adverse reactions with Brimonidine tartrate ophthalmic solution dosed three times daily were somnolence (50-83% in patients ages 2 to 6 years) and decreased alertness. In pediatric patients 7 years of age (>20 kg), somnolence appears to occur less frequently (25%).

Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

Hepatic Impairment

No studies are available for use of Brimonidine Tartrate Ophthalmic Solution in patients with hepatic impairment.

Renal Impairment

Brimonidine Tartrate Ophthalmic Solution has not been studied in patients with renal impairment. The effect of dialysis on brimonidine pharmacokinetics in patients with renal failure is not known.

CONTRAINDICATIONS

Rimoflo™ Soft is contraindicated in neonates and infants (under the age of 2 years).





Rimoflo™ Soft is contraindicated in patients with known hypersensitivity to any ingredient in the formulation.

WARNINGS AND PRECAUTIONS

FOR EXTERNAL USE ONLY. NOT FOR INJECTION

Potiation of Vascular Insufficiency

Brimonidine Tartrate Ophthalmic Solution may potentiate syndromes associated with vascular insufficiency. Brimonidine Tartrate Ophthalmic Solution should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

Severe Cardiovascular Disease

Brimonidine Tartrate Ophthalmic Solution has been shown to produce minimal effect on the blood pressure of patients in clinical studies, still caution should be exercised in treating patients with severe cardiovascular disease.

Contamination of Topical Ophthalmic Products After Use

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 ocular epithelial surface.

DRUG INTERACTIONS

Antihypertensives/Cardiac Glycosides

Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) may reduce blood pressure, henceforth caution in using drugs such as antihypertensives and/or cardiac glycosides with Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) is advised.

CNS Depressants

Although specific drug interaction studies have not been reported with Brimonidine Tartrate Ophthalmic Solution the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.

Tricyclic Antidepressants

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 Brimonidine tartrate ophthalmic solution in humans can lead to resulting interference with the IOP lowering effect. Caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Monoamine Oxidase Inhibitors

Monoamine oxidase (MAO) inhibitors may theoretically interfere with the metabolism of brimonidine and potentially result in an increased systemic side-effect such as hypotension. Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

UNDESIRABLE EFFECTS

Adverse reactions occurring in approximately 10-20% of the subjects receiving brimonidine ophthalmic solution (0.1-0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse

reactions occurring in approximately 5-9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

Adverse reactions occurring in approximately 1-4% of the subjects receiving brimonidine ophthalmic solution (0.1-0.2%) included: abnormal taste, allergic reaction, asthenia, blepharitis, blepharoconjunctivitis, blurred vision, bronchitis, cataract, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspepsia, dyspnea, epiphora, eye discharge, eye dryness, eye irritation, eye pain, eyelid edema, eyelid erythema, fatigue, flu syndrome, follicular conjunctivitis, foreign body sensation, gastrointestinal disorder, headache, hypercholesterolemia, hypotension, infection (primarily colds and respiratory infections), insomnia, keratitis, lid disorder, pharyngitis, photophobia, rash, rhinitis, sinus infection, sinusitis, somnolence, stinging, superficial punctate keratopathy, tearing, visual field defect, vitreous detachment, vitreous disorder, vitreous floaters, and worsened visual acuity.

The following reactions were reported in less than 1% of subjects: corneal erosion, hordeolum, nasal dryness, and taste perversion.

Post Marketing Experience

The following reactions have been identified during postmarketing use of brimonidine tartrate ophthalmic solutions include: bradycardia, depression, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, eyelid pruritus, rash, and vasodilation), syncope, and tachycardia. Apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

Pharmacodynamics

Mechanism of Action:

Brimonidine tartrate is a relatively selective alpha-2 adrenergic receptor agonist with a peak ocular 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

Absorption

After ocular administration of either a 0.1% or 0.2% solution, plasma concentrations peaked within 0.5 to 2.5 hours and declined with a systemic half-life of approximately 2 hours.

Distribution

The protein binding of brimonidine has not been studied.

Metabolism

In humans, brimonidine is extensively metabolized by the liver.

Excretion

Urinary excretion is the major route of elimination of brimonidine and its metabolites. Approximately 87% of an orally-administered radioactive dose of brimonidine was eliminated within 120 hours, with 74% found in the urine.



CLINICAL STUDIES

Elevated IOP presents a major risk factor in glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss. Brimonidine tartrate has the action of lowering intraocular pressure with minimal effect on cardiovascular and pulmonary parameters. Clinical studies were conducted to evaluate the safety, efficacy, and acceptability of brimonidine tartrate ophthalmic solution 0.15% compared with brimonidine tartrate ophthalmic solution 0.2%, administered three-times-daily in patients with open-angle glaucoma or ocular hypertension. Those results indicated that brimonidine tartrate ophthalmic solution 0.15% is comparable in IOP lowering effect to brimonidine tartrate ophthalmic solution 0.2%, and effectively lowers IOP in patients with open-angle glaucoma or ocular hypertension by approximately 2-6 mmHg.

OVERDOSE

Very limited information exists on accidental ingestion of brimonidine in adults; the only adverse reaction reported to date has been hypotension. Symptoms of brimonidine overdose have been reported in neonates, infants, and children receiving Brimonidine Tartrate Ophthalmic Solution as part of medical treatment of congenital glaucoma or by accidental oral ingestion. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

INFORMATION FOR PATIENTS

- Rimoflo™ Soft is sterile when packed. Patient are advised not to allow the dropper tip/ dispensing tip to touch any surface, as this may contaminate the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.
- If solution changes color or becomes cloudy, it is advised that patients must not use it.
- Do not use the product after the expiration date marked on the bottle.
- If patients have ocular surgery or develop an intercurrent ocular condition (e.g. trauma or infection), immediately seek physician's advice concerning the continued use of the present multidose container.
- If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart and only after consultation with medical practitioner.
- As with other similar medications, Rimoflo™ Soft may cause fatigue and/or drowsiness in some cases.
- Patients who engage in hazardous activities are cautioned of the potential for a decrease in mental alertness.

INCOMPATIBILITIES

No incompatibility studies are reported.

SHELF LIFE

Please see Mfg. Date/ Expiry Date printed on pack. Do not use the product after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

PACKAGING INFORMATION

Rimoflo™ Soft (Brimonidine Tartrate Ophthalmic Solution 0.15% w/v) are supplied in a 5 ml plastic bottle with a white cap.

STORAGE AND HANDLING INSTRUCTIONS

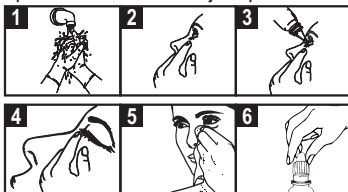
Keep in a cool place. Protect from light. DO NOT FREEZE.
Use the solution within one month after opening the container.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN

REFERENCES:

Pl of Alphagan-P, Allergan, 06/2011 Information compiled in December 2011

Tips for Safe Administration of Eye Drops[®]



- Wash your hands thoroughly before administration.
- Bend your head backwards and gently pull your lower eyelid down.
- Turn the bottle upside down and squeeze it to release one drop into each eye that needs treatment.
- Let go of the lower lid, and close your eye for 30 seconds.
- Wipe away any liquid that falls onto your cheek with a tissue.
- Close the cap immediately after use.

Take Care of your eye drops:

- Do not let the dropper or dispensing tips touch your eye, finger, or any other surface.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If more than one type of Eye Drops are used, wait for at least five minutes before administering the second medication to avoid washout of the previous drug.
- Consult your physician if eye symptoms become worse after using eye drops.

**Read this entire leaflet carefully before you start using this medicine.*

Keep this leaflet. You may need to read it again. If you have any further questions, ask your Physician.

Marketed by: BAUSCH & LOMB EYECARE (I) PVT. LTD.

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Manufactured in India by:
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