1.3.1 South African Product Information

1.3.1.1 Professional Information (PI)

1.3.1.1.1 Professional Information–Approved

Enclosed.

APPROVED CLEAN PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

AGOBRIM 0.15% *w/v* EYE DROPS.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

AGOBRIM 0.15% *w/v* EYE DROPS

Each vial contains Brimonidine tartrate 0.15% *w/v* equivalent to (1.5 mg/mL) of **AGOBRIM 0.15% *w/v* EYE DROPS** Ophthalmic solution.

Excipients with known effect: Preservative: Benzalkonium Chloride 0.005 % *w/v*.

For full list of excipients, (See section 6.1)

3. PHARMACEUTICAL FORM

AGOBRIM 0.15% *w/v* EYE DROPS (Brimonidine Tartrate Eye Drops 0.15% *w/v*) is Clear greenish yellow solution, practically free from visible particle.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

AGOBRIM 0.15% *w/v* EYE DROPS is indicated for the lowering of intraocular pressure in patients with open angle glaucoma or ocular hypertension.

4.2. Posology and method of administration

The recommended dose is one drop of **AGOBRIM 0.15% *w/v* EYE DROPS** in the affected eye(s) twice daily, approximately 12 hours apart.

AGOBRIM 0.15% *w/v* EYE DROPS ophthalmic solution may be used concomitantly with other topical ophthalmic medicinal products to lower intraocular pressure. If more than one topical ophthalmic product is being used, the product should be administered at least 5 minutes apart.

Method of administration: Ocular use.

4.3. Contraindications

AGOBRIM 0.15% *w/v* EYE DROPS is contraindicated in patients who have exhibited hypersensitivity to brimonidine tartrate, benzalkonium chloride or to any of the excipients listed in section 6.1.

AGOBRIM 0.15% *w/v* EYE DROPS is contraindicated in neonates and infants (under the age of 2 years).

4.4. Special warnings and precautions for use

Severe cardiovascular disease

Although Brimonidine eye drops 0.15% w/v has minimal effects on the blood pressure of patients, caution should be exercised in treating patients with severe or unstable and uncontrolled cardiovascular disease.

Potentiation of vascular insufficiency

AGOBRIM 0.15% *w/v* EYE DROPS may potentiate syndromes associated with vascular insufficiency.

AGOBRIM 0.15% *w/v* EYE DROPS should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangitis obliterans.

Patients using IOP-lowering medication should be routinely monitored for IOP (intraocular pressure).

Eye disorders

If allergic reactions are observed, treatment with **AGOBRIM 0.15% *w/v* EYE DROPS** should be discontinued.

Delayed ocular hypersensitivity reactions have been reported with brimonidine, as contained in **AGOBRIM 0.15% *w/v* EYE DROPS,** with some reported to be associated with an increase in (IOP) Intraocular pressure.

Contamination of **AGOBRIM 0.15% *w/v* EYE DROPS** after use

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products such as **AGOBRIM 0.15% *w/v* EYE DROPS**.

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 "Information for patients").

Special populations

Paediatric use

AGOBRIM 0.15% *w/v* EYE DROPS is contra-indicated in children under the age of 2 years (see 'CONTRAINDICATIONS').

The safety and efficacy of brimonidine tartrate have not been studied in children below the age of 2 years. During post-marketing surveillance, apnoea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine either for congenital glaucoma or by accidental ingestion.

Children 2 years of age and above, especially those weighing ≤ 20 kg, should be treated with caution and closely monitored due to the high incidence and severity of somnolence. In a clinical study conducted in paediatric glaucoma patients (ages 2 to 7 years) the most commonly observed adverse reactions with brimonidine tartrate ophthalmic solution 0,2 % dosed three times daily
were somnolence (50 - 83 % in patients ages 2 to 6 years) and decreased alertness. In paediatric patients 7 years of age (> 20 kg), somnolence appears to occur less frequently (25 %). Approximately 16 % of patients on brimonidine tartrate ophthalmic solution discontinued from the study due to somnolence.

Elderly use

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

Patients with hepatic and renal impairment

AGOBRIM 0.15% *w/v* EYE DROPS has not been studied in patients with hepatic impairment.

AGOBRIM 0.15% *w/v* EYE DROPS has not been studied in patients with renal impairment. The effect of dialysis on brimonidine pharmacokinetics in patients with renal

failure is not known.

Caution should be used in treating patients with hepatic and renal impairment.

Information for patients

Patients should be instructed 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. Always replace the cap after using. If solution changes colour or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

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

If more than one topical ophthalmic medicine is being used, the medicine should be administered at least five minutes apart.

Benzalkonium chloride

The preservative in **AGOBRIM 0.15% *w/v* EYE DROPS,** benzalkonium chloride, may cause eye irritation, symptoms of dry eyes, and may affect the tear film and corneal surface. Patients should remove contact lenses prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses. Patients should avoid contact with soft contact lenses.

AGOBRIM 0.15% *w/v* EYE DROPS should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

4.5. Interaction with other medicines and other forms of interaction

Antihypertensives

Because **AGOBRIM 0.15% *w/v* EYE DROPS** may reduce blood pressure, caution in using antihypertensives with **AGOBRIM 0.15% *w/v* EYE DROPS** is advised.

Digoxin

Caution is advised when using **AGOBRIM 0.15% *w/v* EYE DROPS** with digoxin.

CNS depressants

Although specific interaction studies have not been conducted with **AGOBRIM 0.15% *w/v* EYE DROPS**, the possibility of an additive or potentiating effect with CNS-depressants (alcohol, barbiturates, opiates, sedatives, or anaesthetics) should be considered.

Alpha-agonists, as a class, may reduce pulse and blood pressure. Caution in using concomitant medicines such as beta-blockers (ophthalmic and systemic), anti-hypertensives and/or digoxin is advised.

Tricyclic antidepressants

Tricyclic antidepressants have been reported to blunt the hypotensive effects of systemic clonidine. It is not known whether the concurrent use of these medicines with **AGOBRIM 0.15% *w/v* EYE DROPS** 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 interfere with the metabolism of **AGOBRIM 0.15% *w/v* EYE DROPS** 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 amine.

No data on the level of circulating catecholamines after Alphagan administration are available. Caution, however, is advised in patients taking medications which can affect the metabolism and uptake of circulating amines e.g. chlorpromazine, methylphenidate reserpine.

4.6. Fertility, pregnancy, and lactation

Pregnancy

The safety of use during human pregnancy has not been established.

AGOBRIM 0.15% *w/v* EYE DROPS should not be used during pregnancy

Breastfeeding

It is not known if brimonidine is excreted in human milk. Because of the potential for serious adverse reactions from **AGOBRIM 0.15% *w/v* EYE DROPS** in nursing infants **AGOBRIM 0.15% *w/v* EYE DROPS** should not be used by women nursing infants.

Fertility

No data is available

4.7. Effects on ability to drive and use machines

AGOBRIM 0.15% *w/v* EYE DROPS 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. **AGOBRIM 0.15% *w/v* EYE DROPS** may also cause blurred vision or visual disturbance in some patients. The patient should wait until these symptoms have cleared before driving or using machinery.

4.8 Undesirable effects

The most reported ADRs are oral dryness, ocular hyperaemia, and burning/stinging. They are usually transient and not commonly of a severity requiring discontinuation of treatment.

Adverse reactions reported are included in the table below.

a. Tabulated list of adverse reactions

Skin and subcutaneous tissue disorders:	
• Rash • Face oedema	Frequent
• Vasodilatation	Frequency not known
Immune system disorders	
• Allergic reactions	Frequent
Psychiatric disorders	
• Depression, insomnia • Drowsiness	Frequent
Nervous system disorders	
• Headache, • Dizziness	Frequent

• Taste perversion, • Somnolence in adults and infants. • Syncope	Less frequent
Eye disorders	
• Eyelid erythema, • Eyelid oedema, • Conjunctival hyperaemia, Eye pruritus, Allergic conjunctivitis. • Burning sensation, • Stinging, foreign body sensation, • Follicular conjunctivitis, • Photophobia, • Eye pain, • Eye dryness, • Conjunctival oedema, • Blepharitis, • Eye irritation, • Eye discharge, • Conjunctival haemorrhage. • Conjunctival folliculosis, • Conjunctivitis, • Epiphora, • Visual field defects, visual disturbances, • Worsened visual acuity, • Superficial punctate keratopathy, • Vitreous floaters. • Blurred vision • Blepharoconjunctivitis • Cataract • Conjunctival blanching • Keratitis • Lid disorder • Tearing	Frequent

• Vitreous detachment • Vitreous disorder • Ocular allergic reaction	
• Corneal erosion. • Hordeolum	Less frequent
• Iritis, • Miosis	Frequency not known
Cardiac disorders	
• Palpitations	Less frequent
• Bradycardia in adults. Neonates and infants, tachycardia.	Frequency not known
Vascular disorders	
• Hypertension, hypotension	Frequent
Respiratory, thoracic, and mediastinal disorders	
• Cough, dyspnoea	Frequent
• Nasal dryness,	Less frequent
• Apnoea in neonates and infants.	Frequency not known
Infections and infestations	
• Sinusitis, • Flu syndrome, • Bronchitis, • Rhinitis, • Pharyngitis	Frequent
General disorders and administration site conditions	
• Asthenia • Fatigue	Frequent
• Hypothermia in infants	Frequency not known
Musculoskeletal disorders	

• Hypotonia in infants	Frequency not known
Blood and lymphatic system disorders	
• Hypercholesterolaemia	Frequent
Gastrointestinal disorders	
• Dyspepsia • Oral dryness • Gastrointestinal disorder	Frequent

In cases where brimonidine has been used as part of the medical treatment of congenital glaucoma, symptoms of brimonidine overdose such as loss of consciousness, lethargy, somnolence, hypotension, hypotonia, bradycardia, hypothermia, cyanosis, pallor, respiratory depression and apnoea have been reported in neonates and infants receiving brimonidine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9. Overdose

Very limited information exists on accidental ingestion of brimonidine in adults and children; the only adverse reaction reported to date has been hypotension. Treatment, in the event of an oral overdose, includes supportive and symptomatic therapy. A patent airway should be maintained.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological Classification: A.15.4 Ophthalmic preparations. Other.

Pharmacotherapeutic group: Sympathomimetics in glaucoma therapy,

ATC code = S01EA 05.

Brimonidine is an alpha-2 adrenergic receptor agonist that is 1000-fold more selective for the alpha-2 adrenoceptor than the alpha-1 adrenoreceptor.

This selectivity results in no mydriasis and the absence of vasoconstriction in micro vessels associated with human retinal xenografts.

Topical administration of brimonidine tartrate decreases intraocular pressure (IOP) in humans with minimal effect on cardiovascular or pulmonary parameters.

Limited data are available for patients with bronchial asthma showing no adverse effects.

Brimonidine has a rapid onset of action, with peak ocular hypotensive effect seen at two hours post-dosing. In studies, Brimonidine lowered IOP by mean values of approximately 4-6 mmHg.

Fluorophotometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action. It is thought that Brimonidine may lower IOP by reducing aqueous humour formation and enhancing uveoscleral outflow.

5.2 Pharmacokinetic properties

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 metabolised by the liver.

Elimination

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

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzalkonium chloride Ph. Eur.

Polyvinyl alcohol Ph. Eur.

Sodium citrate Dihydrate Ph. Eur.

Citric acid Ph. Eur.

Sodium chloride Ph. Eur.

Sodium hydroxide Ph. Eur.

Water for injection Ph. Eur.

6.2. Incompatibilities

Not Applicable

6.3. Shelf life

Proposed shelf-life for unopened vial: 24 months.

Proposed shelf-life for opened vial: 28 days

6.4. Special precautions for storage

- Store at temperature not exceeding 30°C. Protect from light.
- Keep away medicines from the reach of children.
- Discard remaining contents 28 days after opening.

6.5. Nature and contents of container

LDPE vial

A clear greenish yellow solution, practically free from visible particle. It is available in 5mL labelled LDPE vial with insert cap packed in a carton with pack insert.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product.

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

FDC SA (PTY) LTD
Unit J3, Willows Office Park
Farm Road, The Willows
Pretoria, 0081
South Africa

8. REGISTRATION NUMBER

57/15.4/0378

9. DATE OF FIRST AUTHORISATION

15 JULY 2025

10. DATE OF REVISION OF TEXT

Not Applicable

11. DATE OF PUBLICATION OF THE PACKAGE INSERT

15 JULY 2025