SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
NAZETIN 0.14 mg/spray nasal spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active substance(s):
One spray (0.14 ml) contains 0.14 mg azelastine hydrochloride.

Excipient(s):
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Nasal spray
Solution

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
NAZETIN is an antiallergic / antihistaminic agent.
It is indicated for the treatment of seasonal allergic rhinitis (hay fever) and non-seasonal (perennial) allergic rhinitis and vasomotor rhinitis symptoms such as runny nose, nasal congestion and postnasal drip.

4.2. Posology and method of administration
Posology/frequency of administration and duration of the treatment:
Unless otherwise prescribed by doctor;
Spray once into each nostril twice daily (mornings and evenings; total daily dose equivalent to 0.56 mg azelastine hydrochloride).
In the symptomatic treatment of vasomotor rhinitis, spray the solution into each nostril twice daily.
The duration of treatment with NAZETIN depends on the type, severity and the development of the symptoms. NAZETIN may be used for long-term treatment.

Method of administration:
To be sprayed into the nose.
The spray and head should be kept upright during use.

Additional information for special populations:
Renal/Hepatic failure:
It can be used in normal doses. No dose adjustment is required.

Pediatric population:
The safety and efficacy in seasonal allergic rhinitis and perennial (non-seasonal) allergic rhinitis in children younger than 6 years has not been established. It is used in doses recommended for children older than 6 years. There is no need for dose adjustment. It is used in the symptomatic treatment of vasomotor rhinitis in children aged 12 years and above.

Geriatric population:
It can be used in normal adult dosage. There is no need for dose adjustment.

4.3. Contraindications

- in patients with hypersensitivity to Azelastine or any of the substances in NAZETIN
- in children under 6 years of age

4.4. Special warnings and precautions for use

Not reported.

4.5. Interaction with other medicinal products and other forms of interaction

No interactions with NAZETİN have been reported.

Additional information for special populations:
No interaction studies for special populations have been conducted.

Pediatric population:
No interaction studies in the pediatric population have been performed.

4.6. Fertility, pregnancy and lactation

General advise
Pregnancy category C

Women of childbearing potential/Birth control (contraception)
~~There is not enough data on the use of NAZETIN in pregnant women..~~ Caution should be exercised when it is given to women with childbearing potential.

Pregnancy
There is insufficient data on the use of NAZETIN in pregnant women.

Animal studies are insufficient for effects on pregnancy / and / or / embryonal / fetal development / and / or / birth / and-or / postnatal development (See section 5.3). The potential risk for humans is unknown.

NAZETIN should not be used during pregnancy unless necessary.

Although there is no evidence of a teratogenic effect at doses above the therapeutic dose range tested in laboratory animals, the current therapeutic approach does not recommend the use of NAZETIN in the first trimester of pregnancy.

Breast-feeding
NAZETİN should not be used in breastfeeding mothers since there is insufficient evidence for safety during breastfeeding.

Reproductive ability / Fertility
In animal studies, effects on fertility have been observed after oral administration (see section 5.3).

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 NAZETIN. 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.

During NAZETİN treatment, patients should be instructed to be careful while driving and using machines.

4.8. Undesirable effects

The following terms and frequency levels are used:
Very common (≥1/10); common (≥1/100 to <1/10); not common (≥1/1.000 to <1/100); rare (≥1/10.000 to <1/1.000); very rare (<1/10.000), not known (can not be estimated based on available data).

Undesirable effects reported for NAZETİN are:

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, thoracic and mediastinal disorders
Not common: Irritations of the inflamed nasal mucosa can occur on spraying (e.g. stinging, itching), sneezing and nasal bleeding.

Gastrointestinal disorders
Rare: Nausea

Skin and subcutaneous tissue disorders
Very rare: Skin rash, itching, urticaria

General disorders and administration site conditions
Very rare: Fatigue (weariness, exhaustion), dizziness or weakness that may also be caused by the disease itself

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 Turkish Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel.: 0 800 314 00 08; fax: 0 312 218 35 99)

4.9. Overdose and treatment

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 (dizziness, confusion, coma, tachycardia and hypotension) are to be expected on the basis of results of animal experiments.

Recommended treatment
The treatment of the developing diseases is symptomatic. There is no known antidote. Gastric lavage is recommended if an overdose has just occurred.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Azelastine.
ATC Code: R01AC03

Azelastine hydrochloride is an H_1-antagonistic and therefore an anti-allergically active substance with a relatively long half-life ($t_{1/2}$ ≅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 platelet activating factor.

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 hyperreactivity. The significance of the findings obtained in animals for the therapeutic application of azelastine in humans is unclear.

5.2. Pharmacokinetic properties

Absorption:
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.

After oral administration, azelastine hydrochloride is rapidly and almost completely absorbed in animals and humans.

Distribution:
It is 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.

Biotransformation:
The most important metabolic pathways are ring hydroxylation, N-dimethylation and oxidative opening of the azepine ring.

Elimination:
Azelastine hydrochloride and its metabolites were excreted approx. 75 % via the faeces and approx. 25 % via the kidneys. Its half-life is about 20 hours.

Linearity/non-linearity:
Its pharmacokinetics are linear.

5.3. Preclinical safety data

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

When the oral daily therapeutic dose used in humans is exceeded more than 200 times, depending on body weight, liver (increased serum enzyme activity of ASAT, ALAT, and

AP as well as increased organ weight, cellular hypertrophy, fat infiltration) and kidneys (increase in urea nitrogen, increased urine volume, increased sodium / potassium and chloride secretion as well as increased organ weight) were observed as target organs.

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 azelastine hydrochloride (rat: approx. 130, dog: approx. 25 times the intranasal therapeutic dose in humans related to body weight) yielded no local or organ-specific toxicity finding.

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 was 30 mg/kg/day in all three species.

Fertility disorders were observed in female rats following oral administration of doses of 3mg / kg / day or more.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium EDTA
Hydroxy propyl methyl cellulose
Disodium monohydrogen phosphate dodecahydrate
Citric acid monohydrate
Sodium chloride
Sucralose
Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months
It should not be used for more than 6 months after opening the bottle.

6.4. Special precautions for storage

Store at room temperature below 25 ° C. Do not store in the refrigerator (below + 8 ° C).

6.5. Nature and contents of container

It is available in dose-adjusted, amber colored glass bottle (Type III) with PE piston and PP cap. One bottle contains 10 ml and 20 ml of solution.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed in accordance with regulations "Medical Waste Control Regulation" and "Packaging Waste Control".

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

2018/548

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28.09.2018
Date of latest renewal: -

10. DATE OF REVISION OF THE TEXT

25.04.2021