Translation from the German Language

EXPERT INFORMATION

(= German Summary of Product Characteristics / SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Allergodil 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 of azelastine hydrochloride.

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.

Clear, colorless 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:
Unless otherwise prescribed, the usual dosage in adults and children 4 years and older is one drop in each eye twice daily. This dosage can be increased, if necessary to up to four times daily. If allergen exposure is anticipated Allergodil Eye Drops should be administered prophylactically, prior to the exposure.

Non-seasonal (perennial) allergic conjunctivitis:
Unless otherwise prescribed, the usual dosage in adults and children 12 years and older is one drop in each eye twice daily. This dosage can be increased, if necessary to up 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 course should be limited to a maximum of 6 weeks.

Advice for use without prescription: Patients should be advised to contact their doctor if symptoms worsen or do not improve after 48 hours. It should be pointed out to the patient, that use for more than 6 weeks must take place under medical supervision even in case of seasonal allergic conjunctivitis.

4.3 Contra-indications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special Warnings and Precautions for Use

Allergodil Eye Drops is not intended for treatment of eye infections.

Benzalkonium chloride may cause eye irritation. Any contact with soft contact lenses should be avoided. Contact lenses should be removed before using this product and should not be reinserted before at least 15 minutes after instillation of the drops. It is known that this product causes discoloration of soft contact lenses.

4.5 Interactions with other Medicaments and other Forms of Interaction

No specific interaction studies with Allergodil Eye Drops have been performed. Interaction studies at high oral doses have been performed; however, they bear no relevance to Allergodil Eye Drops, as systemic plasma levels after ocular administration are in the picogram range.

4.6 Fertility, Pregnancy and Lactation

Fertility
In animal studies, effects on fertility have been seen after oral admininstration.

Pregnancy
There is insufficient information available to establish the safety of azelastine hydrochloride in human pregnancy. At high oral doses, azelastine hydrochloride (the active substance in this product) has shown to induce foetal death, growth retardation and skeletal malformation in experimental animals. Local ocular application will result in minimal systemic exposure (plasma levels are in the picogram range only). However, caution should be exercised when using Allergodil Eye Drops during pregnancy.

Breast feeding
Azelastine is excreted into the breast milk in low quantities. For that reason, Allergodil 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 Allergodil Eye Drops is unlikely to affect/impair 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 convention has been used for the classification of undesirable effects in terms of frequency:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Rare (≥1/10,000 to <1/1000)
Very rare (<1/10,000)
Not known (frequency 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 but 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 Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger-Allee 3, D-53175 Bonn, Germany (website: http://www.bfarm.de).

4.9 Overdose

No specific reactions after overdosage in the eye are known, and with this route of administration, overdosage reactions are not anticipated.

There is no experience after administration of toxic doses of azelastine hydrochloride in humans. In the case of overdosage or intoxication, disturbances of the central nervous system are to be expected on the basis of 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:
Anti-allergic agents.

ATC Code: SO1GX07.

Azelastine hydrochloride, a phthalazinone derivative is classified as a potent long-acting anti-allergic compound with selective H1 antagonist properties. An additional anti-inflammatory effect has been detected after topical ocular administration.

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

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

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

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

5.2 Pharmacokinetic Properties

General pharmacokinetics (systemic pharmacokinetics)
Following oral administration, azelastine hydrochloride 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 peripheral compartments. Due to the relatively low level of protein binding (80 - 90%), the probability of drug displacement reactions is unlikely.

Plasma elimination half-times after a single dose of azelastine hydrochloride are approximately 20 hours for azelastine hydrochloride and about 45 hours for the therapeutically active main metabolite N-desmethyl azelastine. Excretion of the pharmaceutically active substance 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.

Kinetics in patients (ocular pharmacokinetics)
After repeated ocular application of Allergodil Eye Drops (one drop in each eye, up to four times daily), C_{max} steady state plasma levels were very low and were detected at or below the limit of quantification.

5.3 Preclinical Safety Data

In studies in the guinea pig, azelastine hydrochloride displayed no sensitizing potential. Azelastine hydrochloride demonstrated no genotoxic potential in in-vitro and in-vivo tests, nor any carcinogenic potential in rats or mice.

In male and female rats, azelastine hydrochloride 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 pregnant 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, Sorbitol solution (crystallizing), Sodium hydroxide, and Water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Unopened: 3 years.

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

6.4 Special Precautions for Storage

Don’t store above 25°C. Keep out of reach of children.

6.5 Nature and Content of Container

10-ml bottle made of opaque HD polyethylene and LD polyethylene dropper with white HD polyethylene screw cap. One bottle either contains 6 ml, 8 ml or 10 ml of solution. Not all pack sizes may be marketed.

6.6 Special Precautions for Disposal

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

MEDA Pharma GmbH & Co. KG
Benzstrasse 1
61352 Bad Homburg (Germany)
Phone: (06172) 888-01
Fax: (06172) 888-2740
medinfo@medapharma.de

8. MARKETING AUTHORIZATION NUMBER(S)

43763.00.00

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 23 October 1998
Date of latest renewal: 17 February 2008

10. DATE OF REVISION OF THE TEXT

April 2015

11. DISPENSING STATUS/CLASSIFICATION FOR SUPPLY

Pharmacy-only medicine