Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Azelastine Eye Drops 0.5 mg/ml Eye Drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Azelastine hydrochloride 0.05% (0.5 mg/ml). Each drop contains 0.015 mg azelastine hydrochloride.

Excipient with known effect: 1 ml contains 0.125 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.
Clear, colourless solution.

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

Seasonal allergic conjunctivitis: The usual dosage in adults and children 4 years and older is one drop in each eye twice daily that can be increased, if necessary, to four times daily. If allergen exposure is anticipated Azelastine eye drops 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 one 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.

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 eye drops is not intended for treatment of eye infections.
Azelastine 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.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

Fertility
Effects on human fertility have not been investigated.

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 eye drops during pregnancy.

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

4.7 Effects on ability to drive and use machines

The mild, transient irritation which can be experienced after application of Azelastine eye drops 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 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

No specific reactions after ocular overdosage are known, and with the ocular route of administration, overdosage 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: 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.

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

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-Desmethyl azelastine. 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 Allergodil eye drops (up to one drop in each eye, four times daily), Cmax 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 3.0 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, disodium edetate, hypromellose, liquid sorbitol (crystallising), sodium hydroxide, water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
Once opened: do not use for longer than 4 weeks.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 ml opaque HDPE bottle and LDPE dropper with white HDPE screw cap. One bottle contains either 6 ml, 8 ml or 10 ml solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Cooper Consumer Health B.V.
Verrijn Stuartweg 60
Diemen
Noord-Holland
1112 AX
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA25506/008/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 August 1998

Date of last renewal: 17 February 2008

10 DATE OF REVISION OF THE TEXT

January 2026