

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Relestat, 0.5 mg/ml, eye drops, solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of eye drops, solution, contains 0.5 mg of epinastine hydrochloride (equivalent to 0.436 mg epinastine)

Excipient: benzalkonium chloride 0.1 mg/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.

Product imported from Greece:

A clear and colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of the symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration

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.

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 different medicinal products should be administered at least 10 minutes apart.

Elderly patients

Relestat has not been studied in elderly patients. Post-marketing 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.

Paediatric population

Safety and efficacy in patients ≥ 12 years has been established in clinical trials. 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 3 years of age have not been established. There are limited data on the safety in children aged 3-12 years, see section 5.1.

Hepatic impairment

Relestat has not been studied in patients with hepatic impairment. Post-marketing 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. 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

Relestat has not been studied in patients with renal impairment. Post-marketing safety data from the tablet formulation of epinastine hydrochloride (up to 20 mg once daily) indicate that there are no particular safety issues for patients with renal impairment. As such, no dosage adjustment is considered to be necessary.

4.3 Contraindications

Hypersensitivity to epinastine or to any of the excipients.

4.4 Special warnings and precautions for use

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

Benzalkonium chloride is commonly used as a preservative in ophthalmic products and has been reported rarely to cause punctate keratopathy and/or toxic ulcerative keratopathy.

Benzalkonium chloride may be absorbed by and discolour soft contact lenses and therefore patients should be instructed to wait until 10-15 minutes after instillation of Relestat before inserting contact lenses. Relestat should not be administered while wearing contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a limited number (11) of exposed pregnancies indicate no adverse effects of epinastine on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3).

Caution should be exercised when prescribing to pregnant women.

Lactation

Epinastine is excreted in the breast milk of rats, but it is not known if epinastine is excreted in human milk. Due to the lack of experience, caution should be exercised when prescribing to breast-feeding women.

Fertility

There are no adequate data from the use of epinastine on fertility in humans.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamic profile, reported adverse reactions and specific psychometric studies, epinastine has no or negligible influence on the ability to drive and use machines.

If transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

In clinical studies, the overall incidence of adverse drug reactions following Relestat was less than 10%. No serious adverse reactions occurred. Most were ocular and mild. 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 decreased seriousness. The following terminologies have been used in order to classify the occurrence of undesirable effects: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$); not known (cannot be estimated from the available data).

The following adverse drug reactions were reported during clinical trials with Relestat:

Nervous system disorders

Uncommon: headache

Eye disorders

Common: burning sensation/ eye irritation

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

Respiratory, thoracic and mediastinal disorders

Uncommon: asthma, nasal irritation, rhinitis

Gastrointestinal disorders

Uncommon: dysgeusia

*Increased lacrimation and eye pain have been identified during postmarketing use of Relestat in clinical practice.

Paediatric population

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

There is limited experience in children 3-12 years of age regarding frequency, type and severity of adverse reactions.

4.9 Overdose

After instillation of 0.3% 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 hydrochloride. A tablet formulation is marketed at a once 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 whole content of the bottle is swallowed.

No case of overdose has been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals; Decongestants and Antiallergics; Other antiallergics
ATC code: S01G X10

Epinastine is a 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 -receptor. It has low affinity for cholinergic, dopaminergic and a variety of other receptor sites. Epinastine does not penetrate the blood/brain barrier and, therefore, does not induce side effects of the central nervous system, i.e., it is non-sedative.

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.

Paediatric population

A 6-week, randomised, double-masked, vehicle controlled study (2:1) involving 96 ocular-wise non-symptomatic, healthy children aged 3-12 years, indicated that Relestat was well tolerated and did not identify any significant differences between the groups for any safety variable. Treatment related reactions were conjunctival follicles (6.3% in both epinastine and vehicle-treated subjects) and conjunctival hyperaemia (1.6% of epinastine treated subjects and none in the vehicle group). Safety and efficacy in patients ≥ 12 years has been established in clinical trials.

5.2 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 renally 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.

5.3 Preclinical safety data

Non clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride (as preservative)
Disodium edetate
Sodium chloride
Sodium dihydrogen phosphate dihydrate
Sodium hydroxide/hydrochloric acid (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on outer package of the product on the market in the country of origin.

After first opening: 28 days

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

A plastic bottle with a screw cap. Each bottle contains 5ml of solution.

Each pack contains 1 bottle.

6.6 Special precautions for disposal

No special requirements

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

7 PARALLEL PRODUCT AUTHORISATION HOLDER

B & S Healthcare
Unit 4, Bradfield Road
Ruislip
Middlesex, HA4 0NU
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1328/196/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th January 2013

10 DATE OF REVISION OF THE TEXT