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 with known effect:

Benzalkonium chloride 0.1 mg/ml and phosphate 4.75 mg/ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution (eye drops)
A clear colourless sterile solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of the symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration

Posology

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.

Elderly

Relestat has not been studied in elderly people. 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 compared with adult patients. As such, no dosage adjustment is considered to be necessary.

Paediatric population

The safety and efficacy in children ≥ 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 aged less than 3 years have not been established. No data are available. There are limited data on the safety in children aged 3-12 years described in section 5.1.

Patients with 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.

Patients with 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.

Method of administration

Relestat is for topical ophthalmic use only.

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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

Excipients with known effect

Benzalkonium chloride

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 soft contact lenses and may change the colour of the contact lenses. Patients should be instructed to remove contact lenses before using this medicine and put them back 15 minutes afterwards.

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

Phosphates

Relestat also contains phosphates. Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas (see section 4.8)

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.

Breast-feeding

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, Relestat 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

Summary of the safety profile

In clinical studies, the overall incidence of adverse 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.

Tabulated list of adverse reactions

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 (≥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 reactions have been reported with epinastine:

System Organ Class	**Frequency**	**Adverse reaction**
Immune system disorders	Not known	Hypersensitivity reaction including symptoms or signs of eye allergy and extra-ocular allergic reactions, including angioedema, skin rash and redness
Nervous system disorders	Uncommon	Headache
Eye disorders	Common	Burning sensation, eye irritation
	Uncommon	Conjunctival/ocular hyperaemia, eye discharge, eye dryness, eye pruritus, visual disturbance
	Not known	Increased lacrimation, eye pain, eye swelling, eyelid oedema
Respiratory, thoracic and mediastinal disorders	Uncommon	Asthma, nasal irritation, rhinitis
Gastrointestinal disorders	Uncommon	Dysgeusia

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 aged 3-12 years regarding frequency, type and severity of adverse reactions.

Adverse reactions reported in phosphate containing eye drops

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard.

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

Mechanism of action

Epinastine is a topically active, direct H_1-receptor antagonist. Epinastine has 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 penetrate the blood/brain barrier and, therefore, does not induce side effects of the central nervous system, i.e., it is non-sedative.

Pharmacodynamic effects
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

Absorption

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.

Distribution

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

plasma proteins.

Biotransformation

Less than 10% is metabolised.

Elimination

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

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, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

List of excipients

Benzalkonium chloride
Disodium edetate
Sodium chloride
Sodium dihydrogen phosphate dihydrate
Sodium hydroxide/hydrochloric acid (pH adjustment)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

After first opening: 4 weeks.

6.4 Special precautions for storage

Keep the bottle in the outer carton in order to protect from light.

Do not store above 25°C

6.5 Nature and contents of container

10 ml polyethylene bottle with a white polystyrene screw cap.

The fill volume is 5 ml.

6.6 Special precautions for disposal

No special requirements.

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

7 MARKETING AUTHORISATION HOLDER

AbbVie Ltd.
Maidenhead
SL6 4UB

8 MARKETING AUTHORISATION NUMBER(S)

PL 41042/0075

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18th October 2002 / 18th October 2007

10 DATE OF REVISION OF THE TEXT

13/01/2025