SIMBRINZA®
(brinzolamide/brimonidine tartrate ophthalmic suspension)
1%/0.2%

Two medications in one bottle

INDICATIONS AND USAGE
SIMBRINZA® (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination indicated in the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION
Contraindications
SIMBRINZA® Suspension is contraindicated in patients who are hypersensitive to any component of this product and neonates and infants under the age of 2 years.

For additional information about SIMBRINZA® Suspension, please see continued Important Safety Information on the following pages and full Prescribing Information.
Be sure to carefully follow your doctor’s instructions for replacement therapy with SIMBRINZA® Suspension.

Your doctor is replacing one of your current treatment eye drops with SIMBRINZA® Suspension.

It’s important that you follow your doctor’s instructions for the use of SIMBRINZA® Suspension. Your eye drops should be administered at least five (5) minutes apart.

**INDICATIONS AND USAGE (cont’d)**

**Dosage and Administration**
The recommended dose is one drop of SIMBRINZA® Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA® Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

**IMPORTANT SAFETY INFORMATION (cont’d)**

**Warnings and Precautions**

*Sulfonamide Hypersensitivity Reactions*—Brinzolamide is a sulfonamide, and although administered topically, is absorbed systemically. Sulfonamide attributable adverse reactions may occur. Fatalities have occurred due to severe reactions to sulfonamides. Sensitization may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

*Corneal Endothelium*—There is an increased potential for developing corneal edema in patients with low endothelial cell counts.

*Severe Hepatic or Renal Impairment (CrCl <30 mL/min)*—SIMBRINZA® Suspension has not been specifically studied in these patients and is not recommended.

*Acute Angle-Closure Glaucoma*—The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. SIMBRINZA® Suspension has not been studied in patients with acute angle-closure glaucoma.

*Contact Lens Wear*—The preservative in SIMBRINZA® Suspension, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA® Suspension but may be reinserted 15 minutes after instillation.

*Severe Cardiovascular Disease*—Brimonidine tartrate, a component of SIMBRINZA® Suspension, had a less than 5% mean decrease in blood pressure 2 hours after dosing.
Eligible patients may pay no more than $25*

The OPENINGSTM Patient Support Program offers:

A program savings card that may help you save money on your prescriptions. You’ll also receive educational information, practical tips, convenient reminders, and more.

Learn more and enroll at OpeningsProgram.com, or ask your doctor for more information.

*Offer not valid for patients who are enrolled in Medicare Part D, Medicaid, Medigap, VA, DOD, Tricare, or any other government-run or government-sponsored health care program with a pharmacy benefit. Complete terms and conditions available at OpeningsProgram.com.

in clinical studies; caution should be exercised in treating patients with severe cardiovascular disease.

Potentiation of Vascular Insufficiency—Brimonidine tartrate, a component of SIMBRINZA® Suspension, may potentiate syndromes associated with vascular insufficiency. It should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud’s phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

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 have been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Adverse Reactions

SIMBRINZA® Suspension

In two clinical trials of 3 months’ duration with SIMBRINZA® Suspension, the most frequent reactions associated with its use occurring in approximately 3-5% of patients in descending order of incidence included: blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Adverse reaction rates with SIMBRINZA® Suspension were comparable to those of the individual components.

For additional information about SIMBRINZA® Suspension, please see continued Important Safety Information on the previous pages and full Prescribing Information.

SIMBRINZA®
(brinzolamide/brimonidine tartrate ophthalmic suspension)
1%/0.2%
At the Pharmacy
Show this information to the pharmacist when filling your prescription for SIMBRINZA® Suspension

This patient was prescribed SIMBRINZA® Suspension:
- NDC 0065-4147-27
- Multi-dose 8 mL bottle

There is no FDA-approved therapeutic equivalent for SIMBRINZA® Suspension.¹

IMPORTANT SAFETY INFORMATION (cont’d)
Adverse Reactions
SIMBRINZA® Suspension (cont’d)
Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA® Suspension patients.

Brinzolamide 1%
In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse events reported in 5-10% of patients were blurred vision and bitter, sour, or unusual taste. Adverse events occurring in 1-5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus, and rhinitis.

Brimonidine Tartrate 0.2%
In clinical studies of brimonidine tartrate 0.2%, adverse events occurring in approximately 10-30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus. Events occurring in approximately 3-9% of the subjects, in descending order, included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision, and muscular pain.

Drug Interactions—Consider the following when prescribing SIMBRINZA® Suspension:
Concomitant administration with oral carbonic anhydrase inhibitors is not recommended due to the potential additive effect. Use with high-dose salicylate may result in acid-base and electrolyte alterations. Use with CNS depressants may result in an additive or potentiating effect. Use with antihypertensives/cardiac glycosides may result in additive or potentiating effect on lowering blood pressure. Use with tricyclic antidepressants may blunt the hypotensive effect of systemic clonidine and it is unknown if use with this class of drugs interferes with IOP lowering. Use with monoamine oxidase inhibitors may result in increased hypotension.

For additional information about SIMBRINZA® Suspension, please see the accompanying full Prescribing Information.

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%

INDICATIONS AND USAGE

SIMBRINZA™ is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension. (1)

DOSE AND ADMINISTRATION

Shake well before use. Instill one drop in the affected eye(s) three times daily. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart. (2)

DOSE FORMS AND STRENGTHS

Suspension containing 10 mg/mL brinzolamide and 2 mg/mL brimonidine tartrate. (3)

CONTRAINDICATIONS

• Hypersensitivity to any component of this product. (4.1)
• Neovascular and infants (under the age of 2 years). (4.2)

WARNINGS AND PRECAUTIONS

• Potential for sulfonamide hypersensitivity reactions (5.1)
• Potential for corneal endothelium cell loss (5.2)

ADVERSE REACTIONS

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience
6.2 Postmarketing Experience

7 DRUG INTERACTIONS

7.1 Oral Carbonic Anhydrase Inhibitors
7.2 High Dose Salicylate Therapy
7.3 CNS Depressants
7.4 Antibiotics/Cardiac Glycosides
7.5 Tricyclic Antidepressants
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8.1 Pregnancy
8.2 Nursing Mothers
8.3 Contact Lens Wear
8.4 Pediatric Use
8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. (1)

2 DOSAGE AND ADMINISTRATION

The recommended dose is one drop of SIMBRINZA™ in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ ophthalmic suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart. (2)

3 DOSAGE FORMS AND STRENGTHS

Suspension containing 10 mg/mL brinzolamide and 2 mg/mL brimonidine tartrate. (3)

4 CONTRAINDICATIONS

4.1 Hypersensitivity
4.2 Neonates and infants (under the age of 2 years)

5 WARNINGS AND PRECAUTIONS

5.1 Sulfonamide Hypersensitivity Reactions
5.2 Corneal Endothelium
5.3 Severe Renal Impairment
5.4 Acute Angle-Closure Glaucma
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7 DRUG INTERACTIONS

7.1 Oral Carbonic Anhydrase Inhibitors
7.2 High Dose Salicylate Therapy
7.3 CNS Depressants
7.4 Antibiotics/Cardiac Glycosides
7.5 Tricyclic Antidepressants
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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
8.2 Nursing Mothers
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17 PATIENT COUNSELING INFORMATION (17.1)

0.1 Clinical Studies Experience

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

SIMBRINZA™ in two clinical trials of 3 months duration 435 patients were treated with SIMBRINZA™, and 915 were treated with the two individual components. The most frequently reported adverse reactions in patients treated with SIMBRINZA™ occurring in approximately 3 to 5% of patients in descending order of incidence were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Rates of adverse reactions reported with the individual components were comparable. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ patients. Other adverse reactions that have been reported with the individual components during clinical trials are listed below.

Brinzolamide 1%

In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse reactions reported in 5 to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1 to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain,
There is a potential for an additive effect on the known effects of oral carbonic anhydrase inhibitors. 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

Pregnancy Category C: Developmental toxicity studies with brinzolamide in rabbits at oral doses of 1, 3, and 6 mg/kg/day (60, and 120 times the recommended human ophthalmic dose) produced maternal toxicity at 6 mg/kg/day and a significant increase in the number of fetal variations, such as accessory skull bones, which was only slightly higher than the historic value at 1 and 6 mg/kg. In rats, statistically decreased body weights of fetuses from dams receiving oral doses of 18 mg/kg/day (180 times the recommended human dose) during gestation were proportional to the reduced maternal weight gain, with no statistically significant effects on organ or tissue development. Increases in unossified sterna, reduced ossification of the skull, and uns ossified hoof that occurred at 6 and 18 mg/kg were not statistically significant. No treatment-related malformations were seen. Following oral administration of 1% brimonidine to pregnant rats, radioactivity was found to cross the placenta and was present in the fetal tissues and blood. Developmental toxicity studies performed in rats with oral doses of 0.66 mg brinzolamide base/kg revealed no evidence of harm to the fetus. Dosing at this level resulted in a plasma drug concentration approximately 100 times higher than that seen in humans at the recommended human ophthalmic dose. In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. There are no adequate and well-controlled studies in pregnant women. SIMBRINZA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

In a study in rabbits, brinzolamide in lactating rats, decreases in body weight gain in offspring at an oral dose of 15 mg/kg/day (150 times the recommended human ophthalmic dose) were observed during lactation. No other effects were observed. However, following oral administration of 1% brinzolamide to lactating rats, radioactivity was found in milk at concentrations below those in the blood and plasma. In animal studies, brimonidine was excreted in breast milk. It is not known whether brinzolamide and brimonidine tartrate are excreted in human milk following topical ocular administration. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%, 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.

8.4 Pediatric Use

The individual component, brinzolamide, has been studied in pediatric glaucoma patients 4 weeks to 5 years of age. The individual component, brimonidine tartrate, has been studied in pediatric patients 2 to 7 years old. Somnolence (50-83%) and decreased alertness was seen in patients 2 to 6 years old. SIMBRINZA® is contraindicated in children under the age of 2 years (see Contraindications (4.3)).

8.5 Geriatric Use

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

8.6 Antihypertensives/Cardiac Glycosides

Because brimonidine tartrate, a component of SIMBRINZA®, may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with SIMBRINZA® is advised.

8.7 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 SIMBRINZA™ 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.

8.9 MONOAMINE OXIDASE INHIBITORS

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

11 DESCRIPTION

SIMBRINZA® (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist.

Brinzolamide is described chemically as: (R)(+)-4-Ethylamino-2-(3-methoxypropyl)-3,4-dihydr-2H-thieno[3,2-b]thiazol-1-yl-2H-thieno[3,2-b]thiazole-1,2-dione. Its empirical formula is C_{13}H_{14}N_{2}O_{5}S and its structural formula is:

![Structural formula of brinzolamide](image)

Brinzolamide has a molecular weight of 338.5. It is a white powder, which is insoluble in water, very soluble in methanol and soluble in ethanol.

Brimonidine tartrate is described chemically as: 5-bromo-2-[(3,2-e)-1,2-thiazine-6-sulfonamide-1,1-dioxide. Its empirical formula is C_{13}H_{14}N_{2}O_{5}S and its structural formula is:

![Structural formula of brimonidine](image)

Brimonidine tartrate has a molecular weight of 442.2. It is a white to yellow powder that is soluble in water (34 mg/ml) at pH 6.5.

SIMBRINZA® (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is supplied as a sterile, aqueous suspension which has been formulated to be readily suspended following shaking. It has a pH of approximately 6.5 and an osmolality of approximately 270 mOsm/kg.

Each mL of SIMBRINZA® (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% contains:

**Active ingredients:**
- Brinzolamide 10 mg, brimonidine tartrate 2 mg (equivalent to 1.32 mg as brinzolamide free base).
- Preservative: benzalkonium chloride 0.03 mg.

**Inactive ingredients:**
- propylene glycol, carbomer, 9740, boric acid, mannitol, sodium chloride, polysorbate 80 and purified water. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

SIMBRINZA® is comprised of two components: brinzolamide (carbonic anhydrase inhibitor) and brimonidine tartrate (alpha 2 adrenergic receptor agonist). Each of these two components decreases increased intraocular pressure. Increased 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.

Brimonidine inhibits carbonic anhydrase in the ciliary processes of the eye to decrease aqueous humor secretion, presumably by slowing the flow of bicarbonate ions with subsequent reduction in sodium and fluid transport. Brinzolamide has a peak ocular hypotensive effect occurring 3 to 4 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. Brimonidine tartrate has a peak ocular hypotensive effect occurring at two hours post-dosing. The result is a decrease in intraocular pressure (IOP).

12.3 Pharmacokinetics

Following topical ocular administration, brinzolamide is absorbed into the systemic circulation. Due to its affinity for CA-11, brinzolamide distributes extensively into the RBCs and exhibits a long half-life in whole blood (approximately 111 days). In humans, the metabolite N-desethyl brinzolamide is formed which also binds to CA and accumulates in RBCs. This metabolite binds mainly to CA-1 in the presence of brinzolamide. In plasma, both parent brinzolamide and N-desethyl brinzolamide are removed primarily by renal route.
brinzolamide concentrations are <10 ng/mL. Binding to plasma proteins is approximately 60%. Brinzolamide is eliminated predominantly in the urine as unchanged drug. N-Desethyl brinzolamide is also found in the urine along with lower concentrations of the N-desmethylpropyl and N-desmethyl metabolites.

After ocular administration of a 0.2% solution of brimonidine tartrate, plasma concentrations peaked within 1 to 4 hours and declined with a systemic half-life of approximately 3 hours. In humans, systemic metabolism of brimonidine is extensive and metabolized primarily by the liver. Urinary excretion is the major route of elimination of the drug and its metabolites. Approximately 87% of an orally-administered radioactive dose was eliminated within 120 hours, with 74% found in the urine.

In humans, a study was conducted to evaluate the pharmacokinetics of the fixed combination of brinzolamide (brinzolamide) and brimonidine (brimonidine tartrate 1%/0.2% ophthalmic suspension). Healthy volunteers were randomly assigned to receive twice or three times a day either the fixed combination, or to brinzolamide or brimonidine. Subjects who were assigned to the brinzolamide alone or combination arms were administered oral brinzolamide capsules for two weeks prior to beginning dosing with the topical ocular suspension. The results demonstrate that the systemic plasma exposure (AUC and Cmax) to brinzolamide and brimonidine in humans is similar after dosing with the fixed combination to that observed following dosing with the individual components.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The following tests for mutagenic potential of brinzolamide were negative: (1) in vivo mouse micronucleus assay; (2) in vivo sister chromatid exchange assay; and (3) Ames E. coli test. The in vitro mouse lymphoma transformation assay was negative in the absence of activation, but positive in the presence of microsomal activation. In this assay, there was no consistent dose-response relationship to the increased mutation frequency and cytotoxicity likely contributed to the high mutation frequency. Carboxic anhydrase inhibitors, as a class, are not mutagenic and the weight of evidence supports that brinzolamide is consistent with the class. In reproduction studies of brinzolamide in rats, there were no adverse effects on fertility or reproductive capacity of males or females at doses up to 18 mg/kg/day (180 times the recommended human ophthalmic dose).

Brimonidine tartrate was not carcinogenic in either a 21-month mouse or 24-month rat study. In these studies, dietary administration of brimonidine tartrate at doses up to 2.5 mg/kg/day in mice and 1 mg/kg/day in rats resulted in plasma drug concentrations 80 and 120 times higher than the human plasma drug level at the recommended clinical dose, respectively. Brimonidine tartrate was not mutagenic or cytotoxic 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 cytogenetic studies in mice, and a dominant lethal assay. In reproductive studies performed in rats with oral doses of 0.66 mg brimonidine base/kg (approximately 100 times the plasma drug concentration level seen in humans following multiple ophthalmic dosing), fertility was not impaired.

14 CLINICAL STUDIES

Two clinical trials of 3 months duration were conducted in patients with open-angle glaucoma or ocular hypertension to compare the IOP-lowering effect of SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% dosed three times daily (TID) to individually administered 1% brinzolamide three times daily and 0.2% brimonidine tartrate three times daily. Mean IOP values at baseline are presented in Table 1.

**Table 1. Mean (SD) IOP Values at Baseline**

<table>
<thead>
<tr>
<th>Study</th>
<th>SIMBRINZA™</th>
<th>Brinzolamide</th>
<th>Brimonidine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=209)</td>
<td>(n=224)</td>
<td>(n=216)</td>
</tr>
<tr>
<td>Week 2</td>
<td>20.4</td>
<td>22.0</td>
<td>21.6</td>
</tr>
<tr>
<td>8 AM</td>
<td>22.4</td>
<td>21.7</td>
<td>20.9</td>
</tr>
<tr>
<td>10 AM</td>
<td>23.8</td>
<td>23.2</td>
<td>22.6</td>
</tr>
<tr>
<td>3 PM</td>
<td>23.7</td>
<td>23.2</td>
<td>23.2</td>
</tr>
<tr>
<td>Week 4</td>
<td>21.5</td>
<td>22.1</td>
<td>21.9</td>
</tr>
<tr>
<td>8 AM</td>
<td>22.6</td>
<td>21.9</td>
<td>21.8</td>
</tr>
<tr>
<td>10 AM</td>
<td>23.8</td>
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</tr>
<tr>
<td>3 PM</td>
<td>23.7</td>
<td>23.0</td>
<td>23.3</td>
</tr>
</tbody>
</table>

The IOP-lowering effect of SIMBRINZA™ was 1% to 3 mmHg greater than monotherapy with either 1% brinzolamide or 0.2% brimonidine tartrate throughout the duration of the trials. Least Square Mean IOP (mmHg) and the results at Week 2, Week 6 and Month 3 for each study are provided in Table 2.

**Table 2. Mean IOP (mmHg) by Treatment Group and Treatment Difference in Mean IOP**

<table>
<thead>
<tr>
<th>Study</th>
<th>SIMBRINZA™</th>
<th>Brinzolamide</th>
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</tr>
<tr>
<td>3 PM</td>
<td>23.7</td>
<td>23.2</td>
<td>23.2</td>
</tr>
<tr>
<td>Week 4</td>
<td>21.5</td>
<td>22.1</td>
<td>21.9</td>
</tr>
<tr>
<td>8 AM</td>
<td>22.6</td>
<td>21.9</td>
<td>21.8</td>
</tr>
<tr>
<td>10 AM</td>
<td>23.8</td>
<td>23.1</td>
<td>22.8</td>
</tr>
<tr>
<td>3 PM</td>
<td>23.7</td>
<td>23.0</td>
<td>23.3</td>
</tr>
</tbody>
</table>

16 HOW SUPPLIED/STORAGE AND HANDLING

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is supplied in white low density polyethylene (LDPE) DROP-TAINER® bottles with a natural LDPE dispensing-tip and light green polypropylene cap as follows:

- 8 ml in a 10 ml bottle
- NDC 0065-4147-27

Storage and Handling


17 PATIENT COUNSELING INFORMATION

17.1 Sulfonamide Reactions

Advise patients that if serious or unusual occurs or systemic reactions or signs of hypersensitivity occur, they should discontinue the use of the product and consult their physician.

17.2 Temporary Blurred Vision

Vision may be temporarily blurred following dosing with SIMBRINZA™. Care should be exercised in operating machinery or driving a motor vehicle.

17.3 Effect on Ability to Drive and Use Machinery

As with other drugs in this class, SIMBRINZA™ may cause fatigue and/or drowsiness in some patients. Caution patients who engage in hazardous activities of the potential for a decrease in mental alertness.

17.4 Avoiding Contamination of the Product

Instruct patients that ophthalmic 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 (5.9)). Always replace the cap after use. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

17.5 Intercurrent Ocular Conditions

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.

17.6 Concomitant Topical Ocular Therapy

If more than one topical ophthalmic drug is being used, the tip of the dispensing container contacts the eye of the patient or surrounding structures, the topical ophthalmic drug should be instilled 15 minutes after dosing with SIMBRINZA™. Care should be exercised in operating machinery or driving a motor vehicle.

17.7 Contact Lens Wear

The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™, but may be reinserted 15 minutes after instillation.

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Part Number: 0909970

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