Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Azelastinehydrochloride Devatis 0,5 mg/ml, oogdruppels, oplossing in verpakking voor éénmalig gebruik

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 0.5 mg azelastine hydrochloride in a preservative free formulation.
One drop contains 0.015 mg azelastine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FROM

Eye drop solution in single dose container for administration by instillation in the conjunctival sac.
Clear, colourless to nearly colourless, slightly viscous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment and prevention of the symptoms of seasonal allergic conjunctivitis in adults and children aged 4 years and older.
- Treatment of the symptoms of non-seasonal (perennial) allergic conjunctivitis in adults and children aged 12 years and older.

4.2 Posology and method of administration

Ocular use

Posology

Seasonal allergic conjunctivitis
The usual dosage in adults and children aged 4 years and older is one drop in each eye twice daily (in the morning and in the evening) that can be increased if necessary to four times daily.

Non-seasonal (perennial) allergic conjunctivitis
The usual dosage in adults and children aged 12 years and older is one drop in each eye twice daily (in the morning and in the evening) 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 treatment cycle should be limited to a maximum of 6 weeks.

Avoid contact with soft contact lenses (See section 4.4).

Paediatric population
Safety and efficacy of Azelastine Devatis in children aged less than 4 years has not been established.

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

Azelastine Devatis is not intended for treatment of eye infections.

As with other ophthalmic solutions, Azelastine Devatis is not recommended for use whilst wearing contact lenses.

Further warnings see 4.5 and 4.6.

4.5 Interactions with other medicinal products and other forms of interaction

No specific interaction studies with Azelastine Devatis 0.5 mg/ml have been performed.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
There is insufficient information available to establish the safety of azelastine in human pregnancy. At high oral doses azelastine has shown to induce adverse effects (foetal death, growth retardation and skeletal malformation) in experimental animals. Local ocular application will result in minimal systemic exposure (picogram range). However, caution should be exercised when using Azelastine Devatis during pregnancy.

Breast-feeding
Azelastine is excreted into the milk in low quantities. For that reason Azelastine Devatis is not recommended during lactation.

4.7 Effects on the ability to drive and use machines

Azelastine Devatis has minor influence on the ability to drive and use machines.

The mild, transient irritation which can be experienced after application of Azelastine Devatis 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 assessment of undesirable effects is based on the following frequencies:

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 rash 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 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 the national reporting system listed in Appendix V*.

[*For the printed material, please refer to the guidance of the annotated QRD template.]

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 must be symptomatic. There is no known antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: DECONGESTANTS AND ANTIALLERGICS, other antiallergics.
ATC code: S01GX07

Azelastine, a phthalazinone derivative is classified as 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.

5.2 Pharmacokinetic properties

General characteristics (systemic pharmacokinetics)

Following oral administration azelastine is rapidly absorbed showing an absolute bioavailability of 81%. Food has no influence on absorption. The volume of distribution is high indicating distribution predominantly into the periphery. The level of protein binding is relatively low (80 - 90%, a level too low to give concern over drug displacement reactions).

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-desmethylazelastine. Excretion occurs mainly via the faeces. The sustained excretion of small amounts of the dose in the faeces suggests that some entero-hepatic circulation may take place.

Characteristics in patients (ocular pharmacokinetics)
After repeated ocular application of azelastine ophthalmic solution (up to one drop in each eye, four 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 sensitising 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 30 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 50 mg/kg/day).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol, liquid (cristallizing) (E420)
Hypromellose (E464)
Disodium edetate (E386)
Sodium hydroxide (E524)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years in the outer packaging

After first opening of the sachet: use the single dose container within 28 days.

After first opening of the single-dose container: use immediately and discard the single-dose container after use.

6.4 Special precautions for storage

Store in the original package. Do not refrigerate or freeze.

For storage conditions of the opened medicinal product, see section 6.3.

6.5 Nature and contents of container

0.3 ml transparent LDPE single-dose containers in PET aluminium/PE sachets containing 5 single dose containers each.

Pack-sizes: 5 x 0.3 ml, 10 x 0.3 ml, 20 x 0.3 ml, 30 x 0.3 ml, 50 x 0.3 ml, 60 x 0.3 ml and 120 x 0.3 ml single dose containers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. MARKETING AUTHORISATION HOLDER

Devatis GmbH
Spitalstr. 22
79539 Lörrach
Duitsland

8. MARKETING AUTHORISATION NUMBER(S)

RVG 113365

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 29 april 2015
Datum van laatste verlenging: 17 maart 2020

10. DATE OF REVISION OF THE TEXT

Laatste gedeeltelijke wijziging betreft rubriek 9: 16.11.2019