07 July 2003

Scheduling Status:

Proprietary Name (and dosage form): Zaditen Eye Drops

Composition:

Each 1 ml contains:

Ketotifen fumarate 0,345mg equivalent to ketotifen 0,25 mg

Preservative:

Benzalkonium chloride 0,01 %m/v

Pharmacological Classification:

A15.4 Ophthalmic preparations - Other

Pharmacological 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. After oral administration, the absorption of ketotifen is almost complete.

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%. 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.

Indications:

For the temporary prevention of itching of the eye due to seasonal allergic conjunctivitis. Safety and efficacy beyond 4 weeks have not been established.

Contra-Indications:

Patients with a history of hypersensitivity to the active ingredient or any of the excipients of this medicine.

The safety of administration in pregnancy and lactation has not yet been established. Use of contact lenses (see warnings).

Warnings:

Use only for ocular instillation. Contact lenses should not be worn during instillation of the drug because benzalkonium chloride may be deposited in soft contact lenses. The lenses should be removed before application and not re-inserted earlier than 15 minutes after instillation.

When other ophthalmic preparations are used concomitantly, an interval of at least 5 min should be observed between the medications, in order to avoid washing out of the drug.

Blurred vision may occur; patients with blurred vision should refrain from driving or operating heavy machinery.

Zaditen eye drops may cause drowsiness.

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

The possibility of adverse effects on corneal permeability and the danger of disruption of corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations cannot be excluded, therefore regular ophthalmological examinations are required.

Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.

Dosage and Directions for Use:

Adults and children (age 3 years and older) : instil 1 drop into the lower conjunctiva! sac of the eyes two to three times daily.

Side-effects and Special Precautions:

In controlled clinical studies, conjunctiva! 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.

The following ocular and non-ocular adverse events were reported at an incidence of less than 5% :

Ocular : Allergic reactions, burning or stinging, conjunctivitis, discharge, dry eyes, eye pain, eyelid disorder, itching, keratitis, lacrimation disorder, mydriasis, photophobia and rash.

Non-ocular : Flu syndrome, pharyngitis, drowsiness.

Known symptoms of overdosage and particulars of its treatment:

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

Identification:

Zaditen is a colourless to faintly yellow, odourless, aqueous solution, free of any particulate matter.

Presentation:

5ml solution in a white, opaque 5ml LDPE plastic bottle with a LDPE plastic dropper and a white HDPE plastic cap.

Storage Instructions:

Store in a well-closed container below 25 °C.

Do not use for more than 30 days after opening.

KEEP OUT OF REACH OF CHILDREN.

Registration Number:

350076

Name and Business Address of the Applicant:

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