PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

OMNAIR® Nasal spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

OMNAIR® Nasal spray is a metered-dose, manual pump spray formulation containing a hypotonic aqueous suspension of ciclesonide. Once primed, each puff (actuation) of the pump delivers 50 micrograms (µg) of ciclesonide in a volume of 70 microlitres (µl) from the nasal actuator.

Each bottle contains: 7,9 g of suspension/bottle (10 ml bottle) and 13,5 g of suspension/bottle (15 ml bottle).

Preservatives: Contains potassium sorbate 0,12 % and edetate disodium 0,01 %

For full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

OMNAIR® Nasal spray, 50 µg (60 or 120 puff metered spray): An amber glass bottle containing a white to off-white suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

OMNAIR® Nasal spray is indicated for:

- the treatment of nasal symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older.
- OMNAIR® Nasal spray is indicated for the treatment of nasal symptoms associated with perennial allergic rhinitis in adults and children 12 years of age and older.

4.2 Posology and method of administration

Posology

OMNAIR® Nasal spray should only be administered by the intranasal route.

Seasonal Allergic Rhinitis: Adults and children (6 years of age and older): The recommended dose of OMNAIR® Nasal spray is 200 µg per day administered as 2 sprays (50 µg/spray) in each nostril once daily. The maximum total daily dosage should not exceed 2 sprays of 50 µg in each nostril once daily (200 µg/day).

Perennial Allergic Rhinitis: Adults and children (12 years of age and older):

The recommended dose of OMNAIR® Nasal spray is 200 µg per day, administered as 2 sprays (50 µg/spray) in each nostril once daily. The maximum total daily dosage should not exceed 2 sprays in each nostril (200 µg/day).

Dosage in special populations:

Hepatic impairment

Dose adjustment in liver impairment is not necessary. The systemic exposure (C_{max} and AUC) in patients with liver impairment increased up to 2,7-fold after high doses of **OMNAIR®** Nasal spray, when compared to healthy subjects (see Pharmacokinetics: Special populations*)*.

Dosage in children

Corticosteroids may cause a reduction in growth velocity when administered to paediatric patients. The potential growth effects of prolonged treatment should be weighed against clinical benefits. To minimise the systemic effects of intranasal corticosteroids, **OMNAIR®** Nasal spray, each patient should be titrated to his/her lowest effective dose (see section 4.4*)*.

Dosage in the elderly

No dosage adjustment is required in elderly patients. The adverse reactions reported in this population were similar in type and incidence to those reported by younger patients, but an increased sensitivity of some older individuals cannot be ruled out (see section 4.4*)*.

Method of administration

Prior to initial use, OMNAIR® Nasal spray must be shaken gently and then the pump must be primed by actuating (pushing the pump) 8 times. If the product is not used for 4 or more consecutive days, it should be shaken gently and re-primed with 1 spray or until a fine spray appears.

Shake gently before use. Read the instructions “Preparing for use” and “Using the spray”, below. Also see diagrams provided.

Preparing For Use

1. Remove **OMNAIR®** Nasal spray from its foil pouch. Count 4 months from this date and write this date (that is 4 months from removing the bottle from the foil pouch) on the sticker provided on the carton. Peel off this sticker and place it in the space provided on the nasal spray bottle. It’s important to throw away the nasal spray bottle after this date.
2. Prior to initial use, **OMNAIR®** Nasal spray must be gently shaken and then the pump must be primed by actuating eight times. If the product is not used for four consecutive days, it should be gently shaken and re-primed with one spray or until a fine mist appears.

Precautions for use

SHAKE CONTAINER GENTLY BEFORE USE. Do not spray in eyes.

Using the Spray

1. Blow the nose to clear nostrils if needed.
2. Shake the bottle gently and remove the dust cap.
3. Hold the bottle firmly with index and middle finger on either side of the spray tip while supporting the base of the bottle with the thumb **(Figure 1)**.

Figure 1

4. Insert spray tip into one nostril and close the other nostril with a finger (Figure 2).

Figure 1

5. Tilt the head forward slightly and keep the bottle upright, press the pump quickly and firmly and inhale through the nose while spraying **(Figure 3)**. Avoid spraying in eyes or directly onto the

nasal septum (the wall between the two nostrils).

Figure 2

4.3 Contraindications

OMNAIR® Nasal spray is contra-indicated in patients with:

- a hypersensitivity to any of its ingredients.
- active pulmonary tuberculosis

4.4 Special warnings and precautions for use

Systemic steroid replacement by a topical steroid

The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency. In addition, some patients may experience symptoms of corticosteroid withdrawal, e.g., joint and/or muscular pain, lassitude, and depression.

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

In those patients who have asthma or other clinical conditions requiring long-term systemic corticosteroid treatment, rapid decreases in systemic corticosteroid dosages may cause a severe exacerbation of their symptoms.

Immunosuppression

Immediate hypersensitivity reactions or contact dermatitis may occur after the administration of intranasal corticosteroids. Patients with a known hypersensitivity reaction to other corticosteroid preparations should use caution when using **OMNAIR®** Nasal spray since cross reactivity to other corticosteroids including ciclesonide may also occur.

Patients who are using medicines that suppress the immune system 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 using corticosteroids. In patients who have not had these

diseases or been properly immunised, particular care should be taken to avoid exposure.

How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known.

If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated.

If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated.

If chickenpox develops, treatment with antiviral agents may be considered.

Impaired wound healing

Due to the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or nasal trauma should not use a nasal corticosteroid until healing has occurred.

Glaucoma and cataracts

Nasal and inhaled corticosteroids may result in the development of glaucoma and/or cataracts. Therefore, close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma and/or cataracts.

Adrenal Hypercorticism and Adrenal Suppression

Doses of **OMNAIR®** Nasal spray larger than the recommended dose should be avoided. When used at excessive doses, systemic corticosteroid effects may occur, such as adrenal hypercorticism and adrenal suppression. If such changes occur, the dosage of **OMNAIR®** Nasal spray should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

Infection

Corticosteroids should be used in caution, if at all, in patients with quiescent tuberculosis infections of the respiratory tract; or in patients with untreated local or systemic fungal or bacterial infections, systemic viral or parasitic infections, or ocular herpes simplex because of potential for worsening of these infections (see section 4.3).

In clinical studies with **OMNAIR®** Nasal spray, the development of localised infections of the nose and pharynx with *Candida albicans* has occurred. When such an infection develops, it may require treatment with appropriate local therapy and discontinuation of **OMNAIR®** Nasal spray. Therefore, patients using **OMNAIR®** Nasal spray over several months or longer should be examined periodically

for evidence of *Candida* infection or other signs of adverse effects on the nasal mucosa.

Effect on growth

Controlled clinical studies have shown that intranasal corticosteroids may cause a reduction in growth velocity in paediatric patients. This effect has been observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA)-axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in paediatric patients than some commonly used tests of HPA-axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown.

The potential for "catch-up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied. The growth of paediatric patients receiving **OMNAIR®** Nasal spray, should be monitored routinely (e.g., via stadiometry). The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of safe and effective non corticosteroid treatment alternatives. To minimise the systemic effects of intranasal corticosteroids, each patient should be titrated to the lowest dose that effectively controls his/her symptoms (see section 4.2*)*.

Use in the elderly

Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see section 4.2*)*.

4.5 Interactions with other medicines and other forms of interaction

Based on *in vitro* studies in human liver microsomes, des-ciclesonide appears to have no inhibitory or induction potential on the metabolism of other drugs metabolised by CYP 450 enzymes. The inhibitory potential of ciclesonide on CYP450 isoenzymes has not been studied.

In vitro studies demonstrated that the plasma protein binding of des-ciclesonide was not affected by warfarin or salicylic acid, indicating no potential for protein binding-based interactions.

In an interaction study, co-administration of orally inhaled ciclesonide and oral erythromycin, an inhibitor of cytochrome P450 3A4, had no effect on the pharmacokinetics of either des-ciclesonide or erythromycin. In another interaction study, co-administration of orally inhaled ciclesonide and oral ketoconazole, a potent inhibitor of cytochrome P450 3A4, increased the exposure (AUC) of des-

ciclesonide by approximately 3,6-fold at steady state, while levels of ciclesonide remained unchanged. Therefore, ketoconazole should be administered with caution with **OMNAIR®** Nasal spray.

4.6 Fertility, pregnancy, and lactation

Pregnancy

There are no adequate and well-controlled studies with OMNAIR Nasal Spray in pregnant women. Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

Breast-feeding

Safety in breastfeeding has not been established. It is not known if ciclesonide is excreted in human milk. However, other corticosteroids are excreted in human milk.

4.7 Effects on ability to drive and use machine

The effects of this medicine on a person's ability to drive and use machines were not assessed.

4.8 **Undesirable effects**

The table below displays adverse events (reactions) that occurred with an incidence of 1% or greater in controlled clinical trials for patients treated with 200 micrograms per day. The displayed frequency categories in the table below, use the following convention: 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); and not known (cannot be estimated from the available clinical trial data).

System Organ Class	**Frequency**	**Side effect**
Respiratory, thoracic and mediastinal disorders	Common	Cough, pharyngitis, epistaxis, nasopharyngitis, sinusitis
	Uncommon	Nasal dryness, pharyngolaryngeal pain, rhinorrheoea, nasal septum disorder, throat irritation
General disorders and site application disorders	Common	Headache, nasal passage irritation, pharyngolaryngeal pain
Nervous system	Uncommon	Dysgeusia
Infections and infestations	Common	Upper respiratory tract infection, influenza
	Uncommon	Candidiasis, rhinitis
Gastrointestinal disorders	Common	Vomiting

	Uncommon	Dry mouth, dyspepsia
Investigations	Uncommon	Laboratory test abnormal, increased white blood cell count

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to Acino Pharma via email to drugsafety_ZA@acino.swiss or to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

There are no data available on the effects of acute or chronic overdosage with **OMNAIR®** Nasal spray.

Because of low systemic bioavailability, acute overdose is unlikely to require any therapy other than observation. A single oral dose up to 10 mg of ciclesonide in healthy volunteers was well tolerated and serum cortisol levels were virtually unchanged in comparison with placebo treatment.

Chronic overdosage with any corticosteroid may result in signs or symptoms of hypercorticism (see section 4.4).

5. PHARMACOLOGICAL PROPERTIES

PHARMACOLOGICAL CLASSIFICATION

A 21.5.1 Corticosteroids and analogues.

5.1 Pharmacodynamics properties

Ciclesonide is a topical glucocorticosteroid delivered as a hypotonic suspension that has local anti-inflammatory properties.

The effects of ciclesonide nasal spray on the HPA (hypothalamic-pituitary-adrenal) axis were investigated in clinical trials. No appreciable effects of intranasally administered ciclesonide on serum or urinary cortisol levels were **detected.**

Mechanism of Action

Ciclesonide is a pro-drug that is enzymatically hydrolysed to a pharmacologically active metabolite, C21-desisobutyryl-ciclesonide (des-ciclesonide or RM1) following intranasal application. Des-ciclesonide has anti-inflammatory activity with affinity for the glucocorticoid receptor that is 120 times higher than the parent compound.

The precise mechanism through which ciclesonide affects allergic rhinitis symptoms is not known. Corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g. mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g. histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic inflammation.

5.2 Pharmacokinetics properties

Absorption

Ciclesonide and des-ciclesonide have negligible oral bioavailability (both less than 1 %) due to low gastrointestinal absorption and high first-pass metabolism. The intranasal administration of ciclesonide at recommended doses results in negligible serum concentrations of ciclesonide. However, low levels of the known active metabolite (des-ciclesonide) are detected in the serum of some patients after nasal inhalation of ciclesonide. In healthy adults treated for two weeks with 50 to 800 µg of ciclesonide nasal spray daily, the peak serum concentrations of des-ciclesonide in all subjects were below 30 pg/ml. Of those treated with 800 µg and 400 µg daily, 100 % and 67 % had detectable levels of des ciclesonide, respectively.

With daily doses of 200 µg or less, detectable serum levels of des-ciclesonide were not observed. The bioanalytical assay used has a lower limit of quantification of 25 pg/ml and 10 pg/ml, for ciclesonide and des-ciclesonide, respectively.

In paediatric subjects with 25 µg to 200 µg of ciclesonide nasal spray daily, serum concentrations of des-ciclesonide were below 45 pg/ml, with the exception of one single value of 64,5 pg/ml.

In a 12-week study in children 6 to 11 years of age with perennial allergic rhinitis, des-ciclesonide was detected in 50 % of the subjects treated with 200 µg and in 5 % of those treated with 100 µg ciclesonide nasal spray daily.

Distribution

Following intravenous administration of 800 µg of ciclesonide, the volumes of distribution of ciclesonide and des-ciclesonide were approximately 2,9 l/kg and 12,1 l/kg, respectively. The

percentage of ciclesonide and des-ciclesonide bound to human plasma proteins averaged ≥ 99 % each, with ≤ 1 % of unbound drug detected in the systemic circulation. Des-ciclesonide is not significantly bound to human transcortin.

Metabolism

Intranasal ciclesonide is hydrolysed to a biologically active metabolite, des-ciclesonide, by esterases in the nasal mucosa. Des-ciclesonide undergoes further metabolism in the liver to additional metabolites mainly by the cytochrome P450 (CYP) 3A4 isozyme and to a lesser extent by CYP 2D6. The full range of potentially active metabolites of ciclesonide has not been characterised.

After intravenous administration of 14C-ciclesonide, 19,3 % of the resulting radioactivity in the plasma is accounted for by ciclesonide or des-ciclesonide; the remainder may be a result of other, as yet unidentified multiple metabolites.

Elimination

Following intravenous administration of 800 µg of ciclesonide, the clearance values of ciclesonide and des-ciclesonide were high (approximately 152 L/h and 228 L/h, respectively). ^{14}C-labeled ciclesonide was predominantly excreted via the faeces after intravenous administration (66 %) indicating that excretion through bile is the major route of elimination. Approximately 20 % or less of drug related radioactivity was excreted in the urine.

Special Populations

The pharmacokinetics of intranasally administered ciclesonide have not been assessed in patient subpopulations because the resulting blood levels of ciclesonide and des-ciclesonide are insufficient for pharmacokinetic calculations. However, population pharmacokinetic analysis showed that characteristics of des-ciclesonide after oral inhalation of ciclesonide were not appreciably influenced by a variety of subject characteristics such as body weight, age, race, and gender.

Hepatic impairment:

Compared to healthy subjects, the systemic exposure (Cmax and AUC) in patients with liver impairment increased in the range of 1,4 to 2,7-fold after 1280 µg ex-actuator ciclesonide by oral inhalation and dose adjustment in liver impairment is not necessary (see section 4.2).

Renal impairment:

Studies in renal impaired patients were not conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Other ingredients include: Microcrystalline cellulose and carboxymethylcellulose sodium, hydroxypropyl methylcellulose, potassium sorbate, disodium edetate and hydrochloric acid to adjust the pH to 4,5.

Preservatives: Contains potassium sorbate 0,12 % and edetate disodium 0,01 %

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 25 °C. Do not refrigerate. Do not freeze.

SHAKE CONTAINER GENTLY BEFORE USE.

Discard OMNAIR® 4 months after opening foil pouch.

6.5 Nature and contents of container

OMNAIR® Nasal spray is supplied in an amber glass bottle covered with a plastic sleeve, with a snapped-on white, plastic metered-pump, packed together in an aluminium foil pouch. The glass bottle is available as a 10 ml bottle (60 puffs/bottle) and a 15 ml bottle (120 puffs/bottle).

Handle glass bottle with care, do not use if pouch or bottle is damaged or broken.

Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Acino Pharma (Pty) Ltd

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South Africa

Tel: 087 742 1860

8. REGISTRATION NUMBER

OMNAIR® Nasal spray: 43/21.5.1/0008

NAMIBIA: NS2
Reg. No.: 13/21.5.1/0272

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

01 March 2013

10. DATE OF REVISION OF THE TEXT

20 May 2026