Summary of Product Characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

<Product name> 1 mg/ml nasal spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 1mg azelastine hydrochloride.
One application (0.14 mL) contains 0.14 mg azelastine hydrochloride equivalent to 0.13 mg azelastine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, solution.
Clear colourless solution.
The pH of the solution is between 6.4 -7.2

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Azelastine is indicated for the symptomatic treatment of seasonal allergic rhinitis (e.g hayfever) and acute exacerbations of perennial allergic rhinitis in adults, adolescents and children from 6 years of age.

4.2 Posology and method of administration

Route of application is topical – nasal mucosa.

One application (0.14 ml) in each nostril twice daily (0.56 mg of azelastine hydrochloride).

There have been no specific studies in the elderly.

For children aged 6 years and older, one application (0.14 ml) in each nostril twice daily (0.56 mg of azelastine hydrochloride).
Azelastine should not be used in children below 6 years of age due to lack of data on safety and efficacy.

Method of administration
Nasal use

Precautions to be taken before handling or administering the medicinal product:
Spray with head held upright.
Before the first use, press the pump several times until an even spray emerges (3-4 times).
When azelastine has not been used for 6 or more days, the pump must be reprimed by pressing down and releasing the pump a sufficient number of times until a fine mist emerges.

After administration, wipe the pump nozzle and replace the protective cap.

4.3 Contraindications

Children under 6 years of age.
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The spray should be used with the head held upright, see section 4.8.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies with azelastine nasal spray have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of azelastine in pregnant women. At high oral doses reproductive toxicity has been seen in animals (see section 5.3). Therefore, caution should be exercised when using azelastine during pregnancy.

Breast-feeding
It is unknown whether azelastine/metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when azelastine is administered to a nursing woman.

Fertility
Effects on fertility were seen in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Azelastine has minor influence on the ability to drive and use machines.
In isolated cases fatigue, weariness, dizziness or weakness that may also be caused by the disease itself, may occur when using azelastine. In these cases, the ability to drive and use machines may be impaired. Alcohol may enhance this effect.

4.8 Undesirable effects

Frequencies are defined as: Very common (≥1/10), Common (≥1/100, <1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10000, <1/1000), Very Rare (<1/10,000), Not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Hypersensitivity reactions

Nervous system disorders
Common: a substance-specific bitter taste may be experienced after administration (often due to incorrect method of application, namely tilting the head too far backwards during administration) which, in rare cases, may lead to nausea.
Very rare: dizziness, somnolence (drowsiness, sleepiness)

Respiratory, thoracic and mediastinal disorders
Uncommon: a mild, transient irritation of the inflamed nasal mucosa may occur with symptoms such as stinging, itching and sneezing, epistaxis.

Gastrointestinal disorders
Rare: nausea

General disorders
Very rare: fatigue (weariness, exhaustion), dizziness or weakness.

Skin and subcutaneous tissue disorders and immune system disorders
Very rare: rash, pruritus, urticaria

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 national reporting system listed in Appendix V.

4.9 Overdose

The results of animal studies show that toxic doses can produce CNS symptoms, e.g. excitation, tremor, convulsions. Should these occur in humans, symptomatic and supportive treatment should be instigated as there is no specific antidote. Gastric lavage is recommended if the overdose is recent.

With the nasal route of administration overdosage reactions are not anticipated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use, Antiallergic agents, excl.corticosteroids, ATC code: R01AC03

Azelastine is classified as a potent long-acting antiallergic compound (t ½ ~ 20 hours) with selective H1-antagonist properties.
Furthermore, data from in vivo (guinea pig) studies show that azelastine applied in therapeutically relevant dosages inhibits leukotriene- and PAF-induced bronchoconstriction. Inhibition of inflammation of the respiratory tract as the basis for hyperreactivity reactions as shown in animal experiments with azelastine hydrochloride can be ascribed to these properties. The relevance of these findings from animal experiments for human therapy is not clear.

5.2 Pharmacokinetic properties

After repeated nasal application (0.14 mg) into each nostril twice daily, the plasma levels of azelastine were about 0.26 ng/ml. The levels of the active metabolite desmethylazelastine were detected at or below the lower limit of quantification (0.12 ng/ml).

After repeated oral administration, the mean Cmax steady state plasma levels were determined giving 3.9 ng/ml for azelastine and 1.86 ng/ml for desmethylazelastine after 2.2 mg b.i.d. azelastine which represents the therapeutic oral dose for the treatment of allergic rhinitis.

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 to the peripheral tissues. The level of protein binding is low (80-95%, 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 N-desmethylazelastine (a therapeutically active metabolite). Excretion occurs mainly via the faeces. The sustained excretion of small amounts of the dose in the faeces suggest that some enterohepatic circulation may take place.

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.
Embryotoxic and teratogenic effects in rats, mice and rabbits occurred only at maternal toxic doses (for example in mice and rats at doses of 68.6 mg/kg/day).
At high oral doses in animals, 1095 times the proposed intranasal human daily dose, foetal death, growth retardation and an increased incidence of skeletal abnormalities occurred during reproduction toxicity testing."

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose 2910
disodium edetate
citric acid anhydrous
disodium phosphate dodecahydrate
sodium chloride
purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

27 months unopened.
Do not use longer than 6 months after first opening.

6.4 Special precautions for storage

Do not refrigerate or freeze.
Do not store above 25ºC.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Azelastine nasal spray is filled in a multidose plastic container (consisting of high-density polyethylene) fitted with a dosing pump. One bottle contains 10 ml of solution.

6.6 Special precautions for disposal

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu<, and on the website of {name of MS Agency (link)}>.