PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

KETAGEX™ 0,035 % eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 0,345 mg ketotifen fumarate (0,035 % *m/v*), equivalent to 0,25 mg ketotifen (0,025 % *m/v*)

Preservative: Benzalkonium chloride 0,1 mg/ml (0,01 % *m/v*)

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution

The solution is a clear, colourless to yellow liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

KETAGEX is indicated for the temporary prevention of itching of the eye due to seasonal allergic conjunctivitis.

Safety and efficacy beyond 4 weeks have not been established.

4.2 Posology and method of administration

Posology

Adults and children (age 3 years and older): Instil one drop into the lower conjunctival sac of the affected eye(s) twice daily, every 8-12 hours and no more than twice per day.

Paediatric population

The safety and efficacy of the use of KETAGEX in children younger than 3 years have not been established.

Method of administration

Contact lenses should be removed before instillation of the eye drops and may be reinserted after 15 minutes (see section 4.4).

If more than one topical ophthalmic medicine is being used, they should be administered at least 5 minutes apart, in order to avoid washing out of the medicine.

To avoid contamination, do not let the applicator tip touch the surface of the eye, fingers, or any other surface.

Replace cap after each use.

4.3 Contraindications

Hypersensitivity to ketotifen fumarate or any other ingredients listed in section 6.1.

4.4 Special warnings and precautions for use

Use only for ocular instillation.

KETAGEX must not be used:

- if solution changes colour or becomes cloudy
- to treat contact lens related irritation.

Use of contact lenses

Contact lenses may absorb benzalkonium chloride which is known to discolour soft contact lenses. Contact lenses should be removed before instillation of KETAGEX and may be reinserted after 15 minutes (see section 4.2).

Benzalkonium chloride

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface.

KETAGEX 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.

Paediatric population

From the limited data available, there is no difference in the adverse event profile in children compared to adults. Generally, eyes in children show a stronger reaction for a given stimulus than the adult eye. Irritation due to benzalkonium chloride may have an effect on treatment adherence in children.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

The use of KETAGEX may potentiate the effects of central nervous system depressants, antihistamines and alcohol.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are no adequate data from the use of KETAGEX eye drops in pregnant women. Animal studies using maternally toxic oral doses showed increased pre- and postnatal mortality, but no teratogenicity. Systemic levels after ocular administration are much lower than after oral use.

However, the safety of KETAGEX in pregnancy has not been established.

Breastfeeding:

Although animal data following oral administration show excretion into breast milk, topical administration to human is unlikely to produce detectable quantities in breast milk. However, the safety of KETAGEX in lactating women has not been established.

Fertility:

There are no data available on the effect of KETAGEX on fertility in humans.

4.7 Effects on ability to drive and use machines

Instillation of eye drops may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines.

4.8 Undesirable effects

a. Summary of the safety profile

In controlled clinical studies, conjunctival injection, headaches and rhinitis were reported at an incidence of 10 to 25 %. The occurrence of these side effects was generally mild. Some of these events were similar to the underlying ocular disease being studied.

b. Tabulated list of adverse reactions

Category	Frequency	Adverse reactions
Ocular	Very common (≥1/10), (10 – 25 %)	conjunctival injection
	Common (≥1/100; <1/10), (less than 5 %)	allergic reactions, burning or stinging, conjunctivitis, discharge, dry eyes, eye pain, eyelid disorder, itching, punctate keratitis, punctate corneal epithelial erosion, lacrimation disorder, mydriasis, photophobia, rash
Non-ocular	Very common (≥1/10), (10 – 25 %)	Headaches, rhinitis
	Common (≥1/100; <1/10), (less than 5 %)	flu syndrome, pharyngitis, drowsiness

Adverse drug reactions from post-marketing experience (Frequency not known):

The following post marketing events have also been observed: hypersensitivity reactions including local allergic reaction (mostly contact dermatitis, eye swelling, eyelid pruritis and oedema), systemic allergic reactions including facial swelling/oedema (in some cases associated with contact dermatitis) and exacerbation of pre-existing allergic conditions such as asthma and eczema.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit-risk of the medicine. Health care providers are asked to report

any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Suspected adverse reactions may also be reported directly to the Holder of the Certificate of registration using the following e-mail address: PV-SouthAfrica@bausch.com

4.9 Overdose

Oral ingestion of the contents of a 10 ml bottle would be equivalent to 3,45 mg of ketotifen fumarate. Clinical results have shown no serious signs or symptoms after ingestion of up to 20 mg of ketotifen fumarate.

In the event of an overdose, treatment should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 15.4 Ophthalmic preparations: Other

Mechanism of action

Ketotifen is a histamine H1-receptor antagonist. In addition, ketotifen in vitro inhibits the release of mediators (e.g. histamine, leukotrienes and prostaglandins, and Platelet-activating factor) from cells involved in immediate Type I allergic reactions (mast cells, eosinophils, basophils and neutrophils). Ketotifen in vitro also decreases chemotaxis, activation and degranulation of eosinophils. Increased cAMP levels by phosphodiesterase inhibition may contribute to the cell stabilizing effect of ketotifen.

5.2 Pharmacokinetic properties

Absorption

Plasma levels of ketotifen after repeated ocular administration for 14 days were in most cases below the limit of quantitation (20 pg/ml).

Distribution

Bioavailability amounts to approximately 50 % owing to a first-pass effect of about 50 % in the liver. Maximal plasma concentrations are reached within 2 to 4 hours. Protein binding is 75%.

Elimination

Ketotifen is eliminated biphasically, with a short half-life of 3 to 5 hours and a longer one of 21 hours. About 1 % of the substance is excreted unchanged in the urine within 48 hours and 60 to 70 % as metabolites. The main metabolite is the virtually inactive ketotifen-N-glucuronide.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Glycerin

Hydrochloric acid and/or sodium chloride (for pH adjustment)

Water for injection

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Before first opening: 2 years

After opening the container: 60 days

6.4 Special precautions for storage

Store at 4 – 30 °C.

After first opening, use within 60 days (see section 6.3) and discard any remaining solution.

6.5 Nature and contents of container

KETAGEX is supplied as a 10 ml solution in a 10 ml white, round low-density polyethylene bottle with a natural linear low-density polyethylene tip and white polypropylene cap. The bottle is labelled and supplied in a carton with a patient information leaflet.

6.6 Special precautions for disposal and other handling

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

47/15.4/1166

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16 August 2022

10 DATE OF REVISION OF THE TEXT