BRIMONIDINE TARTRATE- brimonidine tartrate solution
Sandoz Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BRIMONIDINE TARTRATE OPHTHALMIC SOLUTION safely and effectively. See full prescribing information for BRIMONIDINE TARTRATE OPHTHALMIC SOLUTION.

BRIMONIDINE TARTRATE OPHTHALMIC SOLUTION, 0.15%, for topical ophthalmic use
Initial U.S. Approval: 1996

RECENT MAJOR CHANGES

- Contraindications, Neonates and Infants (Pediatric Patients Younger than 2 Years Old) (4.1) 11/2025
- Warnings and Precautions, Severe Cardiovascular Disease (5.2) 11/2025
- Warnings and Precautions, Contamination of Topical Ophthalmic Products After Use (5.3) 11/2025

INDICATIONS AND USAGE

Brimonidine tartrate ophthalmic solution, 0.15% is an alpha adrenergic agonist indicated for the lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension (1).

DOSAGE AND ADMINISTRATION

- Instill one drop in the affected eye(s) three-times daily (2).
- If more than one topical ophthalmic product is being used, the products should be administered at least 5 minutes apart (2).

DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing 0.15% (1.5 mg/mL) brimonidine tartrate (3)

CONTRAINDICATIONS

- Neonates and infants (pediatric patients younger than 2 years old) (4.1).
- Hypersensitivity to any component of this product (4.2).

WARNINGS AND PRECAUTIONS

- Potentiation of vascular insufficiency (5.1)

ADVERSE REACTIONS

Most common adverse reactions are allergic conjunctivitis, conjunctival hyperemia, and eye pruritis (6.1).
To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc. at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Concomitant use with systemic beta-blockers may potentiate systemic beta-blockade (7.1).
- Use with CNS depressants may result in an additive or potentiating effect (7.2).
- Tricyclic antidepressants may potentially blunt the hypotensive effect of systemic clonidine (7.3).
- Monoamine oxidase inhibitors may result in increased hypotension (7.4).

USE IN SPECIFIC POPULATIONS

Use with caution in pediatric patients aged 2 years and older (8.4).
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
4.1 Neonates and Infants (Pediatric Patients Younger than 2 Years Old)
4.2 Hypersensitivity Reactions
5 WARNINGS AND PRECAUTIONS
5.1 Potentiation of Vascular Insufficiency
5.2 Severe Cardiovascular Disease
5.3 Contamination of Topical Ophthalmic Products After Use
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Anti-hypertensives / Cardiac Glycosides
7.2 CNS Depressants
7.3 Tricyclic Antidepressants
7.4 Monoamine Oxidase Inhibitors
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Brimonidine tartrate ophthalmic solution, 0.15% is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

2 DOSAGE AND ADMINISTRATION

The recommended dosage is one drop of brimonidine tartrate ophthalmic solution,

0.15% in the affected eye(s) three-times daily, approximately 8 hours apart.

Brimonidine tartrate ophthalmic solution, 0.15% may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic product is being used, the products should be administered at least 5 minutes apart.

3 DOSAGE FORMS AND STRENGTHS

Ophthalmic solution containing 0.15% (1.5 mg/mL) brimonidine tartrate.

4 CONTRAINDICATIONS

4.1 Neonates and Infants (Pediatric Patients Younger than 2 Years Old)

Brimonidine tartrate ophthalmic solution, 0.15% is contraindicated in neonates and infants (pediatric patients younger than 2 years old) *[see Use in Specific Populations (8.4)].*

4.2 Hypersensitivity Reactions

Brimonidine tartrate ophthalmic solution, 0.15% is contraindicated in patients with hypersensitivity to any component of this product *[see Adverse Reactions (6.1) and (6.2)].*

5 WARNINGS AND PRECAUTIONS

5.1 Potentiation of Vascular Insufficiency

Brimonidine tartrate ophthalmic solution, 0.15% may potentiate syndromes associated with vascular insufficiency. Brimonidine tartrate ophthalmic solution, 0.15% should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

5.2 Severe Cardiovascular Disease

Although brimonidine tartrate ophthalmic solution had minimal effect on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

5.3 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.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the

labeling:

- Neonates and Infants (Pediatric Patients Younger than 2 Years Old) *[see Contraindications (4.1)]*
- Potentiation of Vascular Insufficiency *[see Warnings and Precautions (5.1)]*
- Severe Cardiovascular Disease *[see Warnings and Precautions (5.2)]*
- Contamination of Topical Ophthalmic Products After Use *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions occurring in approximately 10 to 20% of the subjects included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritis.

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

Adverse reactions occurring in approximately 1 to 4% of subjects included: allergic reaction, arthralgia, arthritis, asthenia, blepharitis, blepharoconjunctivitis, blurred vision, bronchitis, cataract, chest pain, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, diabetes mellitus, 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, insomnia, joint disorder, keratitis, lid disorder, osteoporosis, 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 adverse reactions were reported in less than 1% of subjects: corneal erosion, nasal dryness, and taste perversion.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of brimonidine tartrate ophthalmic solution. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Bradycardia, iritis, miosis, skin reactions (including erythema, eyelid pruritis, rash, and vasodilation), and tachycardia.
- Apnea, bradycardia, hypotension, hypothermia, hypotonia, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions.

7 DRUG INTERACTIONS

7.1 Anti-hypertensives / Cardiac Glycosides

Alpha-2 agonists, as a class, may reduce blood pressure. Caution in using drugs such as beta-blockers (ophthalmic and systemic), anti-hypertensives and/or cardiac glycosides is advised.

7.2 CNS Depressants

Although specific drug interaction studies have not been conducted with brimonidine tartrate ophthalmic solution, 0.15%, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.

7.3 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, 0.15% in humans can lead to resulting interference with its IOP-lowering effect. Caution, however, is advised in patients taking tricyclic antidepressants, which can affect the metabolism and uptake of circulating amines.

7.4 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with brimonidine tartrate ophthalmic solution, 0.15% in pregnant women. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent *(see Data).* Because animal reproduction studies are not always predictive of human response, brimonidine tartrate ophthalmic solution, 0.15% should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Data

Human Data

Limited available data from postmarketing safety reports and published literature with topical use of brimonidine tartrate ophthalmic solution in pregnant women are insufficient to inform a drug-associated risk of pregnancy-related adverse outcomes including miscarriage, stillbirth, congenital anomaly, and events experiences by offspring while breastfeeding.

Animal Data

Embryofetal studies were conducted in pregnant rabbits administered brimonidine tartrate by daily oral gavage on gestation days 6 to 18, to target the period of organogenesis. Brimonidine caused miscarriage at 5 mg/kg/day (approximately 50-times the recommended human ophthalmic dose (RHOD) based on AUC). The no observed adverse effect level (NOAEL) for developmental toxicity in rabbits was 1 mg/kg/day (approximately 6-fold the RHOD based on AUC). No treatment-related malformations were observed in rabbits. Signs of maternal sedation and fatigue were observed at all dose levels; the lowest observed adverse effect level (LOAEL) for maternal toxicity was 5 mg/kg/day, based on the dose-response for these signs.

Embryofetal studies were conducted in pregnant rats administered brimonidine tartrate by daily oral gavage on gestation days 6 to 15, to target the period of organogenesis. The NOAEL for developmental toxicity was 2.5 mg/kg/day (approximately 750-fold the RHOD based on AUC). No treatment-related malformations were observed in rats. The LOAEL for maternal toxicity was 2.5 mg/kg/day, based on signs of sedation and fatigue. The maternal NOAEL was 1 mg/kg/day (180-fold the RHOD based on AUC).

After pregnant rats received a single oral dose of ^{14}C-brimonidine tartrate, brimonidine and metabolites crossed the placenta and were detectable in fetal blood and organs.

8.2 Lactation

Risk Summary

It is not known whether brimonidine tartrate is excreted in human milk. In animal studies, brimonidine has been shown to cross the blood-brain barrier and is excreted into breast milk after oral administration to lactating rats *(see Data)*. Because of the potential for serious adverse reactions, including central nervous system depression and apnea, from brimonidine tartrate ophthalmic solution, 0.15% in nursing infants, brimonidine tartrate ophthalmic solution, 0.15% is not recommended for use during lactation.

Data

Animal Data

After a single oral dose of ^{14}C-labeled brimonidine tartrate to lactating rats, brimonidine and metabolites were detected in milk. After male and female rats received a single oral dose of ^{14}C-brimonidine tartrate, brimonidine crossed the blood:brain barrier. Radiolabel was detected in the cerebellum, cerebrum, and spinal cord.

8.4 Pediatric Use

Brimonidine tartrate ophthalmic solution, 0.15% is contraindicated in pediatric patients younger than 2 years old *[see Contraindications (4.1)]*. During postmarketing surveillance, apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine.

In a well-controlled clinical study conducted in pediatric glaucoma patients aged 2 to 7 years old, the most commonly observed adverse events with brimonidine tartrate ophthalmic solution 0.2% dosed three-times-daily were somnolence (50% to 83% in pediatric patients aged 2 to 6 years old) and decreased alertness. In pediatric patients aged 7 years and older (>20 kg), somnolence appears to occur less frequently (25%).

Approximately 16% of pediatric patients on brimonidine tartrate ophthalmic solution discontinued from the study due to somnolence.

8.5 Geriatric Use

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

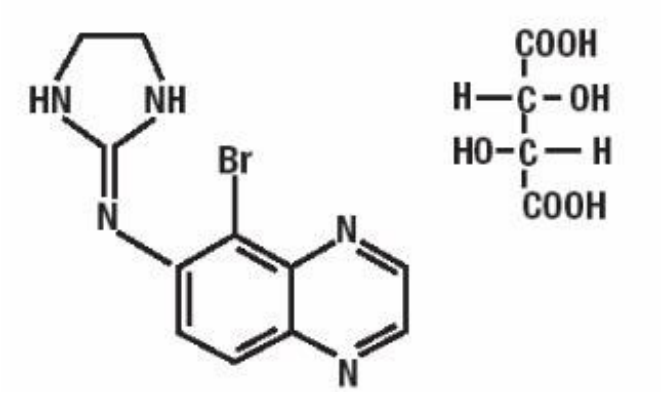
10 OVERDOSAGE

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 as part of medical treatment of congenital glaucoma or accidental oral ingestion *[see Use In Specific Populations (8.4)]*. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

11 DESCRIPTION

Brimonidine tartrate ophthalmic solution, 0.15% (1.5 mg brimonidine tartrate per mL equivalent to 1.0 mg brimonidine free base per mL) is a relatively selective alpha-2-adrenergic agonist for topical ophthalmic use. The chemical name of brimonidine tartrate is 5-bromo-6-(2-imidazolidinylideneamino) quinoxaline L-tartrate. It is a white to off-white,

pale yellow to yellow powder. It has a molecular weight of 442.24 as the tartrate salt, and is both soluble in water (1.5 mg/mL) and in the product vehicle (3.0 mg/mL) at pH 7.2. The structural formula is:



Formula: $C_{11}H_{10}BrN_5 \bullet C_4H_6O_6$

CAS Number: 59803-98-4

In solution, brimonidine tartrate ophthalmic solution, 0.15% has a clear, pale yellow to greenish yellow color. It has an osmolality of 250 - 350 mOsmol/kg and a pH of 6.6 to 7.4.

Contains: **Active ingredient:** brimonidine tartrate 1.5 mg/mL (1.5 mg/mL), **Preservative:** Polyquad (polyquaternium-1) 0.001% (0.01 mg/mL), **Inactives:** boric

acid, calcium chloride, magnesium chloride, mannitol, potassium chloride, povidone, purified water, sodium borate, sodium chloride, with hydrochloric acid and/or sodium hydroxide to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Brimonidine tartrate ophthalmic solution, 0.15% 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.

12.2 Pharmacodynamics

Brimonidine tartrate ophthalmic solution, 0.15% has a peak ocular hypotensive effect occurring at two hours post-dosing.

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.

12.3 Pharmacokinetics

Absorption

In a pharmacokinetic study, 14 healthy subjects (4 males and 10 females) received a single topical ocular administration of brimonidine tartrate ophthalmic solution, 0.15%, one drop per eye. The peak plasma concentrations (C_{max}) and $AUC_{0\text{-}inf}$ were 73 ± 19 pg/mL and 375 ± 89 pg•hr/mL, respectively. T_{max} was 1.7 ± 0.7 hours after dosing. The systemic half-life was approximately 2.1 hours.

Distribution

Brimonidine was approximately 29% bound to plasma proteins in healthy subjects.

Elimination

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% of the radioactivity recovered in the urine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No compound-related carcinogenic effects were observed in either mice or rats following a 21-month and a 24-month study, respectively. In these studies, dietary administration of brimonidine tartrate at doses up to 2.5 mg/kg/day in mice and 1.0 mg/kg/day in rats achieved 120 and 76 times the recommended human ophthalmic dose (RHOD) based on C_{max}.

Mutagenesis

Brimonidine tartrate was not mutagenic or cytogenic in a series of *in vitro* and *in vivo* studies including the Ames test, chromosomal aberration assay in Chinese hamster ovary (CHO) cells, a host-mediated assay and cytogenic studies in mice, and dominant lethal assay.

Impairment of Fertility

A reproduction and fertility study in rats with brimonidine tartrate demonstrated no adverse effect on male or female fertility at oral doses up to 1 mg/kg (approximately 180 times the recommended human ophthalmic dose (RHOD) based on estimated AUC).

14 CLINICAL STUDIES

A clinical study was conducted to evaluate the safety and efficacy of brimonidine tartrate ophthalmic solution, 0.15% compared to Alphagan® P** administered three times daily in patients with open-angle glaucoma or ocular hypertension. The results indicated that brimonidine tartrate ophthalmic solution, 0.15% is equivalent in IOP-lowering effect to Alphagan® P (brimonidine tartrate ophthalmic solution), 0.15%, and effectively lowers IOP in patients with open-angle glaucoma or ocular hypertension by 2 - 6 mmHg.

16 HOW SUPPLIED/STORAGE AND HANDLING

Brimonidine tartrate ophthalmic solution, 0.15% is supplied sterile in opaque white LDPE plastic bottles and natural tips with purple polypropylene caps as follows:

5 mL in 8 mL bottle NDC 61314-144-05

10 mL in 10 mL bottle NDC 61314-144-10

15 mL in 15 mL bottle NDC 61314-144-15

Storage: Store at 15°C to 25° C (59°F to 77°F). After opening, Brimonidine tartrate ophthalmic solution, 0.15% can be used until the expiration date on the bottle.

17 PATIENT COUNSELING INFORMATION

Handling the Container

Instruct patients that ocular solutions, if handled improperly or if the tip of the dispensing container contacts 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 *[see Warnings and Precautions (5.3)]*. Always replace the cap after using. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

When to Seek Physician Advice

Advise patients that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

Use with Other Ophthalmic Drugs

Advise patients that if more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart.

Potential for Decreased Mental Alertness

As with other drugs in this class, brimonidine tartrate ophthalmic solution, 0.15% may cause fatigue and/or drowsiness in some patients. Patients who engage in hazardous activities should be cautioned of the potential for a decrease in mental alertness.

Rx Only

**ALPHAGAN P is a registered trademark of Allergan, Inc.

Manufactured by

Alcon Laboratories, Inc.

Fort Worth, Texas 76134 for

Sandoz Inc.

Princeton, NJ 08540

300069925-1125

PRINCIPLE DISPLAY PANEL

NDC 61314-144-05

Brimonidine

Tartrate

Ophthalmic

Solution

0.15%

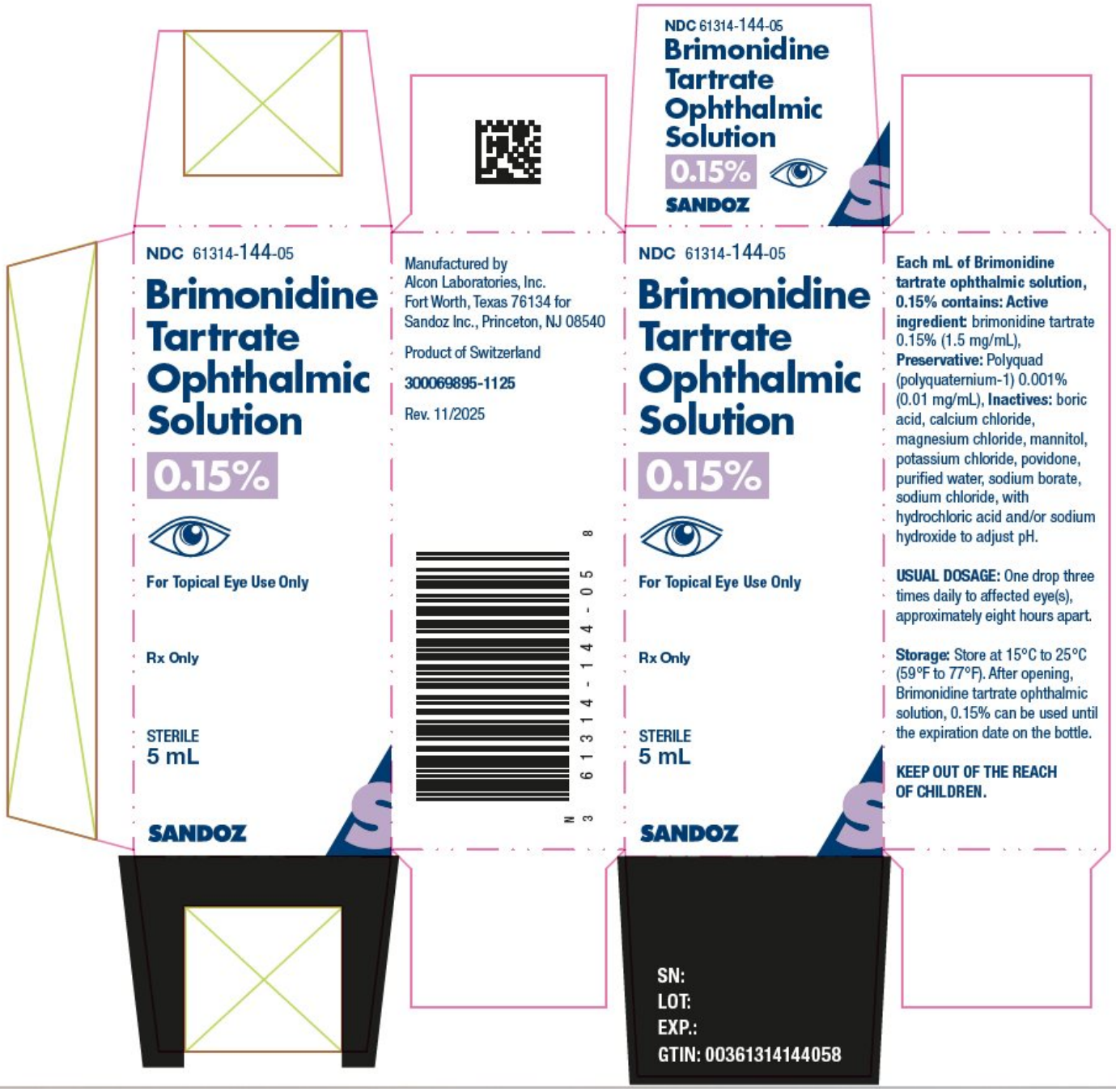
For Topical Eye Use Only

Rx Only

STERILE

5 mL

SANDOZ



BRIMONIDINE TARTRATE

brimonidine tartrate solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:61314-144
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
BRIMONIDINE TARTRATE (UNII: 4S9CL2DY2H) (BRIMONIDINE - UNII:E6GNX3HHTE)	BRIMONIDINE TARTRATE	1.5 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
BORIC ACID (UNII: R57ZHV85D4)	
SODIUM BORATE (UNII: 91MBZ8H3QO)	
CALCIUM CHLORIDE (UNII: M4I0D6VV5M)	
POTASSIUM CHLORIDE (UNII: 660YQ98I10)	
MANNITOL (UNII: 3OWL53L36A)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:61314-144-05	1 in 1 CARTON	10/02/2010	
1		5 mL in 1 BOTTLE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
2	NDC:61314-144-10	1 in 1 CARTON	10/02/2010	
2		10 mL in 1 BOTTLE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		
3	NDC:61314-144-15	1 in 1 CARTON	10/02/2010	
3		15 mL in 1 BOTTLE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021764	10/02/2010	

Labeler - Sandoz Inc (005387188)

Revised: 11/2025 Sandoz Inc