

DATA SHEET

NAME OF MEDICINE

RELESTAT[®] (epinastine hydrochloride) 0.5 mg/mL eye drops.

PRESENTATION

RELESTAT[®] is a clear, colourless, sterile ophthalmic solution. Epinastine hydrochloride is a white to off-white crystalline substance and is freely soluble in water, ethyl alcohol, methyl alcohol, acetic acid and practically insoluble in diethyl ether.

USES

Actions

Pharmacotherapeutic group: Antihistamine.

Epinastine is a potent, topically active, direct H₁-receptor antagonist. Epinastine has a high binding affinity for the histamine H₁-receptor and a 400 times lower affinity for the histamine H₂-receptor. Epinastine also possesses affinity for the α_1 -, α_2 -, and the 5-HT₂-receptors. It has low affinity for cholinergic, dopaminergic and a variety of other receptor sites.

After oral administration in humans, epinastine revealed antihistaminic and antiallergenic effects in the histamine-induced wheal and flare reaction, as well as in histamine and antigen-induced bronchospasm.

Pharmacokinetics

Following administration of one drop of RELESTAT[®] in each eye twice daily, an average maximum plasma concentration of 0.04 ng/mL is reached after about two hours, indicating low systemic exposure.

Following a single intravenous dose of 5 mg epinastine the volume of distribution observed was 417 litres with 64% bound to plasma proteins. The clearance was 56 L/hr and the terminal plasma elimination half-life is about 8.5 hours. Epinastine is mainly excreted unchanged. About 60% of an intravenous dose is recovered unchanged in the urine and about 30% in faeces. Less than 10% is metabolised. The renal elimination is mainly via active tubular secretion.

Indications:

RELESTAT[®] is indicated for the treatment and/or prevention of the signs and symptoms of seasonal allergic conjunctivitis, for a period of no longer than 12 weeks.

CLINICAL STUDIES

Epinastine hydrochloride 0.05% (RELESTAT[®]) has been shown to be significantly superior to vehicle for improving ocular itching and conjunctival hyperemia in patients with allergic conjunctivitis in clinical studies using three different models: (1) conjunctival antigen challenge (CAC) where patients were dosed and then received antigen instilled into the inferior conjunctival fornix; (2) environmental field studies where patients were dosed and evaluated during allergy season in their natural habitat; and (3) Vienna challenge chamber (VCC) where patients were dosed and exposed to airborne antigen in a chamber with controlled environment. RELESTAT[®] administered 15 minutes prior to conjunctival antigen challenge demonstrated a rapid onset of action within 3 to 5 minutes after conjunctival antigen challenge. Duration of effect was shown to be at least 8 hours, making a twice daily regimen suitable. This dosing regimen was shown to be safe and effective for up to 8 weeks, without evidence of tachyphylaxis. Additional results of the CAC study indicated RELESTAT[®] was superior to vehicle in reducing the secondary efficacy variables of ciliary and episcleral hyperemia, chemosis, lid swelling, and tearing. In another environmental study RELESTAT[®] was shown to be superior to levocabastine for improving ocular itching.

DOSAGE AND ADMINISTRATION

The recommended dosage in adults and children is one drop in each affected eye twice daily.

Treatment should be continued throughout the period of exposure (i.e., until the pollen season is over or until exposure to the offending allergen is terminated).

If more than one topical ophthalmic medication is to be used, the other medication should not be used within 5 minutes of using RELESTAT[®] eye drops.

Paediatric Use

The safety and effectiveness of RELESTAT[®] in children less than 9 years of age has not been evaluated.

Use in Elderly

RELESTAT[®] has not been studied in elderly patients over the age of 65 years. Safety data from the tablet formulation of epinastine hydrochloride (up to 20 mg once daily) indicates that there are no particular safety issues for elderly patients compared with adult patients. As such, no dosage adjustment is considered to be necessary.

CONTRAINDICATIONS

RELESTAT[®] eye drops are contraindicated in patients with hypersensitivity to epinastine, or any other ingredient in this product.

WARNINGS AND PRECAUTIONS

Preclinical Findings:

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

Carcinogenicity and Mutagenicity:

In 18 month or 2 year dietary carcinogenicity studies in mice or rats, respectively, epinastine was not carcinogenic at doses which were 40,000 times higher than the maximum recommended ocular human dose (MROHD).

Epinastine was negative for mutagenicity in the Ames/*Salmonella* assay and *in vitro* chromosome aberration assay using human lymphocytes. Epinastine was negative in the *in vivo* clastogenicity studies, including the mouse micronucleus assay and chromosome aberration assay in Chinese hamsters. Epinastine was also negative in the cell transformation assay using Syrian hamster embryo cells, V79/HGPRT mammalian cell point mutation assay, and *in vivo/in vitro* unscheduled DNA synthesis assay using rat primary hepatocytes.

Impairment of Fertility:

Epinastine had no effect on fertility of male rats and decreased fertility in female rats at an oral dose up to 120,000 times the MROHD.

Pregnancy and Lactation:

Pregnancy Category B3

In an embryofetal developmental study in pregnant rats, maternal toxicity with no embryofetal effects was observed at an oral dose that was 120,000 times the MROHD. Resorptions and abortion were observed in an embryofetal study in pregnant rabbits at an oral dose that was 75,000 times the MROHD.

Epinastine had no effect on pup growth or behaviour following an oral dose to pregnant or lactating rats that was 120,000 times the MROHD.

The safety of epinastine HCl tablets (10 or 20 mg once daily) has been evaluated in 11 pregnant women. No adverse drug reactions were observed and there was no influence of epinastine on the pregnant woman, the birth or the newborn baby.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, RELESTAT[®] eye drops should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

A study in lactating rats revealed excretion of epinastine in the breast milk. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RELESTAT[®] eye drops is administered to a nursing woman.

Effects on ability to drive and use machines:

Based on the pharmacodynamic profile, epinastine is not expected to affect the ability to drive and use machines. As with any ocular medication, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machinery.

Hepatic Impairment Use:

RELESTAT[®] has not been studied in patients with hepatic impairment. Safety data from the tablet formulation of epinastine hydrochloride (up to 20 mg once daily) indicates that the incidence of adverse reactions was higher in this group compared with adult patients without hepatic impairment. It should be noted however, that the daily dose of a 10 mg epinastine hydrochloride tablet is more than 100-fold higher than the daily dose following RELESTAT[®]. In addition, the metabolism of epinastine in humans is minimal (<10%). Therefore, no dosage adjustment is considered to be necessary.

Renal Impairment Use:

Safety and effectiveness of RELESTAT[®] has not been studied in patients with renal impairment. The systemic safety of epinastine tablets (10 or 20 mg once daily) has been evaluated in over 60 patients with renal impairment. No adverse drug reactions were reported. The daily dose of a 10 mg epinastine tablet is more than 100-fold higher than the daily dose following RELESTAT[®]. Therefore, dosing of RELESTAT[®] in patients with renal impairment would be expected to be the same as in adults without renal impairment.

Information for patients:

Contact lenses should be removed prior to instillation of RELESTAT[®] and may be reinserted after 10-15 minutes following its administration. Patients should be advised that RELESTAT[®] contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses.

To prevent contaminating the dropper tip and solution, patients should be advised that care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

If more than one topical ophthalmic medication is to be used, the other medication should not be used within 5 minutes of using RELESTAT[®] eye drops.

ADVERSE EFFECTS

In clinical studies, the overall incidence of treatment-related adverse events following RELESTAT[®] was less than 10%. No serious adverse events occurred. Most of the treatment-related events were ocular and mild.

The most common treatment-related adverse event occurring in approximately 4% of patients was burning sensation in the eye. Other treatment-related events reported in less than 1% of patients included allergic conjunctivitis, blepharoptosis, conjunctival oedema, conjunctival hyperemia, eye discharge, eye dryness, eye irritation and stinging, ocular itching, increased ocular sensitivity, photophobia, visual disturbance, headache, asthma, nasal irritation, rhinitis, oral dryness, taste perversion, and pruritus.

INTERACTIONS

No drug-drug 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. Specific interaction studies with other medicinal products have not been performed with RELESTAT[®].

OVERDOSAGE

After instillation of 0.3% (3 mg/mL) epinastine hydrochloride eye drops 3 times daily (corresponds to 9 times the recommended daily dose) reversible miosis, without influence on visual acuity or other ocular parameters, was observed.

The 5 mL bottle of RELESTAT[®] contains 2.5 mg of epinastine. A tablet formulation is marketed overseas at a daily dose of up to 20 mg epinastine hydrochloride, as such, intoxication after oral ingestion of the ophthalmic formulation is not expected even if the entire contents of the bottle is swallowed. No case of overdose with RELESTAT[®] has been reported.

PHARMACEUTICAL PRECAUTIONS

To avoid contamination of the solution, keep container tightly closed. Do not touch dropper tip to any surface. Contents are sterile if seal is intact.

Shelf life: 2 years

Storage: Keep the bottle in the outer carton in order to protect from light. Store below 25°C.

Discard contents 4 weeks after opening the bottle.

MEDICINE CLASSIFICATION

Prescription Medicine

PACKAGE QUANTITIES

RELESTAT[®] (epinastine hydrochloride) 0.5 mg/mL eye drops sterile solution is supplied in 5 mL polyethylene bottles with a white polystyrene screw cap with spike device for opening the bottle.

FURTHER INFORMATION

List of excipients

PRESERVATIVE: benzalkonium chloride

INACTIVES: disodium edetate, sodium chloride, sodium phosphate-monobasic, and purified water. Sodium hydroxide and/or hydrochloric acid may be added to adjust the pH.

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