SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ZELASS-M 0.05% Eye Drops
Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of eye drops contains
Active substance:
Azelastine hydrochloride……..0.5 mg (0.05%) (Equivalent to 0.45 mg azelastine).

Each drop contains 0.015 mg azelastine hydrochloride.

Excipient(s):
Benzalkonium chloride.....0.125 mg/ml
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile eye drops
Clear and colorless solution without visible particles

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prevention of the symptoms of seasonal allergic conjunctivitis in adults and children 4 years and older.

Treatment of the symptoms of non-seasonal (perennial) allergic conjunctivitis in adults and children 12 years and older.

4.2 Posology and method of administration

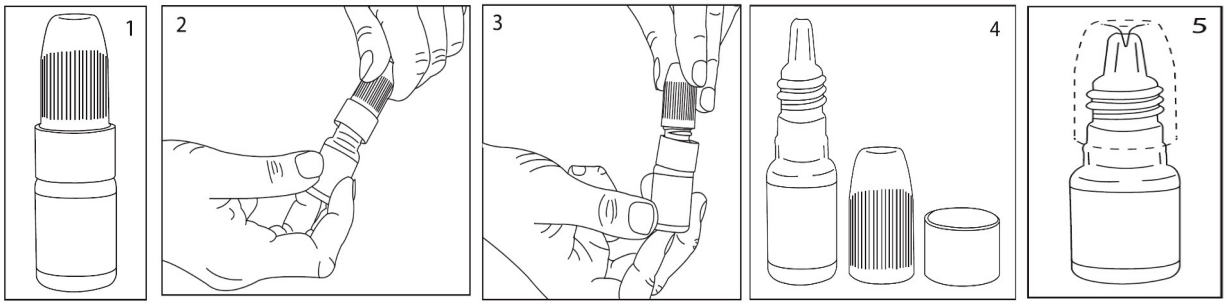
Posology/frequency and duration of administration
Seasonal allergic conjunctivitis:
The usual dosage in adults and children 4 years and older is 1 drop in each eye twice daily that can be increased, if necessary, to four times daily. If allergen exposure is anticipated, ZELASS-M should be administered prophylactically, prior to the exposure.

Non-seasonal (perennial) allergic conjunctivitis:
The usual dosage in adults and children 12 years and older is 1 drop in each eye twice daily that can be increased, if necessary, to four times daily.

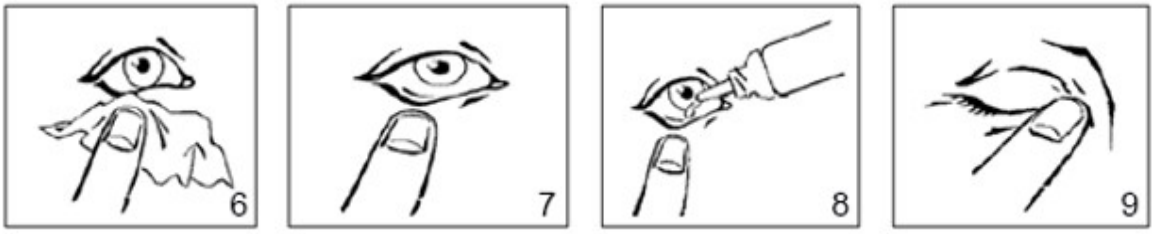
As safety and efficacy have been demonstrated in clinical trials for a period of up to 6 weeks, the duration of any course should be limited to a maximum of 6 weeks. Patients should be advised to contact their doctor if symptoms worsen or do not approve after 48 hours.

Method of administration
Applied into the eyes.

Applied to the conjunctival sac formed by pulling the lower eyelid down with the index finger of one hand. The tip of the dropper should not be allowed to touch any place.



- Take the bottle of ZELASS-M.
- Open the cap of the bottle after washing hands (see Figure 2).
- Remove the ring under the cap (see Figure 3 and Figure 4).
- Close the cap again without the ring. The plastic pin inside the cap will pierce the tip of the bottle (Figure 5).



- Hold the bottle upside down between your thumb and middle finger with the tip pointing down.
- Lean your head back. Open your lower eyelid with your clean finger until a pocket is formed between your eyelid and your eye (see Figure 7). The drop will be instilled here (see Figure 8).
- Bring the tip of the bottle close to your eyes.
- Do not let the dropper touch your eyelids, surrounding areas or other surfaces. The drop can be contaminated with germs.
- Gently press the bottom of the inverted bottle to instill one drop of ZELASS-M at a time.
- After applying ZELASS-M, release your lower eyelid, close your eyes and gently press on the inner corner of your eye against the bridge of your nose. This will help prevent ZELASS-M from spreading to other parts of your body (see Figure 9).
- If you are using the medicine in both eyes, repeat the same steps for your other eye.
- Close the bottle tightly with its cap immediately after each use.
- Fully use up one bottle before opening another one.
- If the drop misses your eye, try again.

Additional information on special populations
Renal/Hepatic impairment
The usual doses can be applied. No dose adjustment is necessary.

Pediatric population
The safety and efficacy for seasonal allergic conjunctivitis in children younger than 4 years of age have not been established. It should be used at recommended doses for children aged 4 years and over. There is no need to adjust the dose.

The safety and efficacy for perennial allergic conjunctivitis in children younger than 12 years of age

have not been established. It should be used at recommended doses for children aged 12 years and over. There is no need for dose adjustment.

Geriatric population
The same dose can be used as recommended for adults. No dose adjustment is necessary.

4.3 Contraindications

It is contraindicated in case of hypersensitivity to the active substance or any of the excipients listed in section 6.1.

4.4 Special warning and precautions for use

ZELASS-M eye drops is not intended for treatment of eye infections. For other warnings, see sections 4.5 and 4.6.

ZELASS-M eye drops contains the preservative benzalkonium chloride which may cause eye irritation. Contact with soft contact lenses should be avoided. Contact lenses should be removed prior to application and the patient should wait at least 15 minutes before reinsertion. Known to discolour soft contact lenses.

Benzalkonium chloride has been reported to cause eye irritation, dry eye symptoms, and may affect the tear film and corneal surface. ZELASS-M 0.05% eye drops should be used with caution in patients with dry eyes and in patients whose cornea may be damaged. In case of long-term use, patients should be monitored.

4.5 Interaction with other medicinal products and other forms of interaction

No specific interaction studies with azelastine have been conducted.

Interaction studies at high oral doses azelastine have been performed, however, they bear no relevance to azelastine, as systemic levels, after administration of the eye drops, are in the picogram range.

Additional information on special populations
There are no data on special populations.

Pediatric population:
There are no data on the pediatric population.

4.6 Fertility, pregnancy and lactation

General recommendation
Pregnancy category is C.

Women of child-bearing potential/Contraception
Caution should be exercised when prescribing it for women of childbearing potential.

Pregnancy
There are no adequate data on the use of azelastine in pregnant women.

There is insufficient information available to establish the safety of azelastine in human pregnancy.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy/ embryonal/fetal development / parturition or postnatal development (see section 5.3).

Caution should be exercised when administered to pregnant women.

At high oral doses, azelastine has shown to induce adverse effects (fetal death, growth retardation and skeletal malformation) in experimental animals. Local ocular application will result in minimal systemic exposure (picogram range).

Lactation
Azelastine is excreted into the milk in low quantities.
ZELASS-M is not recommended during lactation.

Reproductive ability / Fertility
Effects on fertility have not been studied in humans.

4.7 Effects on ability to drive and use machines

The mild, transient irritation that can be experienced after application of ZELASS-M is unlikely to affect vision to any greater extent. However, if there are any transient effects on vision, the patient should be advised to wait until this clears before driving or operating machinery.

4.8 Undesirable effects

The following terms and frequencies are used:
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).

Immune system disorders
Very rare*:* Allergic reactions (such as redness and pruritus)

Nervous system disorders
Uncommon: Bitter taste

Eye disorders
Common*:* Mild, transient irritation in the eye

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 the national reporting system.

4.9 Overdose

No specific reactions after ocular overdose are known, and with the ocular route of administration, overdose reactions are not anticipated.

There is no experience with the administration of toxic doses of azelastine hydrochloride in humans. In the case of overdose or intoxication, disturbances of the central nervous system are to be expected based on the results of animal experiments. Treatment of these disorders should be symptomatic.

There is no known antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, decongestants and antiallergics, other antiallergics
ATC code**:** S01GX07

Azelastine, which is a phthalazinon derivative, is a potent long-acting anti-allergic compound with selective H1 antagonist properties. An additional anti-inflammatory effect could be detected after topical ocular administration.

Data from *in vivo* (pre-clinical) and *in vitro* studies show that azelastine inhibits the synthesis or release of the chemical mediators known to be involved in early and late stage allergic reactions e.g. leukotriene, histamine, PAF and serotonin.

To date, long term therapy ECG evaluations of patients treated with high oral doses of azelastine, have shown that in multiple dose studies, there is no clinically significant effect of azelastine on the corrected QT (QTc) interval.

No association of azelastine with ventricular arrhythmia or "torsade de pointes" was observed in over 3700 patients treated with oral azelastine.

Relief of symptoms of allergic conjunctivitis should be noticed after 15-30 minutes.

5.2 Pharmacokinetic properties

General characteristics (systemic pharmacokinetics)

Absorption

Following oral administration azelastine is rapidly absorbed showing an absolute bioavailability of 81%. Food has no influence on absorption.

Distribution

The volume of distribution is high and mostly peripheral. The level of protein binding is relatively low (80-90%, a very low level in terms of drug interaction reactions).).

Biotransformation

The therapeutically active metabolite is N-Desmethyl azelastine.

Elimination

Plasma elimination half-lives after a single dose of azelastine are approximately 20 hours for azelastine and about 45 hours for the therapeutically active metabolite N-Desmethyl azelastine. Excretion occurs mainly via the feces. The sustained excretion of small amounts of the dose in the feces suggests that some entero-hepatic circulation may take place.

Characteristics in patients (ocular pharmacokinetics)

Linearity/Non-linearity

After repeated ocular application of azelastine (up to one drop in each eye, 4 times daily), C_{max} steady state plasma levels of azelastine hydrochloride were very low and were detected at or below the limit of quantification.

5.3 Preclinical safety data

Azelastine hydrochloride displayed no sensitizing potential in the guinea pig.

Azelastine demonstrated no genotoxic potential in a battery of *in vitro* and *in vivo* tests, nor any carcinogenic potential in rats or mice.

In male and female rats, azelastine at oral doses greater than 3 mg/kg/day caused a dose-related decrease in the fertility index; no substance-related alterations were found in the reproductive organs of males or females during chronic toxicity studies, however.

Embryotoxic and teratogenic effects in rats, mice and rabbits occurred only at maternal toxic doses (for example, skeletal malformations were observed in rats and rabbits at doses of 68.6 mg/kg/day).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Sorbitol (Liquid, 70%)
Hypromellose
Disodium EDTA
Sodium hydroxide
Water for injections

6.2 Incompatibilities

Not known.

6.3 Shelf life

24 months.
Once the bottle is opened, ZELASS-M should be used within 28 days.
During this period, the medicine can be stored at room temperature below 25°C.

6.4 Special precautions for storage

Store at room temperature below 25°C.

6.5 Nature and contents of container

Opaque, low-density polyethylene bottle with a dropper and closed with a white PP screw cap, containing 6 ml of solution, supplied in a cardboard box with a package leaflet.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No.:1
34303 Küçükçekmece-ISTANBUL/TURKEY

8. MARKETING AUTHORIZATION NUMBER

2016/203

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 28.04.2016
Date of renewal:

10. DATE OF REVISION OF THE TEXT

08.05.2023