1.NAME OF MEDICINAL PRODUCT

RIMONAL EYE DROPS 0.15% W/V

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of RIMONAL Eye drops 0.15% w/v contains:

Active Ingredient: Brimonidine Tartrate 0.15% (1.5mg/mL)

Preservative: Benzalkonium chloride 0.005% (0.05mg/mL)

3. PHARMACEUTICAL FORM

Eye drops, solution.

Clear, yellow coloured, practically free from particles solution.

4.CLINICAL PARTICULARS

4.1 Therapeutic indications

RIMONAL is indicated for reduction of elevated intraocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension.

4.2 Posology and method of administration

Posology/frequency and duration of administration:

The recommended dose of RIMONAL is one drop in the affected eyes three times daily in every approximately 8 hours. If more than one topical ophthalmic drug is used, drugs should be administered at least 5 minutes apart.

Method of administration:

It is administrated by instilling into eyes. As with the other eye drops, to reduce possible systemic absorption, it is recommended that the lachrymal sac at the medial canthus is compressed with finger tips for one minute after each drops.

Additional information about special populations:

Renal/Hepatic impairment:

RIMONAL has not been studied in patients with hepatic or renal impairment; caution should be used in treating such patients.

Paediatric population:

Safety and effectiveness in pediatric patients have not been established.

Geriatric population:

Generally, there is no difference for safety or efficacy in elderly and other adult patients.

4.3 Contraindications

RIMONAL is contraindicated in newborns and infants (under 2 years of age).

RIMONAL is contraindicated in patients who are hypersensitive to brimonidine tartrate or any of the other ingredients of its composition.

RIMONAL is contraindicated in patients receiving monoamine oxidase (MAO) treatment.

4.4 Special warnings and precautions for use

RIMONAL may be increased syndromes related to vascular impairment.

RIMONAL should be used carefully in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenology, orthostatic hypotension or thromboangitis obliterans.

In clinical studies, even if, Brimonidine tartrate ophthalmic solution has also a minimal effect on blood pressure of patients, it should be used carefully in patients with severe cardiovascular disease.

This medicinal product contains benzalkonium chloride. Benzalkonium chloride may cause eye irritation. Avoid contact with soft contact lenses. Benzalkonium chloride may occur colour change in soft lenses. Remove lenses before application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

This medicinal product contains less than 23 mg sodium in each dose. However, no warning is required due to the way of use.

4.5 Interaction with other medicinal products and other forms of interaction

Although specific drug interactions studies have not been conducted with RIMONAL, an additive or potentiating effect with central nervous system depressants (alcohol, barbiturates, opiates, sedatives, or anaesthetics) should be considered.

It has been reported that tricyclic antidepressants are blinded hypotensive effect of systemic clonidine. It is not known whether the concomitantly use of these agents with RIMONAL in people interacts with the effect of lowering IOP. It is recommended to be careful in patients using tricyclic antidepressants which affect the metabolism and uptake of circulating amines.

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

Additional information about special populations:

Not reported.

Paediatric population:

Not reported.

4.6 Pregnancy and lactation

General recommendation

Pregnancy category: B

Women of childbearing potential / Contraception

There is no clinical data related to exposure to brimonidine tartrate in pregnancy.

Pregnancy period

Reproductive studies performed in rats with oral doses of 0.66 mg base/kg revealed no evidence of impaired fertility or harm to the fetus due to brimonidine. Dosing at this level produced an exposure that is 189 times higher than the exposure seen in humans following multiple ophthalmic doses. There are no adequate and well-controlled studies in pregnant

women. In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. Brimonidine should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Lactation period

It is not known whether this drug is excreted in human milk; although in animal studies brimonidine tartrate was excreted in breast milk. 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.

Reproductive ability / fertility

Not reported.

4.7 Effects on ability to drive and use machines

As the other similar drugs, RIMONAL may cause fatigue and/or drowsiness, which may affect the ability to drive or use machine in some patients. Patients to be drive and used machine, should be careful that mental alertness may potentially decrease. RIMONAL may cause blurred and/or vision disorders. The patient should wait until these symptoms have cleared before driving or using machinery.

4.8 Undesirable effects

Adverse events occurring in approximately 10-20% of the subjects included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus.

Adverse events occurring in approximately 5-9% of the subjects included: burning sensation in the eye, conjunctival folliculosis, hypertension, oral dryness, and visual disturbance.

Events occurring in approximately 1-4% of subjects included: allergic reaction, asthenia, blepharitis, bronchitis, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspepsia, dyspnea, epiphora, eye discharge, eye dryness, eye irritation, eye pain, eyelid edema, eyelid erythema, flu syndrome, follicular conjunctivitis, ocular stinging sensation, foreign body sensation, headache, pharyngitis, photophobia, rash, rhinitis, sinus

infection, sinusitis, stinging, superficial punctate keratopathy, visual field defect, vitreous floaters, and worsened visual acuity.

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

Post-marketing Experience

The following adverse reactions have been identified during the post-marketing use of brimonidine tartrate 0.15% eye drops in clinical practice.

Eye disorders: Vision blurred, Conjunctivitis
General disorders and administration site conditions: Fatigue, Dizziness
Immune system disorders: Hypersensitivity
Nervous system disorders: Somnolence

4.9 Overdose and treatment

Ophthalmic overdose (Adults):
Reported events in declared cases are generally adverse reactions listed in undesirable effects.

Systemic overdose resulting from accidental ingestion (Adults):
There is very limited data regarding accidental ingestion of brimonidine in adults. The only adverse event reported to date was hypotension. Following hypotensive episode, posthypotensive hypertension was reported.

Overdose treatment includes supportive and symptomatic therapy; it should be careful that patient's airways is open.

Paediatric population:
Symptoms of brimonidine overdose such as apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in paediatric patients following inadvertent ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sympathomimetics used in ophthalmic- glaucoma treatment.
ATC code: S01EA05

Mechanism of action:
Brimonidine tartrate is a quite selective alpha-2 adrenergic receptor agonist with peak ocular hypotensive effective that rise 2 hours after administration.
Fluorophotometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action by reducing aqueous humour formation and enhancing uveoscleral outflow. Brimonidine tartrate has reducing effect of intraocular pressure with minimal effect on cardiovascular or pulmonary parameters.

5.2 Pharmacokinetic properties

General properties

Absorption:
After ocular administration of a 0.2% or 0.1% solution, plasma concentrations were performed peak in 0.5 to 2.5 hours and decreased with systemic half-life within approximately 2 hours.

Distribution:
The protein binding of brimonidine has not been studied.

Biotransformation:
Brimonidine is extensively metabolized by the liver in human.

Elimination:
Urinary excretion is the major route of elimination of brimonidine and its metabolites. Approximately 87% of radioactive brimonidine dose administered orally was eliminated within 120 hours, 74% of it were found in the urine.

Characteristic properties in patients

Properties in elderly patients:

The C_{max}, AUC, and apparent half-life are similar in the elderly when comparing after a single dose of brimonidine tartrate with young adults and therefore, it has been observed that systemic absorption and elimination are not affected by age.

5.3 Preclinical safety data

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 1.0 mg/kg/day in rats achieved 86 and 55 times, respectively, the plasma drug concentration estimated in humans treated with one drop of brimonidine tartrate into both eyes 3 times per day. Brimonidine tartrate was not mutagenic or cytogenic 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 cytogenic studies in mice, and dominant lethal assay.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Boric acid

Calcium chloride dihydrate

Magnesium chloride hexahydrate

Potassium chloride

Sodium borate decahydrate

Hydroxypropyl methyl cellulose

Sodium chloride

Sodium hydroxide

Hydrochloric acid

Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C at room temperature. Use within 4 weeks by keeping below 30°C after first opening.

6.5 Nature and contents of container

RIMONAL 0.15% Eye Drops is packaged in cardboard box with patient information leaflet and in 5 ml Opaque LDPE bottles closed with LDPE-HDPE cap and containing LDPE dropper and 5 ml solution.

6.6 Special precautions for disposal and other handling

Special condition is not required.

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

7. PRODUCT REGISTRANT

Goldplus Universal Pte Ltd.

103 Kallang Avenue #06-02, Singapore 339504

8. PRODUCT REGISTRATION NUMBER

9. DATE OF PRODUCT REGISTRATION/ RENEWAL OF THE REGISTRATION

Date of product registration:

Renewal of the registration:

10. DATE OF REVISION OF THE TEXT

April 2024