PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrNASACORT® AQ

Triamcinolone Acetonide Nasal Spray

Aqueous Nasal Spray 55mcg/Metered Spray

USP

Corticosteroid for Nasal Use

Sanofi Consumer Health Inc.

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Date of Revision:
September 14, 2022

Submission Control Number: 261994

RECENT MAJOR LABEL CHANGES

Section 7, Warnings and Precautions	09/2022

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Sections or subsections that are not applicable at the time of authorization are not listed.

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Children 4 to 12 years of age: NASACORT® AQ is indicated for the topical treatment of the symptoms of perennial and seasonal allergic rhinitis unresponsive to conventional treatment. NASACORT AQ is available only by prescription for children 4 to 12 years of age.

1.1 Pediatrics

Pediatrics (4 to 12 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of NASACORT AQ in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. (See 1 INDICATIONS)

1.2 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

Hypersensitivity to any of the ingredients of NASACORT AQ, and in patients with active or quiescent tuberculosis, or untreated fungal, bacterial and viral infection.

NASACORT AQ is contraindicated in patients who:

- Are hypersensitive to this drug or any ingredient in this formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FROMS, STRENGTHS, COMPOSITION AND PACKAGING.
- Have active or quiescent tuberculosis or untreated fungal, bacterial, and viral infection.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

NASACORT AQ is available only by prescription for children between the ages of 4 and 12 years. NASACORT AQ is not recommended for children under 4 years of age.

Regular usage is essential since maximum relief may not be obtained until after 2 to 3 days of treatment.

Careful attention must be given to patients previously treated for prolonged periods with systemic corticosteroids when transferred to NASACORT AQ, see 7 WARNINGS AND PRECAUTIONS. Initially, NASACORT AQ and the systemic corticosteroid must be given concomitantly, while the dose of the latter is gradually decreased. The usual rate of withdrawal of the systemic steroid is the equivalent of 2.5 mg of prednisone every four days if the patient is under close supervision. If continuous supervision is not feasible, the withdrawal of the systemic steroid should be slower, approximately 2.5 mg of prednisone (or equivalent)

every ten days. If withdrawal symptoms appear, the previous dose of the systemic steroid should be resumed for a week before further decrease is attempted.

4.2 Recommended Dose and Dosage Adjustment

It is always desirable to titrate an individual patient to the minimum effective dose to reduce the possibility of side effects. Therefore, when the maximum benefit has been achieved and symptoms have been controlled, reducing the dose to 110 mcg (one spray in each nostril once daily) has been shown to be effective in maintaining control of the allergic rhinitis symptoms in patients who were initially controlled at 220 mcg/day (see 7 WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS.)

Children 4 to 12 years of age:

NASACORT AQ is available only by prescription for children between the ages of 4 and 12 years. The recommended starting dose is 110 mcg per day given as one spray in each nostril once daily. Patients who do not achieve maximum symptom control may benefit from a dose of 220 mcg given as 2 sprays in each nostril once daily. Once symptoms are controlled, patients should be maintained on 110 mcg (1 spray in each nostril) once daily.

4.4 Administration

The therapeutic effects of corticosteroids, unlike those of decongestants, are not immediate. Since the effect of NASACORT AQ depends on its regular use, patients must be instructed to take the nasal inhalations at regular intervals and not as with other decongestant nasal sprays, as they feel necessary.

In the presence of excessive nasal mucus secretion or edema of the nasal mucosa, the drug may fail to reach the site of action. In such cases it is advisable to use a nasal vasoconstrictor for two to three days prior to NASACORT AQ therapy. Patients should be instructed on the correct method of use, which is to blow the nose, then insert the nozzle firmly into the nostril, compress the opposite nostril and actuate the spray while inspiring through the nose, with the mouth closed.

Children 4 to 12 years of age:

An improvement of symptoms usually becomes apparent within a few days after the start of therapy. However symptomatic relief may not occur in some patients for as long as two weeks. NASACORT AQ should not be continued beyond three weeks in the absence of significant symptomatic improvement.

4.5 Missed Dose

Take the regular dose, which you are on, if a missed dose is less than an hour or so from the designated time. If a dose is missed for over an hour, do not take the dose. Continue regular dosing schedule on the next day, after 24 hours. Do not exceed the maximum daily dose (2 sprays in each nostril once daily).

5 OVERDOSAGE

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.

However, when used chronically in excessive doses or in conjunction with other corticosteroid formulations, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of NASACORT AQ should be discontinued slowly consistent with accepted procedures for discontinuation of chronic steroid therapy. (See 4 DOSEAGE AND ADMINISTRATION)

The restoration of hypothalamic-pituitary axis may be slow; during periods of pronounced physical stress (i.e. severe infections, trauma, surgery) a supplement with systemic steroids may be advisable.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Nasal	Aqueous Nasal Spray 55 mcg/Metered Spray	Benzalkonium chloride, dextrose, edetate disodium, microcrystalline cellulose and carboxymethylcellulose sodium, polysorbate 80, and purified water (hydrochloric acid or sodium hydroxide may be added to adjust the pH to between 4.5 and 6.0.)

NASACORT AQ is an unscented, thixotrophic, water-based metered-dose pump spray formulation unit containing a microcrystalline suspension of triamcinolone acetonide in an aqueous medium.

NASACORT AQ is supplied as a non-chlorofluorocarbon (CFC) containing-metered dose pump spray. It is supplied with a nasal adapter and patient instructions.

Each bottle contains 9.075 mg triamcinolone acetonide. Each actuation releases approximately 55 mcg triamcinolone acetonide from the nasal actuator to the patient (estimated from *in vitro* testing). There are at least 120 actuations in one NASACORT AQ bottle.

7 WARNINGS AND PRECAUTIONS

General

The replacement of a systemic steroid with NASACORT AQ has to be gradual and carefully supervised by the physician. The guidelines under "Dosage and Administration" should be followed in all such cases.

Patients should be informed that the full effect of NASACORT AQ therapy is not achieved until 2 to 3 days of treatment has been completed. Treatment of seasonal rhinitis should, if possible, start before the exposure to allergens.

Patients should be advised to inform subsequent physicians of prior use of corticosteroids.

To ensure the proper dosage and administration of the drug, the patient should be instructed to read the consumer package insert (see PATIENT MEDICATION INFORMATION).

Dependence/Tolerance

Treatment with NASACORT AQ should not be stopped abruptly but tapered off gradually. Systemic absorption of intranasal corticosteroids may occur (especially when used for a prolonged duration) The risks associated with sudden discontinuation of all corticosteroids after prolonged use may include exacerbation or recurrence of the underlying disease, adrenocortical insufficiency or steroid withdrawal syndrome. Typical signs and symptoms of steroid withdrawal syndrome can be either systemic (e.g., arthralgia, myalgia, tremors, weight loss and anxiety) or localized (e.g., nasal bleeding, nasal drip).

In patients previously on prolonged periods or high doses of systemic steroids, the replacement with a topical corticosteroid can be accompanied by symptoms of withdrawal, e.g. joint and/or muscular pain, lassitude, and depression; in severe cases, adrenal insufficiency may occur, necessitating the temporary resumption of systemic steroid therapy. These patients should be carefully monitored for acute adrenal insufficiency in response to stress. Careful attention must be given to patients with asthma or other clinical conditions in whom a rapid decrease in systemic steroids may cause a severe exacerbation of their symptoms.

Ear/Nose/Throat

Because of the inhibitory effect of corticosteroids on wound healing, in patients who have had recent nasal surgery or trauma, a nasal corticosteroid should be used with caution until healing has occurred. As with other nasally inhaled corticosteroids, nasal septal perforations have been reported in rare instances.

The possibility of atrophic rhinitis and/or pharyngeal candidiasis should be kept in mind.

In clinical studies with NASACORT AQ, 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 or systemic therapy and temporary discontinuation of treatment with NASACORT AQ. Therefore, patients using NASACORT AQ over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa.

Endocrine and Metabolism

No apparent evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression was observed in clinical studies following treatment with NASACORT AQ at recommended doses. When intranasal steroids are used at higher than recommended dosages or in susceptible individuals at recommended dosages, systemic corticosteroid effects may occur, such as hypercorticism, suppression of HPA function and/or reduction of growth velocity in children or teenagers. Children should be maintained on the lowest dose which delivers adequate symptom control (see 4 DOSAGE AND ADMINISTRATION).

In order to evaluate the effects of systemic absorption on the Hypothalmic-Pituitary-Adrenal (HPA) axis, a clinical study was performed comparing 220 mcg or 440 mcg NASACORT AQ, or 10 mg prednisone to placebo for 42 days. Adrenal response to a 6-hour cosyntropin stimulation test clearly indicated that NASACORT AQ administered at doses of 220 mcg and 440 mcg had no effect on HPA activity versus placebo. Conversely, oral prednisone at 10 mg/day significantly reduced the response to ACTH.

A six-week study was conducted in 80 pediatric patients to evaluate the effect of 220 mcg or 440 mcg of NASACORT AQ versus placebo on HPA function. No evidence of adrenal axis suppression was observed in the pediatric patients exposed to systemic levels of triamcinolone acetonide higher than the systemic levels observed following administration of the maximum recommended dose of NASACORT AQ.

In a 6-week randomized, double-blind, placebo-controlled clinical study evaluating the effect of NASACORT AQ (once-daily dose of 110 micrograms or 220 micrograms) on HPA axis function (as measured by 24-hour serum cortisol AUC) in 140 children (2 to 11 years of age), no statistically significant difference from placebo was observed. The ratio of NASACORT AQ to placebo was 0.966, 95% CI (0.892, 1.045).

A one-year double-blind, placebo-controlled parallel group study in 298 treated pediatric patients (3 to 9 years of age) was conducted to assess the effect of NASACORT AQ (once-daily dose of 110 microgram) on growth velocity using stadiometry. From the primary analysis of evaluable patients (134 NASACORT AQ and 133 placebo), the estimated growth velocity in the NASACORT AQ group was 0.45 cm/year lower than that in the placebo group with 95% CI ranging between 0.11 to 0.78 cm/year lower than placebo. The clinical long-term relevance of this change in growth velocity associated with nasal corticosteroids is not known. Physicians should closely follow the growth of children and adolescents taking corticosteroids, by any route, and weigh the benefits of corticosteroid therapy against the possibility of growth

suppression. 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.

Osteoporosis is a possible adverse effect associated with a long-term use of large doses of corticosteroids.

Immune

Corticosteroids may mask some signs of infection and new infections may appear. A decreased resistance to localized infections has been observed during corticosteroid therapy; this may require treatment with appropriate therapy or stopping the administration of NASACORT AQ.

Patients who are on immunosuppressant drugs are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in children or adults on immunosuppressant doses of corticosteroids. In such children, or in adults who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG), as appropriate, may be indicated. If chickenpox develops, treatment with antiviral agents may be considered.

Monitoring and Laboratory Tests

During long-term therapy, pituitary-adrenal function and hematological status should be assessed.

Ophthalmologic

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.

Sensitivity/Resistance

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in patients with hypothrombinemia.

The use of NASACORT AQ with alternate day systemic prednisone could increase the likelihood of HPA suppression compared to a therapeutic dose of either one alone. Therefore, NASACORT AQ should be used with caution in patients already receiving alternate-day prednisone treatment for any disease.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of NASACORT AQ in pregnancy has not been established. If used, the expected benefits should be weighed against the potential hazard to the fetus, particularly during the first trimester of pregnancy.

Like other glucocorticosteroids, triamcinolone acetonide is teratogenic to rodents and non-human primates (see 16 NON- CLINICAL TOXICOLOGY). The relevance of these findings to humans has not yet been established. Infants born of mothers who have received substantial doses of glucocorticosteroids during pregnancy should be carefully observed for hypoadrenalism.

7.1.2 Breast-feeding

Glucocorticosteroids are excreted in human milk. It is not known whether triamcinolone acetonide would be secreted in human milk, but it is suspected to be likely. The use of NASACORT AQ in nursing mothers requires that the possible benefits of the drug be weighed against the potential hazards to the infant.

7.1.3 Pediatrics

NASACORT AQ is not presently recommended for children younger than 4 years of age due to limited clinical data in this age group. Oral corticosteroids have been shown to cause growth suppression in children and teenagers, particularly with higher doses over extended periods. If a child or teenager on any corticosteroids appears to have growth suppression, the possibility that they are particularly sensitive to this effect of steroids should be considered.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Systemic and local corticosteroid use may result in the following (see 7 WARNINGS AND PRECAUTIONS):

- Epistaxis, ulcerations, *Candida albicans* infection, nasal septal perforation, impaired wound healing
- Glaucoma and Cataracts
- Immunosuppression
- Hypothalamic-pituitary-adrenal (HPA) axis effects, including reduction of growth velocity

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In placebo-controlled, double-blind and open-label clinical studies, 1483 adults and children 12 years and older received treatment with NASACORT Allergy 24HR. These patients were treated for an average duration of 50.7 days. In the controlled, seasonal allergic rhinitis trials (2-5 weeks duration) from which the following adverse reaction data is derived, 1394 patients were treated with NASACORT Allergy 24HR Nasal Spray for an average of 18.7 days. In the long-term, open-label study, the 172 patients enrolled received treatment for an average of 286 days duration.

The most commonly reported adverse reactions included those involving mucous membranes of the nose and throat. The three most prevalent adverse reactions considered to be at least possibly drug-related in adults and children 12 years and older were rhinitis (1.5%), headache (0.7%), and pharyngitis (0.3%), and in children 4 to 12 years were epistaxis (3.1%), rhinitis (1.4%) and headache (1.2%).

The incidence of specific nasopharyngeal-related adverse reactions considered drug related is summarized as follows:

Table 2: Nasopharyngeal Adverse Reactions

	Placebo (N=176)	Triamcinolone acetonide 110 mcg (N=179)	Triamcinolone acetonide 220 mcg (N=187)	Placebo (N=626)	Triamcinolone acetonide 400 mcg (N=1068)
Nasal AEs (overall)	**15 (8.5%)**	**8 (4.5%)**	**12 (6.4%)**	**20 (3.2%)**	**31 (2.9%)**
Dry mucous membranes	**0**	**0**	**0**	**2 (0.3%)**	**3 (0.3%)**
Epistaxis	**9 (5.1%)**	**6 (3.4%)**	**6 (3.2%)**	**3 (0.5%)**	**17 (1.6%)**
Nasal irritation	**5 (2.8%)**	**0**	**2 (1.1%)**	**3 (0.5%)**	**9 (0.8%)**
Naso-sinus congestion	**0**	**1 (0.6%)**	**1 (0.5%)**	**1 (0.2%)**	**2 (0.2%)**

	Placebo (N=176)	Triamcinolone acetonide 110 mcg (N=179)	Triamcinolone acetonide 220 mcg (N=187)	Placebo (N=626)	Triamcinolone acetonide 400 mcg (N=1068)
Sneezing	**1 (0.6%)**	**0**	**2 (1.1%)**	**6 (1.0%)**	**2 (0.2%)**
Throat discomfort	**1 (0.6%)**	**1 (0.6%)**	**1 (0.5%)**	**6 (1.0%)**	**3 (0.3%)**

These adverse reactions, with the exception of epistaxis (in adults), were reported at approximately the same or lower incidence as placebo treated patients. Only 1% of the patients in the controlled trials discontinued treatment (e.g. pharyngitis, headache). Overall, these studies found the adverse experience profile for triamcinolone acetonide to be similar to placebo.

The following table summarize the adverse events (% of patients) present in at least 5% of patients in the double-blind and open label phase studies in adults.

Table 3: Adverse Events in Adults

	Double-Blind		Open Label
	Placebo N=90	**Triamcinolone acetonide 220 mcg N=88**	**Triamcinolone acetonide 220/110 mcg N=172**
Flu Syndrome	**5 (5.6%)**	**5 (5.7%)**	**17 (9.9%)**
Headache	**12 (13.3%)**	**6 (6.8%)**	**38 (22.1%)**
Epistaxis	**1 (1.1%)**	**6 (6.8%)**	**31 (18.0%)**

Pharyngitis	**5 (5.6%)**	**13 (14.8%)**	**55 (32.0%)**
Rhinitis	**5 (5.6%)**	**6 (6.8%)**	**49 (28.5%)**
Injury Accident	**--**	**--**	**20 (11.6%)**
Back Pain	**--**	**--**	**13 (7.6%)**
Cough Increased	**--**	**--**	**14 (8.1%)**
Sinusitis	**--**	**--**	**27 (15.7%)**
Pain	**--**	**--**	**10 (5.8%)**
Diarrhea	**--**	**--**	**10 (5.8%)**

In the event of accidental overdose, an increased potential for these adverse experiences may be expected, but systemic adverse experiences are unlikely (see 5 OVERDOSAGE).

Hypersensitivity reactions including skin rash and edema of the face or tongue have been reported with other intranasal corticosteroids.

When patients are transferred to NASACORT Allergy 24HR from a systemic steroid, allergic conditions such as asthma or eczema may be unmasked (see 7 WARNINGS AND PRECAUTIONS).

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Children 4 to 12 years of age (n= 622) were studied in 3 controlled clinical trials. Of these, 179 received 110 mcg/day and 215 received 220 mcg/day of triamcinolone acetonide in two, six, or twelve week trials. The longest average duration of treatment for patients receiving 110 mcg/day was 76.3 days and 79.6 days for those receiving 220 mcg/day.

The following tables summarize the adverse events (% of patients) present in at least 5% of patients in controlled studies in children 4 to 12 years of age.

Table 4: Adverse Events in Children 4-12 Years of Age

	Placebo N=202	Triamcinolone acetonide 110 mcg N=179	Triamcinolone acetonide 220 mcg N=215	Triamcinolone acetonide 440 mcg N=26
Fever	**11 (5.4%)**	**8 (4.5%)**	**12 (5.6%)**	**2 (7.7%)**
Flu syndrome	**15 (7.4%)**	**16 (8.9%)**	**4 (1.9%)**	**0**
Headache	**22 (10.9%)**	**18 (10.1%)**	**16 (7.4%)**	**4 (15.4%)**
Infection	**15 (7.4%)**	**13 (7.3%)**	**16 (7.4%)**	**0**
Injury accidental	**3 (1.5%)**	**3 (1.7%)**	**4 (1.9%)**	**2 (7.7%)**
Cough increased	**13 (6.4%)**	**15 (8.4%)**	**15 (7.0%)**	**0**
Epistaxis	**14 (6.9%)**	**8 (4.5%)**	**10 (4.7%)**	**1 (3.8%)**
Pharyngitis	**13 (6.4%)**	**14 (7.8%)**	**16 (7.4%)**	**2 (7.7%)**
Rhinitis	**18 (8.9%)**	**18 (10.1%)**	**18 (8.4%)**	**0**
Sinusitis	**16 (6.4%)**	**7 (3.9%)**	**7 (3.3%)**	**0**

In addition, the most frequent (frequencies ≥ 2%) adverse reactions in adults and children greater than 6 years are: headache, epistaxis, cough, bronchitis, dyspepsia, rhinitis, pharyngitis, flu syndrome, and tooth disorder.

Additional adverse reactions in pediatric patients:

Reduction of growth velocity (see 7 WARNINGS AND PRECAUTIONS – Endocrine and Metabolism section)

In patients aged 2 to 5 years, the following adverse reactions have been observed (frequency ≥ 2%): headache, pharyngolaryngeal pain, nasopharyngitis, excoriation, diarrhea, and upper abdominal pain.

These adverse reactions, with the exception of nasal congestion and sneezing (in children) were reported at approximately the same or lower incidence as placebo treated patients. In children, no patient receiving 110 mcg/day discontinued due to a serious adverse event and one patient receiving 220 mcg/day discontinued due to a serious event that was considered not drug related. Overall, these studies found the adverse experience profile for triamcinolone acetonide to be similar to placebo.

8.3 Post-Market Adverse Reactions

The following additional adverse reactions have been reported during post-marketing experience; they are derived from spontaneous reports and therefore, the frequency of these adverse reactions is not known: nasal irritation, dry mucous membrane, nasal congestion, sneezing alterations of taste and smell, nausea, insomnia, dizziness, fatigue, dyspnea, decreased blood cortisol, cataract, glaucoma, increased ocular pressure, pruritus, rash, hypersensitivity, recurrence of the underlying disease from drug withdrawal and steroid withdrawal syndrome. As with other nasally inhaled corticosteroids, nasal septum perforations have been reported in rare instances.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Triamcinolone acetonide is a potent anti-inflammatory steroid with strong topical and weak systemic activity. Triamcinolone acetonide is a more potent derivative of triamcinolone. Although triamcinolone itself is approximately one to two times as potent as prednisone in animal models of inflammation, triamcinolone acetonide is approximately 8 times more potent than prednisone.

When administered intranasally in therapeutic doses, it has a direct anti-inflammatory action on the nasal mucosa, the mechanism of which is not yet completely defined.

Corticosteroids are very effective. However, when allergic symptoms are very severe, local treatment with recommended doses (microgram) of any available topical corticosteroid are not as effective as treatment with larger doses (milligram) of oral or parenteral formulations. Corticosteroids do not have an immediate effect on allergic signs and symptoms.

Children 4-12 years of age:

An improvement of symptoms may be seen as early as the first day after initiation of treatment and full benefit may be expected in 3 to 4 days. However, symptomatic relief may not occur in some patients for as long as two weeks. NASACORT AQ should not be continued beyond three weeks in the absence of significant symptomatic improvement.

10.2 Pharmacodynamics

Triamcinolone acetonide is a potent derivative of triamcinolone. Although triamcinolone itself is approximately 1-2 times as potent as prednisone in animal models of inflammation, triamcinolone acetonide is much more potent. In cotton oil-induced ear inflammation, triamcinolone acetonide topically applied was 59 times more active than hydrocortisone when given by mouth in equivalent doses. Comparable effects were obtained in rats with cotton and asbestos pellet induced granuloma.

Thymolytic potency was essentially equivalent, when given by the subcutaneous, intramuscular, intravenous and intraperitoneal routes. It was, however, 3-4 times more potent when given orally. Neither triamcinolone nor triamcinolone acetonide produced sodium retention in adrenalectomized rats or androgenic effects in castrated rats.

The precise mechanism of action of the intranasal drug is unknown. However, clinical studies utilizing nasal administration have demonstrated effective local steroid activity with no evidence of systemic effects. Smears of the nasal mucosa obtained during clinical studies demonstrated marked reductions in nasal eosinophils, which are known to release highly active chemical mediators.

10.3 Pharmacokinetics

Absorption

Pharmacokinetic characterization of the NASACORT AQ formulation was determined in both normal adult subjects and patients with allergic rhinitis. Single dose intranasal administration of 220 mcg of NASACORT AQ in normal adult subjects and patients demonstrated minimal absorption of triamcinolone acetonide. The mean peak plasma concentration was approximately 0.5 ng/mL (range: 0.1 to 1.0 ng/mL) and occurred at 1.5 hours post dose. Dose proportionality was demonstrated in normal subjects and in patients following a single intranasal dose of 110 mcg or 220 mcg NASACORT AQ.

Distribution:

Based upon intravenous dosing of triamcinolone acetonide phosphate ester, the volume of distribution (Vd) reported was 99.5 L (SD±27.5).

Metabolism:

Pharmacokinetics studies in animals with radiolabelled triamcinolone acetonide have been carried out by the oral, pulmonary, and intravenous routes in several species. The pharmacokinetic behaviour of the triamcinolone acetonide was similar in all species within

each route of administration. The results of studies in which triamcinolone acetonide was administered as an aerosol showed rapid disappearance of radioactivity from lungs, comparable to that observed following oral administration. Three major metabolites of triamcinolone acetonide have been identified. They are 6-hydroxy-triamcinolone acetonide (much less biologically active than triamcinolone acetonide), 21-carboxytriamcinolone acetonide and 21-carboxy-6-hydroxytriam-cinolone acetonide. The latter two metabolites would also be expected to be substantially less active than the parent compound due to:

a) the dependence of anti-inflammatory activity on the presence of the 21-hydroxyl group,

b) the decreased activity observed upon 6-hydroxylation, and

c) the markedly increased water solubility that favours rapid elimination.

There appeared to be some qualitative differences in the metabolites among the species. No differences were detected in the metabolic pattern as a function of route of administration.

Elimination

Based upon intravenous dosing of triamcinolone acetonide phosphate ester, the half-life of triamcinolone acetonide was reported to be 88 minutes and clearance was 45.2 L/ hour (SD ±9.1) for triamcinolone acetonide. The plasma half-life of corticosteroids does not correlate well with the biologic half-life.

After a **s**ingle dose intranasal administration of 220 mcg of NASACORT AQ in normal adult subjects and patients**,t**he 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.

Studies in animals completed utilizing radiolabelled triamcinolone acetonide given via oral and intravenous routes in several species show the major portion of the drug is eliminated in the feces, irrespective of the route of administration, with only one species (rabbit) showing significant urinary excretion of radioactivity.

Special Populations and Conditions

Pediatrics: Following multiple doses in pediatric patients ages 6 to 12 years old receiving 440 mcg/day, plasma drug concentration, AUC, C_{max} and T_{max} were similar to those values observed in adult patients.

11 STORAGE, STABILITY AND DISPOSAL

Store at 15-25°C.

12 SPECIAL HANDLING INSTRUCTIONS

The bottle should be discarded after 120 sprays or 2 months after starting treatment.

In the PATIENT MEDICATION INFORMATION, patients are provided with a check-off form to track usage.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

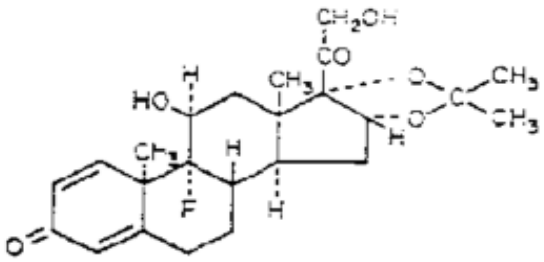
Drug Substance

Proper name: Triamcinolone acetonide

Chemical name: Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,-17- [(1-methyethylidene) bis(oxy)] -,(11β,16α)-

Molecular formula and molecular mass: $C_{24}H_{31}FO_6$; 434.49

Structural formula:



Physicochemical properties: White crystalline powder, sparingly soluble in methanol, acetone, ethyl acetone, with a melting point of 292 - 294 °C.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Perennial and Seasonal Allergic Rhinitis in Children 4 to 12 years of Age

Trial Design and Study Demographics

The safety and efficacy of NASACORT AQ has been evaluated in 10 double-blind, placebo-controlled clinical trials in adults and children 12 years and older with seasonal or perennial allergic rhinitis. The number of patients treated with NASACORT AQ in these studies was 1204; of these patients, 668 were males and 536 were females.

The safety and efficacy of NASACORT AQ, at doses of 110 mcg or 220 mcg once daily, has also been studied in two double blind placebo controlled trials of two and twelve weeks duration in children ages 4 through 12 years with seasonal and perennial allergic rhinitis. These trials included 355 males and 183 females. NASACORT AQ administered at either dose resulted in statistically significant reductions of allergic rhinitis symptoms.

Study Results

Overall, in double-blind clinical trials of two to four weeks duration, analysis of the clinical studies has demonstrated that NASACORT AQ 220 mcg once daily (2 sprays in each nostril) when compared to placebo provides statistically significant relief of nasal symptoms including sneezing, stuffiness, discharge, and itching.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Acute toxicity studies in mice and rats and subacute toxicity studies in rats, rabbits and dogs were done by conventional routes of administration. The findings in these studies were typically those seen following the administration of potent glucocorticosteroids. Subacute toxicity studies in rats and dogs and chronic studies in rats and monkeys were conducted by inhalation of aerosolized triamcinolone acetonide. A one-month intranasal toxicity study in dogs with triamcinolone acetonide aqueous nasal formulation revealed no toxicity other than that expected from triamcinolone acetonide. The findings in these studies generally were minimal and the same as in studies carried out by conventional routes of administration, with changes typical of those seen with potent glucocorticoids. There were no gross histopathological or ultrastructural findings suggestive of untoward effects on the respiratory tract.

An eye irritation study conducted in rabbits with triamcinolone acetonide aqueous nasal formulation revealed only a slight reversible irritation of the conjunctiva and iris.

Carcinogenicity: A recent literature report of a chronic bioassay conducted with several corticosteroids (budenoside, prednisolone, triamcinolone acetonide) indicated that all caused slightly increased incidence of liver tumors at toxic doses over a two-year study period. However, no evidence of treatment-related carcinogenicity was demonstrated after two years of once daily oral administration of triamcinolone acetonide at a maximum daily dose of 1.0 mcg/kg/day (6.1 mcg/m^2/day) in male or female rats and 3.0 mcg/kg/day (12.9 mcg/m^2/day) in male or female mice.

Reproductive and Developmental Toxicology: Teratology studies have been conducted in rats and rabbits by the subcutaneous route and by aerosol inhalation. The known teratogenic effects of glucocorticoids were found to occur following both routes of administration. Triamcinolone acetonide has been shown to be teratogenic in rats and rabbits. Teratogenic effects in both species at 0.02, 0.04 and 0.08 mg/kg/day (approximately 135, 270 and 540 mcg/m^2/day in the rat and 320, 640 and 1280 mcg/m^2/day in the rabbit, as calculated on a surface area basis), included low incidence of cleft palate and/or internal hydrocephaly and

axial skeletal defects. Teratogenic effects, including CNS and cranial malformation have also been observed in non-human primates at 0.5 mg/kg/day (approximately 6.7 mg/m^2/day). The doses of 0.02, 0.04, 0.08 and 0.5 mg/kg/day used in these toxicology studies are approximately 12.8, 25.5, 51 and 318.2 times the minimum recommended dose of 110 mcg of NASACORT AQ per day and 6.4, 12.7, 25.5 and 159.1 times the maximum recommended dose of 220 mcg of NASACORT AQ per day based on a patient body weight of 70 kg.

Administration by aerosol inhalation to pregnant rats and rabbits produced embryotoxic and fetotoxic effects which were comparable to those produced by administration by other routes.

Male and female rats which were administered oral triamcinolone acetonide at doses as high as 15 mcg/kg/day (110 mcg/m^2/day, as calculated on a surface area basis) exhibited no evidence of impaired fertility. The maximum human dose, for comparison, is 6.3 mcg/kg/day (240 mcg/m^2/day). However, a few female rats which received maternally toxic doses of 8 or 15 mcg/kg/day (60 mcg/m^2/day or 110 mcg/m^2/day, respectively, as calculated on a surface area basis) exhibited dystocia and prolonged delivery. Developmental toxicity, which included increases in fetal resorptions and stillbirths and decreases in pup body weight and survival, also occurred at the maternally toxic doses (2.5-15.0 mcg/kg/day or 20-110 mcg/m^2/day, as calculated on a surface area basis). Reproductive performance of female rats and effects on fetuses and offspring were comparable between groups that received placebo and nontoxic or marginally toxic doses (0.5 and 1.0 mcg/kg/day or 3.8 mcg/m^2/day and 7.0 mcg/m^2/day).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrNASACORT® AQ

Triamcinolone Acetonide Nasal Spray

Read this carefully before you start taking **NASACORT AQ** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **NASACORT AQ**.

What is NASACORT AQ used for?

NASACORT AQ is used in children (4 to 12 years of age), to treat the symptoms of:

- **Seasonal allergic rhinitis** (also called "hay fever"); and
- **Perennial allergic rhinitis** (year-round allergies).

How does NASACORT AQ work?

NASACORT AQ belongs to a group of medicines called corticosteroids. NASACORT AQ reduces the irritation and inflammation in the lining of the nose and nasal passages caused by allergies and relieves the blocked up feeling in the nose, runny nose, itching and sneezing.

What are the ingredients in NASACORT AQ?

Medicinal ingredients: Triamcinolone Acetonide

Non-medicinal ingredients: Benzalkonium chloride, carboxymethylcellulose sodium, dextrose, edetate disodium, microcrystalline cellulose, polysorbate 80 and Purified water. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

NASACORT AQ comes in the following dosage forms:
Nasal spray: 55 mcg per metered spray

Do not use NASACORT AQ if:

- You are allergic to any of the ingredients in NASACORT AQ;
- You have active or dormant tuberculosis;
- You have an untreated fungal, bacterial and/or viral infection.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NASACORT AQ. Talk about any health conditions or problems you may have, including if you:

- Have already taken NASACORT AQ or any other corticosteroids and developed an allergy or intolerance to any of them;
- Are allergic to any other substances, such as food, preservatives or dyes;
- Have asthma;
- Are recovering from recent surgery, trauma or sores to your nose;
- Have or are recovering from a fungal infection in your nose;
- Have been exposed to chickenpox or measles. If you think you have been exposed, tell your healthcare professional right away;
- Have hypothyroidism (a condition where the thyroid isn't making enough hormone);
- Have cirrhosis (a damaged liver);
- Have or had a history of any eye disorders such glaucoma or cataracts;
- Are taking other corticosteroid medicines by mouth or as an injection
- Are pregnant or think you are pregnant;
- Are breastfeeding or planning to breastfeed.

Other warnings you should know about:

Eye problems: Medications like NASACORT AQ can cause eye disorders such as:

- **Glaucoma:** An increase in eye pressure, or eye pain. Untreated it may lead to permanent vision loss;
- **Cataracts:** clouding of the lens in the eye, blurry vision or eye pain.

If you haven any changes in your vision, tell your healthcare professional **right away**. You should have regular eye exams.

Growth in Children: Slower growth in children using NASACORT AQ can occur. You and your healthcare professional should monitor your child's growth.

Withdrawal: If you take NASACORT AQ for a prolonged period, do NOT stop taking it without talking to your healthcare professional first. If you stop your treatment abruptly you may experience symptoms of withdrawal such as joint and/or muscle pain, lack of energy, depression, shaking, weight loss, anxiety, nasal drip, bleeding from the nose or the return of symptoms you are trying to treat. If you need to stop taking NASACORT AQ, or have any concerns, talk to your healthcare professional.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with NASACORT AQ:

NASACORT AQ has no known drug interactions.

How to take NASACORT AQ:

- Before use, read the INSTRUCTIONS FOR USE included.
- Use exactly as directed, DO NOT use NASACORT AQ more, or more often than your healthcare professional has told you to.

Usual dose:

Children 4 to 12 years of age: The recommended dose is one spray in each nostril once a day.

DO NOT stop using NASACORT AQ even if you feel better, unless your healthcare professional tells you to. It may take a few days for NASACORT AQ to start working. You will get the best results if you keep using NASACORT AQ regularly each day, without missing a dose.

If your symptoms do not improve after three weeks of treatment, talk to your doctor. If your doctor decides to stop treatment, do not keep any leftover medicine unless your doctor tells you to.

Overdose:

If you think you, or a person you are caring for, have taken too much NASACORT AQ, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose and remember within an hour or so, take the missed dose. However, if you do not remember until later, skip the missed dose and go back to your regular dosing schedule. Do not take double doses.

What are possible side effects from using NASACORT AQ?

These are not all the possible side effects you may have when taking NASACORT AQ. If you experience any side effects not listed here, tell your healthcare professional.

- Nose bleeds, nasal ulcers, pain, burning, irritation, soreness or dryness inside of the nose
- Sore throat, flu-like symptoms, fever, bronchitis, cough, stuffy nose
- Headache
- Unpleasant taste or smell

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Nasal Infection: yellow/green discharge from nose		✓	
RARE			
Nasal septum perforation: (small holes in the wall between the 2 nostrils): constant whistling sounds when you breathe from your nose.		✓	
UNKNOWN FREQUENCY			
Cataracts: clouding of the lens in the eye, blurry vision, and/or eye pain		✓	
Glaucoma (increased pressure in your eyes): eye and head pain, swelling or redness in or around the eye, changes in vision, hazy or blurred vision, sudden sight loss			✓
Slowed growth in children and adolescents		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 15 - 25°C.

Do not use NASACORT AQ after the expiry date which is stated on the carton and the bottle after "EXP".

The bottle should be discarded after 120 sprays or 2 months after starting treatment.

Keep out of reach and sight of children.

If you want more information about NASACORT AQ:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.sanofi.ca, or by calling 1-800-636-3664.

This leaflet was prepared by Sanofi Consumer Health Inc.

Last Revised September 14, 2022

INSTRUCTIONS FOR USE

It is important to shake the bottle gently before each use. The bottle should be discarded after 120 sprays or 2 months after starting treatment. Do not transfer any remaining liquid to another bottle.

PrNASACORT® AQ

(Triamcinolone Acetonide Nasal Spray, USP)

1. IMPORTANT INFORMATION

a. **Read this insert** for complete instructions on how to get a bottle ready (primed), how to use the spray bottle and how to clean the spray nozzle.

b. Keep this insert as it contains important information.

c. NASACORT AQ is for nasal use only.

d. Do not use more than directed.

e. Do not share this bottle with anyone else as this may spread germs.

2. STEPS TO GET A NEW BOTTLE READY FOR USE (PRIMED)

A. Before first use, a new bottle must be primed.

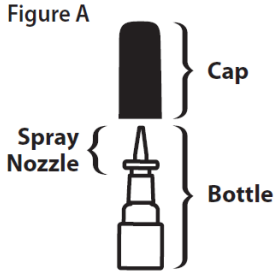
a. Remove purple cap *(Figure A).*

b. Shake the bottle gently before use.

c. Hold the bottle upright. Point the spray away from you or other people while doing this. Press and release spray nozzle until a fine mist is produced, taking care not to spray into eyes or face *(as shown in Figure B).* If you get the spray in your eyes, rinse well with water.

d. The spray is now ready to use.

Figure A



B. If NASACORT AQ has not been used for more than 2 weeks, prime the bottle again. Repeat steps "a" through "c" above.

3. USE INSTRUCTIONS

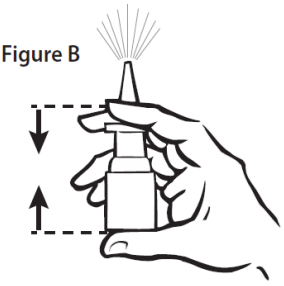
a. Blow nose gently to clear nostrils.

b. Remove cap, then shake the bottle gently.

c. Hold the bottle with thumb under bottle and spray nozzle between your fingers *(as shown in Figure B).*

d. Close off one nostril with your finger.

Figure B



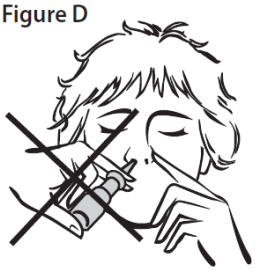
e. Aim nozzle toward back of nose *(Figure C).*

DO NOT spray toward nasal septum (the wall between the 2 nostrils) *(Figure D)*.

Figure C

Correct Position

Figure D



Wrong Position

f. While breathing in gently, press down on the spray nozzle with your fingers to release the spray.

g. Repeat steps "d" through "f" for the other nostril.

h. If you have been prescribed two sprays per nostril, repeat steps "d" through "f" again for both nostrils.

i. After using the nasal spray, wipe nozzle with a tissue and replace cap.

NOTE: Avoid blowing nose for 15 minutes after use.

If nozzle does not spray properly, see cleaning instructions below.

4. IF PUMP DOES NOT SPRAY PROPERLY,

THE NOZZLE MAY BE BLOCKED

a. Never try to unblock nozzle or enlarge the tiny spray hole with a pin or other sharp objects. This can stop the spray from working. *(Figure E)*.

b. Clean the nozzle as shown below.

Figure E

5. CLEANING INSTRUCTIONS

a. Remove the cap.

b. Gently pull off the spray nozzle away from bottle *(Figure F)*.

c. Rinse **SPRAY NOZZLE ONLY** under warm water *(Figure G)*.

d. Shake or tap to remove any water that is left.

e. Re-attach spray nozzle to bottle.

f. Press and release spray nozzle until a fine spray is produced, taking care not to spray in your eyes or face. If you get the spray in your eyes, rinse well with water.

g. Replace the cap over the nozzle.

NASACORT AQ is now ready to use.

Figure F

Figure G

Below is a check-off chart to help you keep track of the number of sprays you have used. This will help assure that you receive the 120 sprays of medication present. The bottle has been filled with extra solution to accommodate the initial priming sprays. Any additional repriming (i.e. other than the initial priming) must be counted below as a spray.

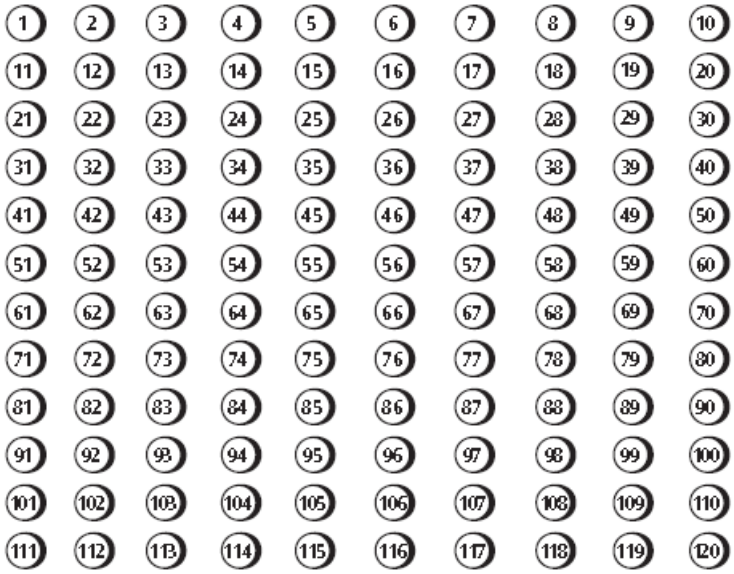
NASACORT AQ 120 Sprays Check-Off

(Include treatment inhalations and repriming sprays)

Check off one circle for one spray.

The bottle should be discarded after 120 sprays or 2 months after starting treatment.

Do not transfer any remaining liquid to another bottle.



Last revised:

September 14, 2022