SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

N-CORT 0.055% Nasal Spray, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance(s):	(w/w %)
Triamcinolone acetonide	0.055

Each application contains 55 micrograms of triamcinolone acetonide.

Excipient(s):	
Benzalkonium chloride 50%	0.03

Each application contains 15 micrograms benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal Spray

N-CORT is an opaque homogenous suspension presented in a bottle containing 120 actuations. Each bottle contains 55 micrograms triamcinolone acetonide.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

It is indicated for the treatment of symptoms of perineal rhinitis and seasonal allergic rhinitis.

4.2. Posology and method of administration

For nasal use.

Posology

Adults and Adolescents 12 Years of Age and Older:
The recommended starting dose is 220 micrograms per day as two sprays in each nostril once daily. When the symptoms have been controlled, the dose can be reduced to 110 mcg per day (one spray in each nostril once a day).

An improvement of symptoms may be seen at the first day after initiation of treatment in some patients. However, for maximum benefit several days of treatment may be necessary.

Children between 6 and 12 years of age:
The recommended dose is 110 micrograms per day as 1 spray in each nostril once daily. In patients with more severe symptoms the dose of 220 micrograms may be used. However once symptoms have been controlled, the dosage may be decreased to minimum effective dose.

Frequency of administration and duration of the treatment:

An improvement of symptoms may be seen at the first day after initiation of treatment in some

patients. However, for maximum benefit several days of treatment may be necessary.

Method of administration:
N-CORT is used by intranasal route only and should be used regularly for optimal efficacy.

Additional information for special populations:
Renal/hepatic failure:
Safety and efficacy of N-CORT in the patients with renal and hepatic failure have not been studied.

Pediatric population:
Efficacy and safety of N-CORT in children under 2 years of age have not been established. Therefore, it is not recommended to be used in children under 2 years of age.
It is not recommended to be used in this age group because of the limited use experience between 2-6 years.
It is not recommended to use for more than 3 months in children under 12 years of age until further evidence is obtained.

Geriatric population:
Efficacy and safety of N-CORT in elderly patients have not been established.

4.3. Contraindications
It is contraindicated in patients with hypersensitivity to any of the ingredient of the drug.

4.4. Special warnings and precautions for use
Due to possible deterioration of the adrenal function, the replacement of a systemic corticosteroid with N-CORT should be made with caution.

Clinically significant adrenal suppression may occur as a result of a higher dose than recommended. Additional systemic corticosteroid protection should be considered during stress or elective surgery if there is evidence of a higher dose than recommended.

Patients previously treated for prolonged periods with systemic corticosteroids and transferred to topical corticosteroids like N-CORT should be carefully monitored for acute adrenal insufficiency in response to stress.

In clinical studies with triamcinolone acetonide, the development of localized infections of the nose and pharynx with *Candida albicans* has rarely occurred. When such an infection develops it may require treatment with appropriate local therapy and discontinuation of N-CORT.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal ulcers, surgery, or trauma should not use N-CORT until healing has occurred.

Nasal corticosteroids including N-CORT at approved doses have been reported to cause growth suppression in children. It is recommended that the height of children receiving treatment with nasal corticosteroids is regularly monitored. Therapy should be managed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to

referring the patient to a specialist. The long-term effects of reduction in growth velocity associated with nasal corticosteroids, including the impact on final adult height are unknown (See Section 5.1).

Glaucoma and/or cataracts have been reported in patients receiving nasal corticosteroids. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma and/or cataracts.

Systemic effects may occur with nasal corticosteroids prescribed at high doses, especially during long-term treatment. These effects are much less common than oral corticosteroids and may vary depending on patients and different corticosteroid preparations. Potential systemic effects include Cushing syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataracts, glaucoma, and more rarely, psychological or behavioral effects such as psychomotor hyperactivity, sleep disturbances, anxiety, depression or aggression (especially in children).

Since it contains benzalkonium chloride, it may cause skin reactions.

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

It has no interaction with other medicines.

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

Pediatric population:
No interaction studies have been conducted on the pediatric population.

4.6. Fertility, Pregnancy and Lactation

General advise
Pregnancy category: C.

Women of childbearing potential/Birth control (Contraception)
No data available.

Pregnancy
The clinical experience of triamcinolone acetonide use in pregnant women is limited.
Corticosteroids, including triamcinolone acetonide, were teratogenic in animal studies. Triamcinolone acetonide should not be administered during pregnancy unless the therapeutic benefit to the mother is considered to outweigh the potential risk to the fetus/baby.

Breast-feeding
Like other corticosteroids, triamcinolone acetonide may be excreted into human milk. N-CORT should not be administered during lactation unless the therapeutic benefit to the mother is considered to outweigh the potential risk to the fetus/baby.

4.7. Effects on ability to drive and use machines

N-CORT has no known effect on the ability to drive or use machines.

4.8. Undesirable effects

Adverse drug reactions are identified below according to their frequency:

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 (cannot be estimated based on available data).

The adverse events reported in clinical trials were generally very rare and most commonly involved the mucous membranes of the nose and throat.

The most common adverse effects reported in adults and children over 6 years of age are:

Infections and infestations
Common: Rhinitis, pharyngitis, flu syndrome

Immune system disorders:
Not known: Hypersensitivity (including rash, urticaria, pruritus and facial edema)

Psychiatric disorders:
Not known: Insomnia

Nervous system disorders:
Common: Headache
Not known: Dizziness, taste and odor changes

Eye diseases:
Not known: Cataract, glaucoma, increased ocular pressure

Respiratory, thoracic and mediastinal disorders:
Common: Epistaxis, cough, bronchitis
Rare: Nasal septum perforation
Not known: Nasal irritation, dryness of mucous membranes, nasal congestion, sneezing, dyspnea

Gastrointestinal disorders:
Common: Dyspepsia, tooth disorder
Not known: Nausea

General Disorders and Administration Site Conditions:
Not known: Fatigue

Investigations:
Not known: Decrease in cortisol levels in the blood

Other adverse effects in pediatric patients
In a post-marketing clinical trial with N-CORT, a reduction in growth rate was observed in children (see section 5.1).

As with other nasal corticosteroids, nasal septum perforations and nasal congestion have been

reported rarely.

Systemic effects of nasal corticosteroids may occur, especially when used at high doses for a long time. Growth retardation has been reported in children using intranasal steroids.

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

Like any other nasally administered corticosteroid, acute overdosing is unlikely in view of the total amount of active ingredient present. In the event that the entire contents of the bottle were administered all at once, via either oral or nasal application, clinically significant systemic adverse events would most likely not result. The patient may experience some gastrointestinal upset if taken orally. In case of a suspected overdose, supportive treatment for the management of related symptoms should be considered.

It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear at chronic treatment with high doses. If such effects occur, N-CORT should be reduced slowly, consistent with accepted procedures for reducing oral steroids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

Pharmacotherapeutic group: Corticosteroid (Topical nasal)
ATC Code: R01ADll

Triamcinolone acetonide is a more potent derivative of triamcinolone and is approximately 8 times more potent than prednisone in animal models.

Although the precise mechanism of corticosteroid antiallergic action is unknown, corticosteroids are very effective in the treatment of allergic diseases in man.

Triamcinolone acetonide does not have an immediate effect on allergic signs and symptoms. An improvement in some patient symptoms may be seen within the first day of treatment with triamcinolone acetonide and relief may be expected in 3 to 4 day. When triamcinolone acetonide is prematurely discontinued symptoms may not recur for several days.

In clinical trials in adults and children older than 6 years, no suppression of the hypothalamic-pituitary-adrenal axis (HPA) has been observed with doses of triamcinolone acetonide administered intranasally up to 440 micrograms per day and intranasally up to 110 micrograms per day in children aged 2-5 years.

In a six-week placebo-controlled clinical trial conducted with 140 children aged 2-11 years, the effect of N-CORT administered at doses of 110 micrograms or 220 micrograms once daily on the HPA axis was assessed by 24-hour serum cortisol AUC (Area Under Curve) value. No statistically significant difference was observed in the study compared to placebo.

The effect of N-CORT on the adrenal function of children in the 2-5 age group cannot be excluded.

In a one-year, double-blind, placebo-controlled, parallel-group study conducted with 298 pediatric patients aged 3-9 years, the effect of N-CORT administered at doses of 110 micrograms once daily on growth rate was evaluated by stadiometry. The primary analysis of evaluable patients (N-CORT 134; placebo 133) showed that the predicted growth rate in the N-CORT group was 0.45 cm / year lower than the placebo group (95% CI was 0.11-0.78 cm / year lower than the placebo). The difference between the treatment groups began 2 months after starting the drug. During the 2-month follow-up period after treatment was discontinued, the average growth rate in the treatment group returned to baseline values (pre-treatment values).

5.2. Pharmacokinetic Properties

General characteristics

Triamcinolone acetonide is a nasal corticosteroid. N-CORT is a homogeneous looking opaque suspension of 120 doses per bottle containing 55 microgram triamcinolone acetonide in each dose.

Absorption:

Single dose intranasal administration of 220 micrograms of triamcinolone acetonide in normal adult subjects and in adult patients with allergic rhinitis demonstrated low absorption of triamcinolone acetonide.

Distribution:

The mean peak plasma concentration was approximately 0.5 ng/mL (range 0.1 to 1 ng/mL) and occurred at 1.5 hours post dose. The mean plasma drug concentration was less than 0.06 ng/mL at 12 hours and below the assay detection limit at 24 hours. The average terminal half-life was 3.1 hours.

Dose proportionality was demonstrated in normal subjects and in patients following a single intranasal dose of 110 micrograms or 220 micrograms triamcinolone acetonide. Following multiple doses in pediatric patients (440 mcg/day), plasma drug concentrations, AUC, Cmax and Tmax were similar to those values observed in adult patients.

Biotransformation:

Three metabolites of triamcinolone acetonide have been identified in human plasma; 6β-hydroxytriamcinolone acetonide, 21-carboxytriamcinolone acetonide and 21-carboxy-6β-hydroxytriamcinolone acetonide. All three metabolites had no significant pharmacological activity compared to the parent compound.

Elimination:

Triamcinolone acetonide is excreted in urine and faeces as unconjugated metabolites. About 94% of the radiologically labeled compound taken orally was excreted in urine and faeces. About 40% of this was detected in urine and about 54% in faeces.

Special Populations

Pediatric Patients

In pediatric patients with allergic rhinitis (children aged 6-12 years), pharmacokinetic

parameters showed a rapid decrease in plasma drug level 6 weeks after the highest dose level of 440 micrograms of triamcinolone acetonide nasal spray; accumulation was too low or no accumulation was detected.

5.3. Preclinical safety data
In pre-clinical studies, only effects typical of glucocorticoids were observed.

Carcinogenicity:
Studies in rodents show no carcinogenicity related with triamcinolone acetonide.

Mutagenicity:
No evidence of mutagenicity was detected from *in vitro* tests (a reverse mutation test in *Salmonella* bacteria and a forward mutation test in Chinese hamster ovary cells) conducted with triamcinolone acetonide.

Teratogenicity:
Like other corticosteroids, triamcinolone acetonide has been shown to be teratogenic in rats and rabbits, resulting in cleft palate and/or internal hydrocephaly and axial skeletal defects. Other teratogenic effects, including CNS and cranial malformations, have also been observed in non-human primates.

Fertility disorders:
Triamcinolone acetonide caused increased fetal resorptions and stillbirths and decreases in pup weight and survival in rodents but no change in pregnancy rate has been observed.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Disodium edetate
Dextrose monohydrate
Microcrystalline cellulose and carboxymethyl cellulose sodium
Polysorbate 80
Benzalkonium chloride 50%
Dilute hydrochloric acid
Dilute sodium hydroxide
Purified water

6.2. Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life
24 months

6.4. Special precautions for storage
Store at room temperature below 25°C in a dry place and in its original packaging.

It should be discarded 2 months later after opening.
Keep out of sight and reach of children in its original packaging.

6.5. Nature and contents of container

16.5 g suspension for 120 actuations compromised of metered dose valve and a nasal applicator; each actuation contains 55 micrograms of triamcinolone acetonide.

6.6. Special precautions for disposal and other handling

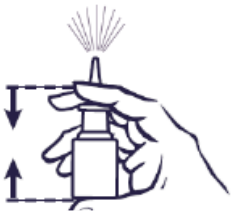
Administration of N-CORT:
N-CORT is only used by spraying into the nose.
Before using N-CORT, clean your nostrils.

1. Preparing the bottle

- Remove the cover by pushing it upwards.
- Shake the bottle gently before use.

2. Before using Nasal Spray for the first time

- Hold the bottle upright.
- Direct the spray away from yourself.
- Fill the pump by pressing the nozzle downwards.
- Press and release 5 times.
- Spray until you get a fine spray.
- Spray is now ready to use.



Correct position Wrong position

3. **Use of spray**

- Close one of your nostrils by pressing with your finger.
- Hold the bottle upright and insert the nozzle into your nostril to the level that will not disturb you.
- While your mouth is closed and breathing smoothly through your nose, apply a spray by pressing the nozzle of the bottle.

Correct position Wrong position

4. Then exhale through your mouth.

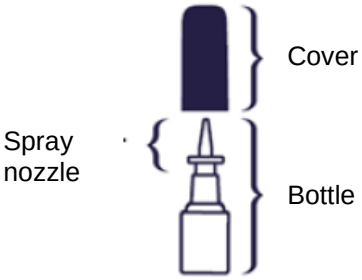
5. Follow the procedures described in item 3 and 4 above for the other nostril.

6. After using the spray

- Carefully wipe the nozzle with a soft cloth or tissue after each use and
- Place the cap on top of the spray nozzle.

If you have not used the nasal spray for more than 2 weeks:

- To fill spray nozzle with spray you should prepare it for use.
- During this application, keep the spraying point of the nozzle away from you.
- Spray once into the air before you start using it.
- Shake the bottle gently before each use.



Cleaning the spray

If the spray does not work, the nozzle may be clogged. **Never** try to open the clogging. Do not attempt to extend the small spray hole with a needle or a hard object, as the spray mechanism could be damaged.

Nasal spray should be cleaned at least once a week. It can be cleaned more often if clogged.

Instructions for cleaning the spray:
1. Remove the cover.
2. Only gently pull the spray nozzle.

3. Soak the cap and spray nozzle in hot water for a few minutes.
4. Then rinse in cold running tap water.

5. Remove excess water by shaking or tapping gently.
6. Allow to dry.
7. Reattach the spray nozzle
8. Spray the unit until a fine spray is reached.
9. Use as usual.

Unused product or waste materials should be disposed of according to the regulations on "Control of Medicinal Wastes" and "Control of Packaging and Packaging Wastes".

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

250/86

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 06.05.2013
Renewal of the authorization: 09.10.2019

10. DATE OF REVISION OF THE TEXT

31.08.2020