

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Azelastine hydrochloride 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 hydrochloride 0.5 mg/ml Eye drops, solution 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 hydrochloride 0.5 mg/ml Eye drops, solution is not intended for treatment of eye infections. Further warnings see 4.5 and 4.6.

Azelastine hydrochloride 0.5 mg/ml Eye drops, solution contains 0.125mg/ml Benzalkonium chloride as preservative which may be deposited in soft contact lenses. Hence, Azelastine hydrochloride 0.5 mg/ml Eye drops, solution should not be used while wearing these lenses. The lenses should be removed before instillation of the drops and not reinserted earlier than 15 minutes after use.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Azelastine hydrochloride 0.5 mg/ml Eye drops, solution should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

### **4.5 Interaction with other medicinal products and other forms of interaction**

No specific interaction studies with Azelastine hydrochloride 0.5 mg/ml Eye drops, solution have been performed.

Interaction studies at high oral doses of Azelastine have been performed however they bear no relevance to Azelastine hydrochloride 0.5 mg/ml Eye drops, solution, 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 hydrochloride 0.5 mg/ml Eye drops, solution during pregnancy.

### Breast feeding

Azelastine is excreted into the milk in low quantities. For that reason Azelastine hydrochloride 0.5 mg/ml Eye drops, solution 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 hydrochloride 0.5 mg/ml Eye drops, solution 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**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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. By reporting side effects you can help provide more information on the safety of this medicine.

## **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 anti-allergic compound with selective H<sub>1</sub> 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 (QT<sub>c</sub>) 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 hydrochloride 0.5 mg/ml Eye drops, solution (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 (E420i),

Sodium hydroxide (E524)

Water for injections.

## **6.2 Incompatibilities**

None known.

## **6.3 Shelf life**

24 months. Discard after 28 days of opening.

## **6.4 Special precautions for storage**

Do not store above 25°C.

## **6.5 Nature and contents of container**

Each carton contains low density polyethylene (LDPE) bottle with LDPE dropper nozzle and white coloured HDPE screw cap with tamper- evident LDPE dust cover sealing the bottle cap.

Each bottle contains 8ml Azelastine eye drops, solution.

## **6.6 Special precautions for disposal**

This medicinal product does not require any special storage conditions.

# **7 MARKETING AUTHORISATION HOLDER**

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25/03/2021

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