SCHEDULING STATUS

Schedule 2

PROPRIETARY NAME AND DOSAGE FORM

RELESTAT Eye drops

COMPOSITION

Epinastine hydrochloride 0,5 mg per ml.

Excipients: Benzalkonium chloride 0,01 % m/v as preservative, disodium edetate, sodium chloride, sodium dihydrogen phosphate dihydrate, purified water.

PHARMACOLOGICAL CLASSIFICATION

A.15.4 Ophthalmic preparations. Other

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Epinastine is a topically active, direct H_1-receptor antagonist, with a high binding affinity for the histamine H_1-receptor and a 400 times lower affinity for the histamine H_2-receptor. Epinastine also possesses affinity for the α_1-, α_2-, and the 5-HT_2-receptor. It has low affinity for cholinergic, dopaminergic and a variety of other receptor sites. Epinastine does not readily penetrate the blood/brain barrier.

Following topical eye application in animals, epinastine showed evidence for antihistaminic activity, a modulating effect on the accumulation of inflammatory cells and mast cell stabilising activity.

In provocation studies with allergens in humans, epinastine was able to ameliorate ocular symptoms following ocular antigen challenge. The duration of the effect was at least 8 hours.

Pharmacokinetic properties

Following administration of one drop of RELESTAT in each eye twice daily, an average maximum plasma concentration of 0,042 ng/ml is reached after about two hours.

Epinastine has a volume of distribution of 417 litres and is 64 % bound to plasma proteins.

The clearance is 928 ml/min and the terminal plasma elimination half-life is about 8 hours. Less

than 10 % is metabolised.

Epinastine is mainly excreted unchanged. The renal elimination is mainly via active tubular secretion.

Preclinical studies *in vitro* and *in vivo* show that epinastine binds to melanin and accumulates in the pigmented ocular tissues of rabbits and monkeys. *In vitro* data indicate that the binding to melanin is moderate and reversible.

INDICATIONS

RELESTAT is indicated for the short-term treatment of the symptoms of seasonal allergic conjunctivitis.

CONTRA-INDICATIONS

Hypersensitivity to epinastine, benzalkonium chloride, or to any of the excipients in RELESTAT.

WARNINGS AND SPECIAL PRECAUTIONS

RELESTAT is for topical ophthalmic use only and not for injection or oral use.

RELESTAT contains benzalkonium chloride as a preservative which has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy.

Benzalkonium chloride may be absorbed by and discolour soft contact lenses. Patients should be instructed to wait until 15 minutes after instillation of RELESTAT before inserting contact lenses.

RELESTAT should not be administered while wearing contact lenses.

As the possibility of adverse effects on the corneal permeability, and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride-preserved ophthalmological preparations cannot be excluded, regular ophthalmological examination is 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 (see DOSAGE AND

DIRECTIONS FOR USE).

Effects on ability to drive and use machines

Transient blurring of vision may occur upon instillation of eye drops. Patients should be cautioned to not drive or operate hazardous machinery unless their vision is clear.

INTERACTIONS

No interaction studies have been performed.

No interactions are anticipated in humans since systemic concentrations of epinastine are extremely low following ocular dosing. In addition, epinastine is mainly excreted unchanged in humans, indicating a low level of metabolism.

PREGNANCY AND LACTATION

Pregnancy

Safe use of RELESTAT in pregnancy has not been established. RELESTAT should not be used during pregnancy.

Lactation

Safe use of RELESTAT during lactation has not been established. RELESTAT should not be used by woman breastfeeding their infants. Alternatively, mothers on RELESTAT should not breastfeed their infants.

DOSAGE AND DIRECTIONS FOR USE

The recommended dose for adults is one drop instilled in each affected eye twice daily, during the symptomatic period.

There is no experience in clinical studies with the use of RELESTAT for more than 8 weeks, and use RELESTAT beyond that time span is therefore not recommended (see WARNINGS AND SPECIAL PRECAUTIONS).

To avoid contamination of the eye or eye drops do not allow the dropper tip to come into contact with any surface.

If more than one topical ophthalmic medicinal product is being used, the medicinal products

should be administered at least 10 minutes apart.

Elderly patients

RELESTAT has not been studied in elderly patients.

Children

RELESTAT may be used in adolescents (12 years of age and older) at the same dosage as in adults. The safety and efficacy of RELESTAT in children less than 12 years of age have not been established.

Hepatic impairment

RELESTAT has not been studied in patients with hepatic impairment.

Renal impairment

RELESTAT has not been studied in patients with renal impairment.

SIDE EFFECTS

The most common adverse reaction was burning sensation in eye (mostly mild); all other adverse reactions were uncommon.

Within each frequency grouping, adverse reactions are presented according to System Organ Class in order of decreasing seriousness. The following terminologies have been used in order to classify the occurrence of undesirable effects: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

The following adverse medicine reactions were reported during clinical trials with RELESTAT.

Eye disorders

Common: Burning sensation/eye irritation

Uncommon: Conjunctival/ocular hyperaemia, eye dryness, eye pruritus, visual disturbance, eye discharge, increased lacrimation*, eye pain*

Nervous system disorders

Uncommon: Headache

Respiratory, thoracic and mediastinal disorders

Uncommon: Asthma, nasal irritation, rhinitis, sinusitis.

Gastrointestinal disorders

Uncommon: Dysgeusia

Post-marketing experience

The following adverse reactions have been identified during post-marketing use of RELESTAT.

Eye disorders

Ocular hyperemia, lacrimation increased, eye pain, eye swelling, eyelid edema

Immune system disorders

Hypersensitivity reaction including symptoms or signs of eye allergy and skin allergic reaction

Paediatric population

Frequency, type and severity of adverse reaction in adolescents ≥ 12 years of age are expected to be the same as in adults.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

See ‘SIDE EFFECTS’. Treatment is symptomatic and supportive.

No case of overdose has been reported.

IDENTIFICATION

A clear colourless solution in a multidose bottle.

PRESENTATION

5 ml LDPE bottle with dropper tip and a white polystyrene screw cap.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Do not use more than 30 days after opening.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER

37/15.4/0691

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

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION

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