

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Azelastine.

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 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 improve 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 is not intended for treatment of eye infections. Further warnings see 4.5 and 4.6.

Azelastine eye drops contains the preservative benzalkonium chloride. Benzalkonium chloride may cause eye irritation, especially with dry eyes or disorders of the cornea. 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 have been performed. Interaction studies at high oral doses of 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.

### **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 during pregnancy.

#### Breast Feeding

Azelastine is excreted into the milk in low quantities. For that reason Azelastine 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 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 ( $\geq 1/10$ )

Common ( $\geq 1/100$  to  $< 1/10$ )

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ )

Rare ( $\geq 1/10,000$  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 Yellow Card Scheme at:

[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

#### **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

Antiallergic, ATC code: S01GX07

Azelastine, a phthalazinone derivative is classified as a potent long-acting antiallergic compound with selective H1 antagonist properties. An additional antiinflammatory 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 Azelastine (up to one drop in each eye, four times daily), C<sub>max</sub> 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 (preservative), disodium edetate, hypromellose, liquid sorbitol (crystallising), sodium hydroxide and water for injections.

### **6.2 Incompatibilities**

None known.

### **6.3 Shelf life**

Unopened: 3 years.

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

### **6.4 Special precautions for storage**

No special precautions for storage.

### **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 volume fill sizes are marketed in all Member States.

### **6.6 Special precautions for disposal**

This medicinal product does not require any special storage conditions.

**7      MARKETING AUTHORISATION HOLDER**

Mylan Products Ltd.,  
Station Close, Potters Bar,  
Hertfordshire, EN6 1TL, UK

**8      MARKETING AUTHORISATION NUMBER(S)**

PL 46302/0067

**9      DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
AUTHORISATION**

12/08/2009

**10     DATE OF REVISION OF THE TEXT**

15/02/2019