INDICATIONS AND USAGE
ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% is an alpha-adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
Neonates and Infants (under the age of 2 years): ALPHAGAN® P is contraindicated in neonates and infants (under the age of 2 years).

Hypersensitivity Reactions: ALPHAGAN® P is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

Please see additional Important Safety Information inside.
All about high eye pressure and ALPHAGAN® P 0.1%

This brochure will help you learn more about how ALPHAGAN® P 0.1% may help to reduce high eye pressure, known as intraocular pressure (IOP), for people who have open-angle glaucoma or ocular hypertension.

We hope that you will find this information useful. If you have any questions, please discuss them with your physicians.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS
Potentiation of Vascular Insufficiency: ALPHAGAN® P may potentiate syndromes associated with vascular insufficiency. ALPHAGAN® P should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud’s phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

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.

What is open-angle glaucoma and ocular hypertension?
Open-angle glaucoma is a disease of the eye marked by increased pressure within the eyeball. This can result in damage to the optic nerve and gradual loss of vision. Ocular hypertension is elevated pressure in the eye without the presence of optic nerve or vision damage.

Remember that open-angle glaucoma is a lifelong disease—there is no cure—so treatment will be lifelong too.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
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.

Please see additional Important Safety Information on following pages.
Why is eye pressure important?

A number of factors may contribute to open-angle glaucoma, but high pressure inside the eye (IOP) plays a very important role.

- Your eyes contain fluid that keeps them nourished and healthy
- Normally, this fluid flows within the eye and drains freely
- In people who have open-angle glaucoma, the fluid does not drain properly
- The buildup of fluid causes pressure inside the eye to rise
- If the pressure remains high for a long time, it can slowly cause damage to the optic nerve, which could lead to glaucoma-related vision loss
- The higher the eye pressure becomes, the greater the risk for optic nerve damage and vision loss

**IMPORTANT SAFETY INFORMATION (continued)**

**DRUG INTERACTIONS**

**Antihypertensives/Cardiac Glycosides:** Because ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with ALPHAGAN® P is advised.

Please see additional Important Safety Information on following pages.
Medication like ALPHAGAN® P 0.1% can lower high eye pressure

What is ALPHAGAN® P 0.1%?
ALPHAGAN® P 0.1% is approved for the lowering of elevated IOP in patients with open-angle glaucoma or ocular hypertension.³

Why has my physician prescribed ALPHAGAN® P 0.1%?
Approximately 2.7 million people (aged 40 and older) in the United States have open-angle glaucoma.⁵ ALPHAGAN® P 0.1% ophthalmic solution is approved to lower high IOP in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
CNS Depressants: Although specific drug interaction studies have not been conducted with ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15%, 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 ALPHAGAN® P 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.

Please see additional Important Safety Information on following pages.
How does ALPHAGAN® P 0.1% work?

ALPHAGAN® P 0.1% is believed to work in 2 different ways:

1. It decreases the amount of fluid produced in the eye.
2. It increases fluid that flows out of the eye (different from tears).

*The exact way ALPHAGAN® P 0.1% may work is unknown.

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS (continued)

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.

ADVERSE REACTIONS

Adverse reactions occurring in approximately 10% to 20% of the subjects receiving brimonidine ophthalmic solution (0.1% to 0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse reactions occurring in approximately 5% to 9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

Please see accompanying full Prescribing Information inside pocket at the back of this brochure.
Why is it important to get the Green Bottle?

Your doctor specifically prescribed ALPHAGAN® P 0.1% for you.

- In clinical trials, ALPHAGAN® P 0.1% had fewer patients discontinue treatment (8.8%) (n = 19/215) than ALPHAGAN® 0.2% (15.1%) (n = 33/218) due to side effects.

- If you experience a hypersensitivity to brimonidine, you can no longer use any medication that contains brimonidine—even if the concentration of brimonidine is lower.

- ALPHAGAN® P 0.1% is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Neonates and Infants (under the age of 2 years):

ALPHAGAN® P is contraindicated in neonates and infants (under the age of 2 years).

Please see additional Important Safety Information on following pages.
How can I make sure I get the Green Bottle?

- Be sure you receive the correct medication—ALPHAGAN® P 0.1% in the Green Bottle—by checking your prescription at the pharmacy.

Is there a generic version of ALPHAGAN® P 0.1%?

There is no FDA-approved generic formulation for ALPHAGAN® P 0.1%.

IMPORTANT SAFETY INFORMATION (continued)
CONTRAINDICATIONS (continued)

Hypersensitivity Reactions: ALPHAGAN® P is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

Please see additional Important Safety Information on following pages.
How much will ALPHAGAN® P 0.1% cost?

The cost of ALPHAGAN® P 0.1% will be determined by your health plan. ALPHAGAN® P 0.1% is covered for most patients with Commercial or Medicare Part D health plans. Individual plans and out-of-pocket costs will vary.

Be sure to ask your physician about any other offers or coupons that may be available at the office.

If you need financial assistance with your prescriptions, visit www.RxHope.com/Allergan for more information on the Allergan PATIENT ASSISTANCE PROGRAM™. It offers free or low-cost prescriptions for those who qualify financially.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Potentiation of Vascular Insufficiency: ALPHAGAN® P may potentiate syndromes associated with vascular insufficiency. ALPHAGAN® P should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud’s phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

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.

Please see additional Important Safety Information on following pages.
How many times a day do I need to take ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1%?

The recommended dosing of ALPHAGAN® P 0.1% is 3 times a day—approximately 8 hours apart. Always follow your physician’s instructions for taking ALPHAGAN® P 0.1%.³

If you take other eyedrops besides ALPHAGAN® P 0.1%, you should take them at least 5 minutes apart.³

Follow these 5 steps:

1. Wash your hands. Tilt your head back and look at the ceiling.

2. Using your index finger, gently pull down your lower eyelid to form a pocket.

3. Gently squeeze 1 drop into the pocket. Do not let the bottle tip touch your eye, your fingers, or anything else.

4. Gently close your eyes and lightly press on the inside corners of your eyes.

5. Then carefully blot away any excess liquid that may be on your skin.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
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.

Handling your eyedrop bottles

It is very important to handle your eyedrop bottles carefully. Always wash your hands before putting drops into your eyes. Don’t allow anything to touch the tip—not even your eyes or the areas around your eyes! Potentially harmful bacteria could enter the bottle and cause a serious eye infection. Always replace the cap after using. Contact your physician if you think your bottle may have been contaminated.

Please see additional Important Safety Information on following pages.
Why is it important to take my ALPHAGAN® P 0.1% drops?

Even if you feel fine, it’s important to continue using ALPHAGAN® P 0.1% every day as your physician prescribed. Make it part of your daily routine. Do not skip or stop treatment before speaking with your physician.

Follow some helpful tips to remember to take your eyedrops every day:

- Associate using your eyedrops with other daily routines you’ve established for yourself, such as brushing your teeth
- Set a daily clock or watch alarm that can remind you to use your eyedrops
- Ask a friend or family member to remind you when it’s time to use your eyedrops

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS

Antihypertensives/Cardiac Glycosides: Because ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with ALPHAGAN® P is advised.

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

Please see additional Important Safety Information on following pages.
What should I expect with ALPHAGAN® P 0.1% therapy?

Large clinical studies have shown that ALPHAGAN® P 0.1% is effective for reducing high eye pressure in patients with open-angle glaucoma and ocular hypertension. In 5% to 20% (n = 215) of patients, the following adverse events were reported3,6:

- Eye allergies and inflammation
- Redness of the eyes
- Itchiness or burning sensation in the eyes
- High blood pressure
- Dryness of the mouth
- Vision changes

ALPHAGAN® P 0.1% ophthalmic solution may cause fatigue and/or drowsiness. If you drive or perform hazardous work, such as operating machinery, make sure you feel appropriately alert.3

These are not the only risks associated with ALPHAGAN® P 0.1%. If you experience these or other side effects, you should immediately contact your physician.

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS (continued)

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 ALPHAGAN® P 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.

Please see additional Important Safety Information on following pages.
Who should NOT use ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1%?

ALPHAGAN® P 0.1% should not be used in neonates and infants (children under the age of 2). You should also not use ALPHAGAN® P 0.1% if you have allergies to any of the ingredients in ALPHAGAN® P 0.1%.³

ALPHAGAN® P 0.1% eyedrops can be absorbed by your body, which may be of concern if you have other medical conditions or are taking other drugs. Tell your physician about your other medications, especially³:

- Heart or blood pressure medicines, such as beta-blockers and calcium-channel blockers
- Sedatives
- Certain types of antidepressants, including those known as “tricyclic antidepressants” and “MAO inhibitors”

It is also very important to tell your physician if you have³:

- Depression
- Heart problems
- Upcoming surgery for your eyes
- Eye injury or infection

These risks are not the only risks associated with ALPHAGAN® P 0.1%. If you experience these or other side effects, you should immediately contact your physician.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions occurring in approximately 10% to 20% of the subjects receiving brimonidine ophthalmic solution (0.1% to 0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse reactions occurring in approximately 5% to 9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

Please see accompanying full Prescribing Information inside pocket at the back of this brochure.
Please see accompanying full Prescribing Information inside pocket.
Visit www.AlphaganP.com for more information about ALPHAGAN® P 0.1% and to download a cost-saving rebate.

3. ALPHAGAN® P Prescribing Information.
7. Brimonidine tartrate ophthalmic solution 0.15% Prescribing Information.
8. Brimonidine tartrate ophthalmic solution 0.2% Prescribing Information.
10. Managed Markets Insight & Technology, LLC, database as of April 2013.
Alphagan P
(brimonidine tartrate ophthalmic solution) 0.1% & 0.05%

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ALPHAGAN® P safely and effectively. See full prescribing information for ALPHAGAN® P.
ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% and 0.15% Initial U.S. Approval: 1996

INDICATIONS AND USAGE
ALPHAGAN® P is an alpha adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. (1)

DOSAGE AND ADMINISTRATION
• One drop in the affected eye(s), three times daily, approximately 8 hours apart. (2)

DOSAGE FORMS AND STRENGTHS
• Solution containing 1 or 1.5 mg/mL, brimonidine tartrate. (3)

CONTRAINDICATIONS
• Neonates and infants (under the age of 2 years). (4, 1)

WARNINGS AND PRECAUTIONS
Potentiation of vascular insufficiency. (5, 1)

ADVERSE REACTIONS
Most common adverse reactions occurring in approximately 5% to 20% of patients receiving brimonidine ophthalmic solution 0.1% - 0.2% included allergic conjunctivitis, burning sensation, conjunctival folliculosis, conjunctival hyperemia, eye pruritus, hypertension, ocular allergic reaction, oral dryness, and visual disturbance. (6, 1)

To report SUSPECTED ADVERSE REACTIONS, contact Allergan at 1-800-433-8871 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
• Antihypertensives/cardiac glycosides may lower blood pressure. (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)
• Nonselective oxiadase inhibitors may result in increased hypotension. (7, 4)

USE IN SPECIFIC POPULATIONS
• Use with caution in children ≥ 2 years of age. (8, 4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 11/2011

FULL PRESCRIBING INFORMATION: CONTENTS
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
4.1 Neonates and Infants (under the age of 2 years)
4.2 Hypersensitivity Reactions
5 WARNINGS AND PRECAUTIONS
5.1 Potentiation of Vascular Insufficiency
5.2 Severe Cardiovascular Disease
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7.1 Antihypertensives/Cardiac Glycosides
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FULL PRESCRIBING INFORMATION
1 INDICATIONS AND USAGE
ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% is an alpha 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 ALPHAGAN® P in the affected eye(s) three times daily, approximately 8 hours apart. ALPHAGAN® P ophthalmic solution 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.

3 DOSAGE FORMS AND STRENGTHS
Solution containing 1 mg/mL or 1.5 mg/mL, brimonidine tartrate.

4 CONTRAINDICATIONS
4.1 Neonates and Infants (under the age of 2 years)
ALPHAGAN® P is contraindicated in neonates and infants (under the age of 2 years).

4.2 Hypersensitivity Reactions
ALPHAGAN® P is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

5 WARNINGS AND PRECAUTIONS
5.1 Potentiation of Vascular Insufficiency
ALPHAGAN® P may potentiate syndromes associated with vascular insufficiency. ALPHAGAN® P should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud’s phenomenon, orthostatic hypotension, or thrombocytopenia 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 (see PATIENT COUNSELING INFORMATION, 17).

6 ADVERSE REACTIONS
6.1 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 rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Adverse reactions occurring in approximately 10% to 20% of the subjects receiving brimonidine ophthalmic solution 0.1% to 0.2% included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse reactions occurring in approximately 5% to 9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

Adverse reactions occurring in approximately 1% to 4% of the subjects receiving brimonidine ophthalmic solution 0.1% to 0.2% included: abnormal taste, allergic reaction, asthma, blepharitis, blepharocconjunctivitis, blurred vision, bronchitis, catarrh, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspnea, dysuria, epistaxis, eye discharge, eye dryness, eye irritation, eye pain, eye lid edema, eye lid erythema, fatigue, flu syndrome, follicular conjunctivitis, foreign body sensation, gastrointestinal disorder, headache, hyperchloremia, hypotension, infection (primarily colds and respiratory infections), iritis, keratitis, lid disorder, mydriasis, photophobia, rash, rhinitis, skin infection, sinusitis, somnolence, stinging, superficial punctate keratopathy, tearing, visual field defect, vitreous detachment, vitreous floaters, and worsened visual acuity.

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

6.2 Postmarketing Experience
The following reactions have been identified during postmarketing use of brimonidine tartrate ophthalmic solutions in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solutions, or a combination of these factors, include: bradycardia, depression, hypersensitivity, iritis, keratoconjunctivitis sicca, mild, nausea, skin reactions (including eczema, erythema, pruritus, rash, and vasodilation), syncope, and tachycardia. Agenesis, brachydactyly, comas, hypotension, hypothermia, hypotonia, lethargy, palmar, respiratory depression, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions.

7 DRUG INTERACTIONS
7.1 Antihypertensives/Cardiac Glycosides
Because ALPHAGAN® P may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with ALPHAGAN® P is advised.
7.2 CNS Depressants

Although specific drug interaction studies have not been conducted with ALPHAGAN® P, 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 ALPHAGAN® P 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.

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

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 (0.5 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 ALPHAGAN® P 0.1% or 0.15%, 1 drop in both eyes three times daily.

There are no adequate and well-controlled studies in pregnant women; however, in animal studies, brimonidine crosses the placenta and entered into the fetal circulation to a limited extent. Because animal reproduction studies are not always predictive of human response, ALPHAGAN® P should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

8.3 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 ALPHAGAN® P 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.

8.4 Pediatric Use

ALPHAGAN® P is contraindicated in children under the age of 2 years (see CONTRAINDICATIONS, 4.1). During postmarketing surveillance, anaphylactic reactions, anaphylactoid reactions, angioedema, hypotension, lethargy, palor, respiratory depression, and somnolence have been reported in infants receiving brimonidine. The safety and effectiveness of brimonidine tartrate have not been studied in children under the age of 2 years.

In a well-controlled clinical study conducted in pediatric glaucoma patients (ages 2 to 7 years) the most common observed adverse reactions with brimonidine tartrate ophthalmic solution 0.2% dosed three times daily were somnolence (52-83% 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 (23%). Approximately 16% of 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.

8.6 Special Populations

ALPHAGAN® P has not been studied in patients with hepatic impairment.

ALPHAGAN® P has not been studied in patients with renal impairment. The effect of dialysis on brimonidine pharmacokinetics in patients with renal failure is not known.

10 OVERDOSAGE

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 ALPHAGAN® P as part of medical treatment of congenital glaucoma by accidental oral ingestion (see USE IN SPECIFIC POPULATIONS, 8.4). Treatment of an oral overdose includes supportive and symptomatic therapy; a patient alway should be maintained.

11 DESCRIPTION

ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15%, sterile, is a relatively selective alpha-2 adrenergic receptor agonist (topical introcular pressure lowering agent).

The structural formula of brimonidine tartrate is:

![Chemical Structure](attachment://chemical_structure.png)

COOH

HO--CH--C--OH

Biochemistry details:

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 (1.4 mg/ml) at pH 7.7.

Each ml of ALPHAGAN® P contains the active ingredient brimonidine tartrate 0.1% (1 mg/ml), or 0.15% (1.5 mg/ml) with the inactive ingredients sodium carboxymethylcellulose; sodium borate; sodium chloride; potassium chloride; calcium chloride; magnesium chloride; PURITE® (0.00% (0.00 mg/ml) as a preservative, purified water, and hydroboric acid and/or sodium hydroxide to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ALPHAGAN® P 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.

12.3 Pharmacokinetics

Absorption

After oral 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 radioative dose of brimonidine was eliminated within 120 hours, with 74% found in the urine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No compound-related carcinogenic effects were observed in either mice or rats following a 21-month and 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 mg/kg/day in rats achieved AUC exposure values 360- and 20-fold higher, or 260- and 15-fold higher, respectively, than similar values estimated in humans treated with ALPHAGAN® P 0.1% or 0.15%, 1 drop in both eyes three times daily.

14 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 hemodynamics.

Clinical studies were conducted to evaluate the safety, efficacy, and acceptability of ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.15% compared with ALPHAGAN® administered three-times-daily in patients with open-angle glaucoma or ocular hypertension. Those results indicated that ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.15% is comparable to IOP lowering effect to ALPHAGAN® (brimonidine tartrate ophthalmic solution) 0.2%, and effectively lowers IOP in patients with open-angle glaucoma or ocular hypertension by approximately 2-6 mmHg. A clinical study was conducted to evaluate the safety, efficacy, and acceptability of ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% compared with ALPHAGAN® administered three-times-daily in patients with open-angle glaucoma or ocular hypertension. Those results indicated that ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% is equivalent in IOP lowering effect to ALPHAGAN® (brimonidine tartrate ophthalmic solution) 0.2%, and effectively reduces IOP in patients with open-angle glaucoma or ocular hypertension by approximately 2-6 mmHg.

16 HOW SUPPLIED/STORAGE AND HANDLING

ALPHAGAN® P is supplied sterile, in tear osseous plastic LFPE bottles and tips, with purple high impact polystyrene (HIPS) caps as follows:

<table>
<thead>
<tr>
<th>Strength</th>
<th>Amount</th>
<th>NDC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1%</td>
<td>5 ml</td>
<td>0293-9231-05</td>
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<td></td>
<td>10 ml</td>
<td>0293-9231-10</td>
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<td>0293-9177-15</td>
</tr>
<tr>
<td></td>
<td>15 ml</td>
<td>0293-9177-17</td>
</tr>
</tbody>
</table>

Storage: Store at 15°C-30°C (59°F-86°F).