Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Azelastine Hydrochloride 0.5mg/ml Eye Drops, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Azelastine hydrochloride 0.05% (0.5 mg/ml). Each drop (30µl) contains 0.015 mg azelastine hydrochloride
Excipients: 1 ml contains 0.125 mg benzalkonium chloride
Liquid sorbitol crystallising

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 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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

As with other ophthalmic solutions, Azelastine hydrochloride Eye drops is not recommended for use whilst wearing contact lenses. 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. Azelastine hydrochloride Eye drops is not intended for treatment of eye infections. Benzalkonium chloride may cause eye irritation. Further warnings see 4.5 and 4.6.

4.5 Interaction with other medicinal products and other forms of interaction

No specific interaction studies with Azelastine hydrochloride Eye drops have been performed.

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

4.6 Fertility, pregnancy and lactation

There is insufficient information available to establish the safety of azelastine in human pregnancy. At high oral doses, azelastine has been shown to induce adverse effects (fetal 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 Eye drops during pregnancy.

Azelastine is excreted into the milk in low quantities. For that reason Azelastine hydrochloride Eye drops is not recommended during lactation.

In male and female rats, azelastine at oral doses greater than 30 mg/kg/day caused a doserelated decrease in the fertility index; no substance-related alterations were found in the reproductive organs of males or females during chronic toxicity studies, however.

4.7 Effects on ability to drive and use machines

The mild, transient irritation which can be experienced after application of Azelastine hydrochloride 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).

Nervous system disorders
Uncommon: Bitter taste.

Eye Disorders
Common: mild, transient irritation in the eye.

Immune system disorders
Very rare: Allergic reactions (such as rash and pruritus).

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 : SO1GX07

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-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 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 30 mg/kg/day caused a doserelated 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 maternally 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

Benzalkonium chloride
Disodium edetate
Hypromellose
Liquid sorbitol crystallising,
Sodium hydroxide (for pH adjustment)
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

This medicinal product does not require any special storage precautions.

6.5 Nature and contents of container

10 ml LDPE Blow Fill Seal (BFS) container with white polypropylene screw cap with shrink wrap around the cap extending upto shoulder of the container. 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

Brown & Burk UK Ltd
5 Marryat Close
Hounslow West
Middlesex
TW4 5DQ
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1648/003/001

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