Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Astepro 1.5 mg/ml nasal spray, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml solution contains 1.5 mg azelastine hydrochloride.
One actuation (0.14 ml) contains 0.21 mg azelastine hydrochloride equivalent to 0.19 mg azelastine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal spray, solution
Clear colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Symptomatic treatment of seasonal allergic rhinitis (hayfever) in adults, adolescents and children 6 years and older.

4.2 Posology and method of administration

Posology
Adults and adolescents 12 years and older
2 sprays in each nostril once a day. In some cases 2 sprays in each nostril twice a day may be required. The maximum daily dose is 2 sprays in each nostril twice daily.

Children 6 to 11 years
1 spray in each nostril twice daily.

Clinical experience of up to 4 weeks duration showed good efficacy and safety in children. Longer experiences in children have not been available; however, clinical trials of up to one year duration using a double higher daily dose showed good safety in adults and adolescents.

Astepro 1.5 mg/ml Nasal Spray, Solution is not recommended for use in children below 6 years of age due to a lack of data on safety and/or efficacy.
Duration of treatment
Astepro 1.5 mg/ml Nasal Spray, Solution is suitable for long-term use. The duration of treatment should be a clinical decision considering the severity of allergic symptoms, safety and should correspond to the period of allergenic exposure.
Use longer than 4 weeks is not recommended in children 6-11 years due to lack of clinical data.

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, the pump must be primed by pressing down and releasing the pump six times. When Astepro 1.5 mg/ml Nasal Spray, Solution has not been used for 3 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.

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

Nothing relevant.

4.5 Interaction with other medicinal products and other forms of interactions

No interaction studies with azelastine nasal spray have been performed.

Interaction studies at high oral doses have been performed. However, they bear no relevance to Astepro 1.5 mg/ml Nasal Spray, Solution as systemic levels after administration reach no more than 1/5 of the levels that were well tolerated after oral administration.

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 Astepro 1.5 mg/ml Nasal Spray, Solution during pregnancy.

Breastfeeding
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

Astepro 1.5 mg/ml Nasal Spray, Solution has minor influence on the ability to drive and use machines.
Rarely, the patient may experience fatigue, weariness, exhaustion, dizziness or weakness due to the disease itself, or when using Astepro 1.5 mg/ml Nasal Spray, Solution. In these cases, the ability to drive and use machines may be impaired. Special attention should be paid to the fact that alcohol may enhance these effects.

4.8 Undesirable effects

Commonly, dysgeusia, a substance-specific unpleasant 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.

Adverse events are listed below by system organ class and frequency. Frequencies are defined as:
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).

Immune system disorders	***Very rare***	Hypersensitivity
Nervous system disorders	***Common***	Dysgeusia (unpleasant taste)
	Rare	Dizziness*, somnolence (drowsiness, sleepiness)
Respiratory, thoracic and mediastinal disorders	***Uncommon***	Nasal discomfort (stinging, itching) Sneezing Epistaxis
Gastrointestinal disorders	***Rare***	Nausea
Skin and subcutaneous tissue disorders	***Very rare***	Rash Pruritus Urticaria
General disorders and administration site conditions	***Rare***	Fatigue* (weariness, exhaustion) Weakness*

* may also be caused by the disease itself (see section 4.7)

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

With the nasal route of administration overdose reactions are not anticipated. In the event of overdose after incidental oral uptake, disturbances of the central nervous system (including drowsiness, confusion, coma, tachycardia and hypotension) are to be expected based on the results of animal experiments. Treatment of these disorders must be symptomatic. Depending on the amount swallowed gastric lavage is recommended. There is no known antidote.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nasal preparations, decongestants and other nasal preparations for topical use, antiallergic agents, excl. corticosteroids.
ATC code: R01AC03

Azelastine, a phthalazinone derivative is classified as a potent long-acting anti-allergic compound with selective H_1-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. leukotrienes, histamine, PAF and serotonin.

Data from clinical studies show that azelastine nasal spray has a faster onset of action than deloratadine and nasally administered mometasone. A relief of nasal allergic symptoms is observed within 15 minutes after administration.

5.2 Pharmacokinetic properties

General characteristics:
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 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 takes place.

After intranasal administration of 2 sprays per nostril (0.822 mg total dose) of Azelastine S 1.5 mg/ml Nasal Spray, the mean azelastine peak plasma concentration (C_{max}) is 409 pg/ml in healthy subjects, the mean extent of systemic exposure (AUC) is 9312 pg•hr/ml and the median time to reach C_{max} (t_{max}) is 4 hours.

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 maximum recommended 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
Sucralose (E 955)
Sorbitol liquid (crystallising)
Disodium edetate
Sodium citrate
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

In-use shelf life (after first use): 6 months

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and contents of container

Brown glass bottle fitted with a spray pump (the pump parts in contact with the solution consists of polypropylene, polyethylene, polyoxymethylene, elastomer and stainless steel):
5 ml fill volume in 10 ml bottles (as sales pack and as sample pack)
10 ml fill volume in 10 ml bottles
17 ml fill volume in 20 ml bottles
20 ml fill volume in 20 ml bottles
22 ml fill volume in 20 ml bottles

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

Mylan IRE Healthcare Limited
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Baldoyle Industrial Estate
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Ireland

8 MARKETING AUTHORISATION NUMBER

PA2010/045/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th September 2013

10 DATE OF REVISION OF THE TEXT