Translation from the German Language

1. Trade Name of the Medicinal Product

Allergodil® Nasal Spray
1 mg / 1 ml
Active substance: Azelastine hydrochloride

2. Qualitative and Quantitative Composition

1 spray puff (0.14 ml) contains:
0.14 mg of Azelastine hydrochloride

3. Pharmaceutical Form

Solution

4. Clinical Particulars

4.1 Therapeutic Indications

Allergodil Nasal Spray is an anti-allergic agent / antihistaminic agent.
For symptomatic treatment of seasonal allergic rhinitis (hay fever) and for symptomatic treatment of non-seasonal (perennial) allergic rhinitis.

4.2 Posology and Method of Administration

To be sprayed into the nose; for nasal application.

Unless otherwise prescribed, spray Allergodil Nasal Spray once into each nostril twice daily (mornings and evenings; equivalent to a daily dose of 0.56 mg Azelastine hydrochloride / day).

Spray the solution into each nostril with head held upright.
Duration of treatment depends on the type, severity and the development of the symptoms.
Allergodil Nasal Spray may be used for long-term treatment; there is no time limit for its use.

4.3 Contra-indications

Not to be used in patients with known hypersensitivity to the active substance, Editic acid, nor in children under 6 years of age.

4.4 Special Warnings and Precautions for Use

None.

4.5 Interactions with other Medicaments and other forms of Interaction

So far, no interactions have been reported.

4.6 Pregnancy and Lactation

Although doses far in excess of the therapeutic dose range tested in laboratory animals failed to generate any evidence of an embryotoxic effect of this medicinal product, current medical concepts discourage use of Allergodil Nasal Spray in the first trimester of pregnancy.

Allergodil Nasal Spray should not be used by nursing mothers, because there is insufficient evidence of the safety of this medicinal product during lactation.

4.7 Effects on Ability to Drive and Use Machines

Very rarely, fatigue, weariness, exhaustion, dizziness or weakness that may also be caused by the disease itself, may occur when using Allergodil Nasal Spray. In these cases, the ability to drive and use machines may be impaired. Special attention should be paid to the fact that this effect may be intensified in combination with alcohol and other medications which for their part have a negative impact on reactivity.

4.8 Undesirable Effects

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 reactions
Nervous system disorders
Common: Improper administration (with head reclined back; see Section 4.2) may produce a bitter taste which may lead to nausea occasionally.
Very rare: Vertigo
Respiratory disorders
Uncommon: Irritations of the inflamed nasal mucosa can occur on spraying (e.g. stinging, itching), sneezing and nasal bleeding.
Gastrointestinal disorders
Rare: Nausea
General disorders
Very rare: Fatigue (weariness, exhaustion), dizziness or weakness that may also be caused by the disease itself.
Skin
Very rare: Rash, itching, nettle fever.

4.9 Overdose

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

ATC Code: R01AC03
Azelastine hydrochloride is an H_1-antagonistic and therefore an anti-allergically active substance with a relatively long half-life (t ½ ≅ 20 hours).

Furthermore, in vivo studies in the guinea pig have shown that, in doses relevant for human therapy, Azelastine also inhibits the bronchial constriction induced by leukotrienes and PAF.

It is due to these properties that, in animal experiments, azelastine hydrochloride has also been able to suppress the inflammation in the respiratory tract causing this hyper-reactivity. The significance of the findings obtained in animals for the therapeutic application of azelastine in humans is unclear.

5.2 Pharmacokinetic Properties

In animals and humans, azelastine hydrochloride was absorbed rapidly and almost quantitatively after oral administration and mainly distributed in the peripheral organs, above all in the lungs, skin, muscles, liver and kidneys, but only to a minor extent in the brain. A dose-linear kinetic effect was demonstrated. Azelastine hydrochloride and its metabolites were excreted approx. 75 % via the faeces and approx. 25 % via the kidneys. The most important metabolic pathways are ring hydroxylation, N-dimethylation and oxidative opening of the azepine ring.

In patients suffering from allergic rhinitis, steady state mean plasma concentrations of azelastine hydrochloride observed two hours after a total daily dose of 0.56 mg azelastine hydrochloride (e. g. one spray puff per nostril twice daily) were about 0.65 ng/ml but these did not result in clinically relevant systemic side-effects. Due to the dose-linear effect, an elevation of mean plasma levels can be expected if the daily dose is increased.

5.3 Preclinical Safety Data

Toxicity with repeated administration

With repeated oral administration of azelastine hydrochloride to rats and dogs, the first general toxic symptoms were observed at doses which exceeded the maximum daily dose used for humans 75 times.

In rats, the liver (increased serum enzyme activity of ASAT, ALAT, and AP as well as increased organ weight, cellular hypertrophy, fat infiltration) and the kidneys (increase in urea nitrogen, increased urine volume and increased excretion of sodium, potassium and chloride as well as increased organ weight) proved to be the target organs and this in doses which, related to body weight, exceeded the oral daily therapeutic dose used for humans 200 times.

The nontoxic dose for both young and adult animals was at least 30 times the maximum oral therapeutic daily dose for humans.

Six months intranasal administration to rats and dogs up to the maximum possible doses of Allergodil Nasal Spray (rat: approx. 130, dog: approx. 25 times the intranasal therapeutic dose in humans related to body weight) yielded no local or organ-specific toxicity findings.

Sensitization

Azelastine hydrochloride displayed no sensitizing properties in studies in the guinea pig.

Mutagenicity / carcinogenicity

In-vivo and in-vitro mutagenicity tests and carcinogenicity studies in mice and rats revealed no mutagenic or tumoragenic potential of azelastine hydrochloride.

Reproductive toxicity

In animal experiments, small quantities of azelastine hydrochloride passed through the placenta and entered in the mother's milk. Embryotoxicity studies after oral administration in rats, mice and rabbits revealed signs of teratogenic effects in the maternal toxic dose range (68.6 mg/kg/day) only in mice. The smallest embryotoxic dose per os was 30 mg/kg/day in all three species.
Fertility disorders were observed in female rats with a dose of 3 mg/kg/day p.o. or more.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sodium edetate, Hypromellose, Sodium monohydrogen phosphate dodecahydrate, Citric acid, Sodium chloride, purified water.

6.2 Incompatibilities

So far, no incompatibilities have been reported.

6.3 Shelf Life

The shelf life of Allergodil Nasal Spray is 3 years in the unopened bottle.
After first opening of the bottle, the solution should not be used for longer than 6 months.

6.4 Special Precautions for Storage

Do not store below +8 °C.

6.5 Nature and Content of Container

Bottle containing 5 ml of solution.
Bottle containing 10 ml of solution (N1).
Bottle containing 17 ml of solution (N2).
Hospital pack containing 10 x 10 ml of solution.
Not all pack sizes may be marketed.

6.6 Special Precautions for Disposal

No special requirements.

7. Marketing Authorization Holder

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8. Marketing Authorization Number(s)

22667.00.00

9. Date of First Authorization / Renewal of the Authorization

17 Sep. 1991 / 15 Sep. 2001 / 23 Oct. 2009

10. Date of Revision of the Text

September 2010

11. General classification for supply

Pharmacy medicine.