Core Safety Profile

<table>
<thead>
<tr>
<th>Active substance:</th>
<th>Epinastine hydrochloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutical form(s)/strength:</td>
<td>0,5 mg/ml eye drops, solution</td>
</tr>
<tr>
<td>P-RMS:</td>
<td>SE/H/PSUR/0042/002</td>
</tr>
<tr>
<td>Date of FAR:</td>
<td>20.09.2013</td>
</tr>
</tbody>
</table>
4.2 Posology and method of administration

/.../ is for topical ophthalmic use only.

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 /.../ 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

/.../ 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. /.../ may be used in adolescents (12 years of age and older) at the same dosage as in adults.

The safety and efficacy of /.../ 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

/.../ 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 /.../. In addition, the metabolism of epinastine in humans is minimal (<10%). Therefore, no dosage adjustment is considered to be necessary.

Renal impairment

/.../ 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

/.../ 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 discolor soft contact lenses and therefore patients should be instructed to wait until 10-15 minutes after instillation of /.../ before inserting contact lenses. /.../ 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 /.../ 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 (≥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 drug reactions were reported during clinical trials with /.../:

**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 /.../ 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 /.../ 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.