Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Rhinolast S, 1 mg/ml Nasal Spray, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Solution containing 1 mg /ml azelastine hydrochloride.
The delivered dose per actuation (0.14 ml) contains 0.14 mg azelastine hydrochloride equivalent to 0.13 mg azelastine

For a 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 allergic rhinitis in adults, adolescents and children 6 years and older.

4.2 Posology and method of administration

Adults and adolescents 12 years and older:
2 applications in each nostril twice daily. This dose should not be exceeded.

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

Rhinolast S Nasal Spray is not recommended for use in children below 6 years of age due to a lack of data on safety and/or efficacy

Rhinolast S Nasal Spray is suitable for long-term use. There is no restriction regarding duration of use.

Method of administration
Nasal use (topical – nasal mucosa)

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 Rhinolast S Nasal Spray 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 azelastine hydrochloride or to any of the excipients.

4.4 Special warnings and precautions for use

Nothing relevant.

4.5 Interaction with other medicinal products and other forms of interaction

No specific interaction studies with azelastine nasal spray have been performed. Interaction studies at high oral doses have been performed. However, they bear no relevance to Rhinolast S Nasal Spray as systemic levels after administration reach no more than 1/6 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 Rhinolast S Nasal Spray 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

Rhinolast S Nasal Spray has minor influence on the ability to drive and use machines.
Very rarely, the patient may experience fatigue, weariness, exhaustion, dizziness or weakness due to the disease itself, or when using Rhinolast S Nasal Spray. 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)
	Very rare	Dizziness* somnolence (drowsiness, sleepiness)
Respiratory, thoracic and mediastinal disorders	***Uncommon***	Nasal discomfort (stinging, itching) Sneezing Epistaxis
Gastrointestinal disorders	***Rare***	Nausea
General disorders	***Very rare***	Fatigue* (weariness, exhaustion) Weakness*

Skin and subcutaneous tissue disorders	***Very rare***	Rash Pruritus Urticaria

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

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: Decongestans and other nasal preparations for topical use, Antiallergent 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 repeated nasal application of a daily dose of 0.56 mg azelastine hydrochloride (referring to one spray per nostril twice daily), the C_{max} of azelastine at steady state was about 0.27 ng/ml in healthy subjects. The levels of the active metabolite N−desmethyl azelastine were detected at or below the lower limit of quantification (0.12 ng/ml).

Characteristics in patients
In patients with allergic rhinitis after a total daily dose of 0.56 mg azelastine hydrochloride (i.e. two sprays per nostril once daily) the steady state mean plasma concentrations of azelastine observed two hours after dose were about 0.65 ng/ml. A doubling of the total daily dose to 1.12 mg azelastine hydrochloride (i.e. two sprays per nostril twice daily) resulted in steady state mean plasma concentrations of 1.09 ng/ml azelastine, suggesting dose proportionality within the dose range.

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, 1875 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, sucralose (E 955), liquid sorbitol, (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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Meda Health Sales Ireland Limited
Unit 34/35, Block A
Dunboyne Business Park
Dunboyne
Co. Meath
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1332/015/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th October 2012

10 DATE OF REVISION OF THE TEXT

July 2014