SCHEDULING STATUS

Schedule 3

PROPRIETARY NAME AND DOSAGE FORM

ALPHAGAN® Purite® Ophthalmic solution

COMPOSITION

Each ml contains: Brimonidine tartrate 1,5 mg

Excipients: Boric acid, calcium chloride dehydrate, magnesium chloride hexahydrate; potassium chloride, purified water, sodium borate decahydrate, sodium carboxymethylcellulose, sodium chloride.

Preservative: Purite® (stabilised oxychloro complex) 0,005 % m/v

PHARMACOLOGICAL CLASSIFICATION

A.15.4 Ophthalmic preparations. Other.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Brimonidine tartrate is a selective alpha-2-adrenergic receptor agonist. Topical administration of brimonidine decreases intraocular pressure (IOP) in humans 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 humour production and increasing uveoscleral outflow.

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.

INDICATIONS

ALPHAGAN® Purite® is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

CONTRA-INDICATIONS

ALPHAGAN® Purite® is contraindicated in patients who have exhibited a hypersensitivity reaction to brimonidine tartrate or any component of ALPHAGAN® Purite®.

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

WARNINGS AND SPECIAL PRECAUTIONS

Severe cardiovascular disease

Although ALPHAGAN® Purite® ophthalmic solution had minimal effects on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

Potentiation of vascular insufficiency

ALPHAGAN® Purite® may potentiate syndromes associated with vascular insufficiency. ALPHAGAN® Purite® should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans. Patients using IOP-lowering medication should be routinely monitored for IOP.

Contamination of ALPHAGAN® Purite® after use

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products such as ALPHAGAN® Purite®. 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").

Paediatric use

ALPHAGAN® Purite® is contra-indicated in children under the age of 2 years (see 'CONTRA-INDICATIONS'). 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.

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

Special populations
ALPHAGAN® Purite® has not been studied in patients with hepatic impairment.

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

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.

Effects on ability to drive and use machines

ALPHAGAN® Purite® 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. ALPHAGAN® Purite® 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.

INTERACTIONS

Antihypertensives

Because ALPHAGAN® Purite® may reduce blood pressure, caution in using antihypertensives with ALPHAGAN® Purite® is advised.

Digoxin

Caution is advised when using ALPHAGAN® Purite® with digoxin.

CNS depressants

Although specific interaction studies have not been conducted with ALPHAGAN® Purite®, 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 agents with ALPHAGAN® Purite® 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 ALPHAGAN® Purite® 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.

PREGNANCY AND LACTATION

Pregnancy

Safety and/or efficacy for ALPHAGAN® Purite® use during pregnancy have not been established.

Lactation

It is not known whether ALPHAGAN® Purite® is excreted in breastmilk. Because of the potential for serious adverse reactions from ALPHAGAN® Purite® in nursing infants, patients should not breastfeed while using ALPHAGAN® Purite®.

DOSAGE AND DIRECTIONS FOR USE

The recommended dose is one drop of ALPHAGAN® Purite® in the affected eye(s) twice daily, approximately 12 hours apart.

ALPHAGAN® Purite® 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.

SIDE EFFECTS

For each indication the frequency of adverse reactions arising from clinical experience is given as follows: Very common (≥1/10); Common (≥1/100, <1/10); Uncommon (≥1/1 000, <1/100); Rare (≥1/10 000, <1/1 000); Very rare (<1/10 000).

Eye disorders

Very common: Allergic conjunctivitis, conjunctival hypaeremia, eye pruritus

Common: Blepharitis, burning sensation, conjunctival folliculosis, conjunctival oedema, conjunctival haemorrhage, conjunctivitis, epiphora, eye discharge, eye dryness, eye irritation, eye pain, follicular conjunctivitis, foreign body sensation, photophobia, stinging, superficial punctuate keratophy, visual disturbance, visual field defects, vitreous floaters, worsened visual acuity, blepharoconjunctivitis, blurred vision, cataract, keratitis, lid disorder, tearing, vitreous detachment, vitreous disorder, ocular allergic reaction, eyelid oedema, eyelid erythema

Uncommon: Corneal erosion, hordeolum

Nervous system disorders

Common: Dizziness, headache

Uncommon: Somnolence, taste perversion

Vascular disorders

Common: Hypertension, hypotension

Psychiatric disorders

Uncommon: Insomnia

Respiratory, thoracic and mediastinal disorders

Common: Cough, dyspnoea

Uncommon: Nasal dryness

Gastrointestinal disorders

Common: Dyspepsia, oral dryness, gastrointestinal disorder

Skin and subcutaneous tissue disorders

Common: Rash

Immune system disorders

Common: Allergic reaction

Infections and infestations

Common: Bronchitis, flu syndrome, pharyngitis, rhinitis, sinus infection, sinusitis

General disorders and administration site conditions

Common: Asthenia, fatigue

Blood and lymphatic system disorders

Common: Hypercholesterolaemia

The following events have been identified during post-marketing use of ALPHAGAN® Purite® ophthalmic solution in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to ALPHAGAN® Purite®, or a combination of these factors, include: bradycardia, depression, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including

erythema, eyelid pruritus, rash and vasodilatation), syncope, and tachycardia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

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

IDENTIFICATION

Clear green-yellow solution, essentially free of any visible particulate matter.

PRESENTATION

ALPHAGAN® Purite® is supplied sterile in opaque teal LDPE plastic bottles and tips with purple high impact polystyrene (HIPS) caps, containing 5 ml of solution.

STORAGE INSTRUCTIONS

Store at or below 25 °C and protect from light. To avoid contamination of the solution keep container tightly closed. Do not touch dropper tip to any surface. Discard contents 30 days after opening the bottle. Contents are sterile if seal is intact.
KEEP OUT OF REACH AND SIGHT OF CHILDREN.

REGISTRATION NUMBER

A39/15.4/0202

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

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DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration: 05 October 2007
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