# NEW ZEALAND DATA SHEET

## 1. PRODUCT NAME
ALPHAGAN® P 1.0 mg/mL eye drops

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each mL of ALPHAGAN® P 1.0 eye drops contains brimonidine tartrate 1.0 mg (equivalent to 0.66 mg as brimonidine free base).

For the full list of excipients, see section 6.1 List of excipients.

## 3. PHARMACEUTICAL FORM
Sterile ophthalmic solution.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications
ALPHAGAN® P 1.0 eye drops are indicated for lowering intraocular pressure in patients with chronic open-angle glaucoma or ocular hypertension.

### 4.2 Dosage and method of administration
The recommended dose for ALPHAGAN P® 1.0 is one drop applied to the affected eye(s) twice a day at approximately 12-hour intervals.

If more than one topical ophthalmic medicine is to be used, other eye drops should not be used within five to ten minutes of using ALPHAGAN® P 1.0 eye drops.

In order to minimise systemic absorption of ALPHAGAN® P 1.0 eye drops, apply pressure to the tear duct immediately following administration.

Paediatric population
ALPHAGAN P® 1.0 eye drops are not recommended for use in children as safety and efficacy have not been established. Severe adverse reactions have been reported when brimonidine tartrate eye drops have been used in children (see section 4.4). ALPHAGAN P® 1.0 eye drops are contraindicated in infants and children <2 years of age (see section 4.3).

### 4.3 Contraindications
ALPHAGAN® P 1.0 eye drops are contraindicated in patients with hypersensitivity to brimonidine tartrate or any of the excipients listed in section 6.1. Brimonidine tartrate eyedrops are also contraindicated in patients receiving monoamine oxidase (MAO) inhibitor therapy.

Brimonidine tartrate eye drops are contraindicated in infants and children <2 years of age.

## 4.4 Special warnings and precautions for use

### Identified precautions

Brimonidine tartrate eye drops should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangiitis obliterans.

During the studies there was a loss of effect in some patients. The IOP-lowering efficacy observed with brimonidine eye drops during the first month of therapy may not always reflect the long-term level of IOP reduction. Patients prescribed IOP-lowering medication should be routinely monitored for IOP.

### Cardiovascular disease

Although brimonidine tartrate eye drops had minimal effect on blood pressure and heart rate of patients in clinical studies, caution should be observed in treating patients receiving brimonidine tartrate eye drops with severe, uncontrolled cardiovascular disease.

### Hypersensitivity

Delayed ocular hypersensitivity reactions have been reported with brimonidine tartrate eye drops, with some reported to be associated with an increase in IOP.

### Use in Renal or Hepatic Impairment

Brimonidine tartrate eye drops have not been studied in patients with hepatic or renal impairment; caution should be used in treating such patients.

### Use in the Elderly

No overall difference in safety and effectiveness has been observed between elderly and other adult patients. The $C_{max}$ and apparent half-life of brimonidine were similar in elderly subjects (65 years or older) and younger adults, indicating that its systemic absorption and elimination were not significantly affected by age.

### Paediatric Population

Brimonidine tartrate eye drops are not recommended for use in children as safety and efficacy has not been established.

Severe adverse reactions have been reported when brimonidine tartrate eye drops have been used in children. During post-marketing surveillance, apnoea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in neonates, infants, and children receiving brimonidine either for congenital glaucoma or by accidental oral ingestion. In a clinical study there was a high incidence and severity of somnolence in children, especially in those weighing ≤20 kg. Brimonidine tartrate eye drops are contraindicated in infants and children <2 years of age (see section 4.3).

## 4.5 Interactions with other medicines and other forms of interaction

Although specific drug interaction studies have not been conducted with ALPHAGAN® P 1.0 eye drops, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.

Because brimonidine tartrate eye drops may reduce blood pressure, caution using concomitant drugs such as beta-blockers (ophthalmic and systemic), anti-hypertensives and/or cardiac glycosides is advised.

Caution is advised when initiating or changing the dose of a concomitant systemic agent which may interact with alpha-adrenergic agonists or interfere with their activity (i.e. sympathomimetic agents, agonists or antagonists of the adrenergic receptor).

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 eye drops can lead to an interference in IOP lowering effect, although in rabbit experiments, tricyclic antidepressants did not alter the IOP response to brimonidine. No data on the level of circulating catecholamines after brimonidine tartrate eye drops are instilled are available. Caution, however, is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

As brimonidine is metabolised primarily by the liver, most likely by cytochrome P450 and aldehyde oxidase, this may affect the metabolism of other drugs that utilise the cytochrome P450 pathway.

## 4.6 Fertility, pregnancy and lactation

### Fertility

Reproduction and fertility studies in rats with brimonidine tartrate demonstrated no adverse effect on male or female fertility at doses which achieve at least 84 times the systemic exposure (based on AUC) following the maximum recommended human ophthalmic dose of brimonidine tartrate eye drops.

### Pregnancy

Pregnancy Category B3

There are no studies of brimonidine in pregnant women. In rats, the drug crosses the placenta and enters the foetal circulation.

In pregnant rats, brimonidine was associated with maternotoxicity and increased early resorptions/post-implantation losses and decreased pup viability and body weights at estimated exposures (based on AUC) of 390 times the expected exposures in humans treated therapeutically. The drug was also maternotoxic in rabbits and caused abortions at exposures about 23 times greater than those expected in humans. In both rats and rabbits, brimonidine was not teratogenic.

**Breast-feeding**

It is not known whether brimonidine is excreted in human milk. Therefore, a decision should be made whether to discontinue the drug, taking into account the importance of the drug to the mother. In lactating rats, levels of the drug in milk were up to 12 times higher than those in maternal plasma; and in a perinatal and postnatal study in rats, brimonidine was associated with decreased pup viability and pup weights during lactation at maternal plasma exposures of about 84 times greater than those expected in humans.

## 4.7 Effects on ability to drive and use machines

As with other alpha-agonists, brimonidine can potentially cause fatigue and/or drowsiness in some patients. Patients who engage in hazardous activities requiring mental alertness, such as driving and operating machinery, should be cautioned of the potential for a decrease in mental alertness.

Brimonidine tartrate eye drops may also cause blurred vision or visual disturbance. The patient should wait until these symptoms have cleared before driving or using machinery.

## 4.8 Undesirable effects

**Clinical trials experience**

Summary of the Safety Profile

Based on the safety data from Study 190342-022 at Month 12, adverse events were reported for 61.5% (64/104) of patients in the Brimonidine Purite 0.1% group and 63.7% (65/102) in the ALPHAGAN P 0.15% group. The most frequently reported events (> 5% in either treatment group) were conjunctival hyperemia, conjunctival folliculosis, hypertension, and infection. There were no statistically significant differences between 2 treatment groups for any of the individual adverse events.

**Table 1 No. (%) of patients with adverse events reported by ≥ 2% of patients in 12 hourly treatment group over 12 months**

| **BODY SYSTEM Preferred Term** | **ALPHAGAN P 1.0 (brimonidine tartrate 0.1%)**<br><br>**N=104** |
|---|---|
| **BODY AS A WHOLE** | |
| Infection | 6 (5.8%) Common |
| **CARDIOVASCULAR** | |
| Hypertension | 7 (6.7%) Common |
| **METABOLIC & NUTRITIONAL** | |
| Diabetes mellitus | 3 (2.9%) Common |

| | |
|---|---|
| **MUSCLOSKELETAL** | |
| Arthritis | 5 (4.8%) Common |
| **RESPIRATORY** | |
| Bronchitis | 4 (3.8%) Common |
| **SPECIAL SENSES** | |
| Conjunctival hyperemia | 17 (16.3%) Very Common |
| Conjunctivial folliculosis | 7 (6.7%) Common |
| Blepharitis | 5 (4.8%) Common |
| Visual disturbence | 3 (2.9%) Common |

**Table 2 All treatment related adverse events: No. (%) of patients by preferred term over 12 months**

| **ADVERSE EVENT Preferred Term** | **ALPHAGAN P 1.0 (brimonidine tartrate 0.1%)**<br><br>**N=104** |
|---|---|
| Conjunctival Hyperemia | 14 (13.5%) Very Common |
| Conjunctival Folliculosis | 6 (5.8%) Common |
| Allergic Conjunctivitis | 2 (1.9%) Common |
| Visual Disturbance | 2 (1.9%) Common |
| Eye Pruritus | 1 (1.0%) Common |
| Erythema eyelid | 1 (1.0%) Common |
| Intraocular pressure | 1 (1.0%) Common |
| Irritation eye | 1 (1.0%) Common |

## Post marketing experience

The following adverse reactions have been identified during postmarketing use of ALPHAGAN® P 1.0 in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made.

**Eye disorders:**

Lacrimation increased, Vision blurred

**Nervous system disorders**

Dizziness, Headache

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

### 4.9 Overdose

Ophthalmic overdose:
In those cases, received, the events reported have generally been those already listed as adverse reactions.

Systemic overdose resulting from accidental ingestion:
There is very limited information regarding accidental ingestion of brimonidine in adults. The only adverse event reported to date was hypotension. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained. Symptoms of brimonidine overdose such as apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in neonates, infants, and children receiving brimonidine tartrate eye drops 0.2% as part of medical treatment of congenital glaucoma or by accidental oral ingestion.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sympathomimetics in glaucoma therapy
ATC code: S01EA05

**Mechanism of action**

Brimonidine is an alpha-2 adrenergic agonist that is 1000-fold more selective for the alpha-2 adrenoreceptor than the alpha-1 adrenoreceptor. Affinity at human alpha-1 and alpha-2 adrenoreceptors are ~2000 nM and ~2 nM, respectively. This selectivity results in no mydriasis and the absence of vasoconstriction in microvessels associated with human retinal xenografts.

Topical administration of brimonidine decreases intraocular pressure (IOP) in humans. When used as directed, brimonidine has the action of reducing elevated IOP with minimal effect on cardiovascular parameters.

**Pharmacodynamic effects**

Brimonidine has a rapid onset of action, with the peak ocular hypotensive effect occurring at two hours post-dosing. The duration of effect is at least 12 hours.

Fluoro photometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action. ALPHAGAN® P 1.0eye drops lower IOP by reducing aqueous humor production and enhancing uveoscleral outflow.

**In vitro and In vivo Studies on Purite®**

ALPHAGAN® P eye drops are the only IOP-lowering product preserved with Purite®. *In vitro* and *in vivo* studies demonstrate a lower rate of corneal epithelial cytotoxicity (an indicator of ocular surface health) and increased cell viability for Purite® - preserved ophthalmic solutions compared to use of other preservatives.

**Clinical efficacy and safety**

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. ALPHAGAN® P 1.0 eye drops have the action of lowering IOP with minimal effect on cardiovascular and pulmonary parameters.

***Studies with ALPHAGAN® P 1.0 eye drops:***

A 3-month (with a double-masked extension to 1 year) clinical study (N=433) was conducted to evaluate the safety, efficacy, and acceptability of ALPHAGAN® P 0.1% compared with ALPHAGAN® 0.2% administered 3 times daily in patients with glaucoma or ocular hypertension.

A 3-month analysis of the pivotal study indicated that ALPHAGAN® P 0.1% is equivalent in IOP-lowering effect to ALPHAGAN® 0.2% and effectively lowers IOP in patients with glaucoma or ocular hypertension (mean change from baseline IOP -3.3 to -5.4 mm Hg). Additionally, 12-month analysis of the pivotal study indicated ALPHAGAN® P 0.1% continued to be equivalent to ALPHAGAN® 0.2% and effectively lowered IOP in patients with glaucoma or ocular hypertension (mean change from baseline IOP at hours 0, 2, and 8 ranged from -2.7 to -5.4 mm Hg).
A 3-month (with a double-masked extension to 1 year) clinical study (N=207) was conducted to evaluate the safety and efficacy of ALPHAGAN® P 0.1% compared with ALPHAGAN® P 0.15%, administered 2 times daily in patients with open-angle glaucoma or ocular hypertension whose IOP was controlled on ALPHAGAN® P 0.15% monotherapy with twice daily dosing.

A 3-month analysis of this study indicated that the IOP-lowering efficacy of ALPHAGAN® P 0.1% was non-inferior to that of ALPHAGAN® P 0.15%. There were no statistically significant differences shown between the 2 treatment groups in mean change from baseline IOP at any follow-up timepoints. Additionally, 12-month analysis of this study indicated that the efficacy of ALPHAGAN® P 0.1% was

maintained. The study confirmed that ALPHAGAN® P 0.1% is well tolerated and effective when dosed 2 times daily for 12 months.

**Pharmacokinetics properties**

### *Absorption*

After ocular administration of a 0.1% and 0.2% solution of brimonidine tartrate eye drops three times daily for 7 days, plasma concentrations were low (mean $C_{max}$ was 0.03 ng/mL and 0.06 ng/mL for the 0.1% and 0.2% solutions, respectively). There was a slight accumulation in plasma after multiple instillations. The area under the plasma concentration-time curve over 8 hours at steady state ($AUC_{0-8h}$) was 0.14 ng.hr/mL and 0.25 ng.hr/mL for the 0.1% and 0.2% solutions, respectively. The mean apparent half-life in the systemic circulation was approximately 2 hours in humans after topical dosing.

Peak plasma brimonidine concentration ($C_{max}$) is predicted to be 0.03 ng/mL when brimonidine tartrate eye drops are administered twice daily for 7 days. Systemic accumulation is unlikely after twice daily administration of a 0.1% solution given the short elimination half-life of brimonidine.

### *Metabolism*

In humans, brimonidine is metabolised extensively by the liver.

### *Excretion*

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.

The pharmacokinetics of ALPHAGAN® P 1.0 eye drops have not been specifically studied in patients with hepatic or renal disease (see 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE) or in paediatric patients (see 4.3 CONTRAINDICATIONS).

## 5.3 Preclinical safety data

***Carcinogenesis, mutagenesis and impairment of fertility***

No compound-related carcinogenic effects were observed in 21 month and 2 year studies in mice and rats given oral doses of 2.5 mg/kg/day and 1.0 mg/kg/day brimonidine respectively. Plasma concentrations of brimonidine in mice and rats in the high dose groups were at least 170 times greater than those expected in humans dosed therapeutically.

Brimonidine tartrate was not mutagenic or clastogenic in a series of in vitro and in vivo studies including the Ames bacterial reversion test, chromosomal aberration assay in Chinese Hamster Ovary (CHO) cells, and three in vivo studies in CD-1 mice: a host-mediated assay, cytogenetic study, and dominant lethal assay.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

PRESERVATIVE: PURITE®

INACTIVES: carmellose sodium, boric acid, borax, sodium chloride, potassium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate and purified water. Hydrochloric acid and/or sodium hydroxide may be added to adjust pH.

## 6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

## 6.3 Shelf life:

18 months

## 6.4 Special precautions for storage:

Store below 30°C

To avoid contamination of the solution, keep container tightly closed. Do not touch dropper tip to any surface. Contents are sterile if seal is intact.

Discard contents 4 weeks after opening the bottle.

## 6.5 Nature and contents of container

ALPHAGAN® P 1.0 is supplied sterile in opaque teal low density polyethylene (LDPE) plastic bottles and droppers with purple high impact polystyrene (HIPS) caps. Each bottle has a fill volume of 5 mL.

## 6.6 Special precautions for disposal

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

# 7. MEDICINE SCHEDULE

Prescription Medicine

# 8. SPONSOR

AbbVie Limited
6th Floor, 156-158 Victoria St
Wellington, 6011
New Zealand
Freephone: 0800 900 030

# 9. DATE OF FIRST APPROVAL

09 Sep 2025

## 10. DATE OF REVISION OF THE TEXT

09 Sep 2025

## SUMMARY TABLE OF CHANGES

| Sections changed | Summary of new information |
|---|---|
| All | New strength registration |