SUMMARY OF PRODUCT CHARACTERISTICS FOR PHARMACEUTICAL PRODUCTS

1 NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

NASOALDO 50 micrograms/spray, nasal spray, suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each spray delivers 50 micrograms of mometasone furoate (as monohydrate).

Excipient(s) with known effect: this medicinal product contains 0.2 mg benzalkonium chloride per gram.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal spray, suspension.
White suspension.

4 CLINICAL PARTICULARS

4.1.*Therapeutic indications*

NASOALDO is indicated for adults and children 3 years of age and older for the symptomatic treatment of seasonal or perennial allergic rhinitis.

NASOALDO is indicated for the treatment of nasal polyps in adults 18 years of age and older.

4.2.*Posology and method of administration*

After priming the NASOALDO pump, each spray provides approximately 100 mg of mometasone furoate suspension, containing mometasone furoate monohydrate equivalent to 50 micrograms of mometasone furoate.

Posology

Seasonal or perennial allergic rhinitis

Adults (including older patients) and children aged 12 years and older: The usual recommended dose is two sprays (50 micrograms/spray) in each nostril once daily (total dose of 200 micrograms). Once symptoms are under control, reducing the dose to one spray in each nostril (total dose of 100 micrograms) may be effective for maintenance.

If symptoms are inadequately controlled, the dose may be increased to a maximum daily dose of four sprays in each nostril once daily (total dose of 400 micrograms). Reducing the dose again is recommended once symptoms are under control.

Children aged 3 to 11 years: The usual recommended dose is two sprays (50 micrograms/spray) in each nostril once daily (total dose of 100 micrograms).

The onset of action of mometasone furoate was evident within 12 hours after the first dose in

some patients with seasonal allergic rhinitis. However, the full benefit of treatment may not be achieved within the first 48 hours. Therefore, the patient should continue with regular use to achieve full therapeutic benefit.

Treatment with NASOALDO may need to be initiated some days before the expected start of the pollen season in patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis.

Nasal polyposis

The usual recommended starting dose for polyposis is two sprays (50 micrograms/spray) in each nostril once daily (total daily dose of 200 micrograms). If after 5 to 6 weeks symptoms are not adequately controlled, the dose may be increased to a daily dose of two sprays in each nostril twice daily (total daily dose of 400 micrograms). The dose should be established at the lowest dose at which effective control of symptoms is achieved. If no improvement in symptoms is seen after 5 to 6 weeks of twice-daily administration, the patient should be re-assessed and the treatment strategy reconsidered.

Efficacy and safety studies on mometasone furoate for the treatment of nasal polyposis lasted four months in duration.

Paediatric population

Seasonal or perennial allergic rhinitis

The safety and efficacy of mometasone furoate in children under the age of 3 have not been established.

Nasal polyposis

The safety and efficacy of mometasone furoate in children and adolescents under the age of 18 have not been established.

4.3.*Method of administration*

Prior to administration of the first dose, shake the container well and press the pump 10 times (until a consistent spray is obtained). If the pump is not used for 14 days or longer, re-prime the pump with 2 sprays until a consistent spray is observed, before the next use.

Shake the container well before each use. The bottle should be discarded after the labelled number of sprays or within 2 months of first use.

4.4.*Contraindications*

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

NASOALDO should not be used in the presence of untreated localised infection involving the nasal mucosa, such as herpes simplex.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have had recent nasal surgery or trauma should not use a nasal corticosteroid until healing has taken place

4.5.*Special warnings and precautions for use*

Immunosuppression

NASOALDO should be used with caution, or avoided completely, in patients with active or

quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial or systemic viral infections.

Patients receiving corticosteroids who are potentially immunosuppressed should be warned of the risk of exposure to certain infections (e.g. chickenpox, measles) and of the importance of obtaining medical advice if such exposure occurs.

Local nasal effects

Following 12 months of treatment with mometasone furoate in a clinical trial with patients with perennial rhinitis, there was no evidence of atrophy of the nasal mucosa; also, mometasone furoate tended to cause the nasal mucosa to revert closer to a normal histological phenotype. Nevertheless, patients using mometasone furoate over several months or longer should be examined periodically for possible changes in the nasal mucosa. If localised fungal infection of the nose or pharynx develops, it may be necessary to discontinue mometasone furoate therapy or start the patient on appropriate treatment. Persistence of nasopharyngeal irritation may be an indication for discontinuing mometasone furoate.

Mometasone furoate is not recommended in cases of nasal septum perforation (see section 4.8).

In clinical trials, the incidence of nosebleed was higher compared to placebo. Nosebleed was generally self-limiting and mild in severity (see section 4.8).

This medicine contains 20 mcg benzalkonium chloride per actuation. Benzalkonium chloride may cause irritation or swelling inside the nose, especially if used for a long time.

Systemic effects of corticosteroids

Systemic effects of nasal corticosteroids may occur, particularly at high doses over prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataracts, glaucoma and, more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Following the use of intranasal corticosteroids, instances of increased intraocular pressure have been reported (see section 4.8).

There is no evidence of suppression of the hypothalamic–pituitary–adrenal axis after prolonged treatment with mometasone furoate. However, patients who are changed from long-term administration of systemically active corticosteroids to mometasone furoate require close monitoring. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of hypothalamic–pituitary–adrenal axis function. If these patients exhibit signs and symptoms of adrenal insufficiency or symptoms of withdrawal (e.g. joint and/or muscle pain, lassitude, and depression initially) despite relief from nasal symptoms, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted. Said treatment change may also unmask pre-existing allergic conditions, such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweights the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Treatment with higher than recommended doses may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used, then additional protection with systemic corticosteroids should be considered during periods of stress or elective surgery.

Nasal polyps

The safety and efficacy of mometasone furoate have not been studied for use in the treatment of unilateral polyps, polyps associated with cystic fibrosis, or polyps that completely obstruct the nasal cavities.

Unilateral polyps that are unusual or irregular in appearance, especially if ulcerating or bleeding, should be further evaluated.

4.6.*Paediatric population*

Effect on growth in paediatric population

It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids be regularly monitored. If delayed growth is detected, therapy should be reviewed with the aim of reducing the dose, if possible, to the lowest dose at which effective control of symptoms is achieved. In addition, consideration should be given to referring the patient to a paediatric specialist.

Non-nasal symptoms

Although mometasone furoate will control the nasal symptoms in most patients, the concomitant use of appropriate additional therapy may provide additional relief of other symptoms, particularly ocular symptoms.

4.7. *Interaction with other medicinal products and others forms of interaction*

(See section 4.5, Special warnings and precautions for use with systemic corticosteroids.)
A clinical interaction study was conducted with loratadine. No interactions were observed.
Co-treatment with CYP3A inhibitors is not recommended (see section 4.5.).

4.8. *Additional information on special populations*

Not applicable.

4.9. *Fertility, pregnancy and lactation*

Pregnancy

There are no or limited amount of data from the use of mometasone furoate in pregnant women. Studies conducted in animals showed reproductive toxicity (see section 5.3). As with other nasal corticosteroid preparations, mometasone furoate should not be used in pregnancy unless the potential benefit to the mother justifies any potential risk to the mother, foetus or infant. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for adrenal insufficiency.

Breastfeeding

It is not known whether mometasone furoate passes into breast milk. As with other nasal corticosteroids, a decision must be made whether to discontinue breastfeeding or to discontinue treatment after taking into account the benefit of breastfeeding for the child and the benefit of treatment for the woman.

Fertility

There are no data concerning the effect of mometasone furoate on fertility. Animal studies have shown reproductive toxicity, but no effects on fertility (see section 5.3).

4.10. *Effects on ability to drive and use machines*

None known.

4.11. *Undesirable effects*

a) Summary of the safety profile

Nosebleed was generally self-limiting and mild in severity, and occurred at a higher incidence compared to placebo (5%), but at a comparable or lower incidence when compared to the active-control nasal corticosteroids studied (up to 15%), as reported in clinical trials for allergic rhinitis. The incidence of all other adverse events was comparable with that of placebo. In patients treated for nasal polyposis, the overall incidence of adverse events was similar to that observed for patients with allergic rhinitis.
Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

b) Tabulated list of adverse reactions

Treatment-related adverse reactions (≥1%) reported in clinical trials in patients with allergic rhinitis or nasal polyposis and post-marketing regardless of indication are shown in Table 1. Adverse reactions are listed according to MedDRA primary system organ class. Within each system organ class, adverse reactions are ranked by frequency. Frequencies are defined as follows: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100). The frequency of post-marketing adverse events are considered as “not known (cannot be estimated from the available data)”.

Table 1: Treatment-related adverse reactions reported by system organ class and frequency

	Very common	Common	Not known
Infections and infestations		Pharyngitis Upper respiratory tract infection†	
Immune system disorders			Hypersensitivity including anaphylactic reactions, angioedema, bronchospasm and dyspnoea.
Nervous system		Headache	
Eye disorders			Glaucoma Increased intraocular pressure Cataracts Vision, blurred (see also
Respiratory, thoracic and mediastinal disorders	Nosebleed*	Nosebleed Nasal burning Nasal irritation	Perforation of the nasal septum
Gastrointestinal		Sore throat*	Altered taste and

*reported with twice-daily dose in nasal polyposis

†reported as uncommon with twice-daily dose in nasal polyposis

b) Description of selected adverse reactions

Not applicable

c) Paediatric population

In the paediatric population, the incidence of adverse events reported in clinical trials, e.g. nosebleed (6%), headache (3%), nasal irritation (2%) and sneezing (2%), was comparable to placebo.

d) Other special populations

Not applicable

4.12. *Overdose*

Symptoms

Inhalation or oral administration of excessive doses of corticosteroids may lead to the suppression of hypothalamic–pituitary–adrenal axis function.

Treatment

Because the systemic bioavailability of mometasone furoate is <1%, overdose is unlikely to require any therapy other than observation, followed by initiation of the appropriate prescribed dosage.

5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use - corticosteroids. ATC code: R01A D09.

Mechanism of action

Mometasone furoate is a topical glucocorticosteroid with local anti-inflammatory properties at doses that are not systemically active.

It is likely that much of the mechanism for the anti-allergic and anti-inflammatory effects of mometasone furoate lies in its ability to inhibit the release of mediators of allergic reactions. Mometasone furoate significantly inhibits the release of leukotrienes from leukocytes of allergic patients. In cell cultures, mometasone furoate demonstrated high potency in inhibiting the synthesis and release of IL-1, IL-5, IL-6 and TNFα; it is also a potent inhibitor of leukotriene production. In addition, it is an extremely potent inhibitor of the production of the Th2 cytokines, IL-4 and IL-5, from human CD4+ T-cells.

Pharmacodynamic effects

In studies conducted with nasal-antigen challenge, mometasone furoate has shown anti-inflammatory activity in both the early- and late-phase allergic responses. This has been demonstrated by decreases (versus placebo) in histamine and eosinophil activity and reductions (versus baseline) in eosinophil, neutrophil and epithelial-cell adhesion proteins.

In 28% of the patients with seasonal allergic rhinitis, mometasone furoate nasal spray demonstrated a clinically significant onset of action within 12 hours after the first dose. The median (50%) onset time of relief was 35.9 hours.

Paediatric population
In a placebo-controlled clinical trial in which paediatric patients (n=49/group) were administered mometasone furoate 100 micrograms daily for one year, no reduction in growth rate was observed.

There are limited data available on the safety and efficacy of mometasone furoate in the paediatric population aged 3 to 5 years, and an appropriate dosage range cannot be established. In a study involving 48 children aged 3 to 5 years treated with intranasal mometasone furoate 50, 100 or 200 µg/day for 14 days, there were no significant differences from placebo in the mean change in plasma cortisol level in response to the tetracosactide stimulation test.

The European Medicines Agency has waived the obligation to submit the results of studies with mometasone furoate in all subsets of the paediatric population in seasonal and perennial allergic rhinitis (see section 4.2 for information on paediatric use).

5.2. Pharmacokinetic properties

Absorption

Mometasone furoate, administered as an aqueous suspension for nasal spray, has a systemic bioavailability of <1% in plasma, using a sensitive assay with a lower quantitation limit of 0.25 pg/ml.

Distribution

Not applicable, as mometasone is poorly absorbed via the nasal route.

Metabolism or biotransformation

The small amount that may be swallowed and absorbed undergoes extensive first-pass hepatic metabolism.

Elimination

Absorbed mometasone furoate is extensively metabolised and the metabolites are excreted in urine and bile.

5.3. Preclinical safety data

No toxicological effects unique to mometasone furoate have been demonstrated. All observed effects are typical of this class of compounds and are related to exaggerated pharmacological effects of glucocorticoids.

Preclinical studies demonstrate that mometasone furoate is devoid of androgenic, anti-androgenic, oestrogenic or anti-oestrogenic activity but, like other glucocorticoids, it exhibits some anti-uterotrophic activity and delays vaginal opening in animal models at high oral doses of 56 mg/kg/day and 280 mg/kg/day.

Like other glucocorticoids, mometasone furoate showed a clastogenic potential in vitro at high concentrations. However, no mutagenic effects are to be expected at therapeutically relevant doses.

In studies of reproductive function, subcutaneous mometasone furoate at 15 micrograms/kg prolonged gestation and prolonged and complicated labour, with a reduction in offspring survival and body weight, or weight gain. There was no effect on fertility.

Like other glucocorticoids, mometasone furoate is teratogenic in rodents and rabbits.

Effects noted were umbilical hernia in rats, cleft palate in mice and gallbladder agenesis, umbilical hernia, and flexed front paws in rabbits. There were also reductions in maternal weight gain, effects on foetal development (lower foetal body weight and/or delayed ossification) in rats, rabbits and mice, and reduced offspring survival in mice.

The carcinogenicity potential of inhaled mometasone furoate (aerosol with chlorofluorocarbon propellant and surfactant) at concentrations of 0.25 to 2.0 micrograms/l was investigated in 24-month studies in mice and rats. Typical glucocorticoid-related effects were observed, including

several non-neoplastic lesions. No statistically significant dose-response relationship was detected for any of the tumour types.

6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Dispersible cellulose (microcrystalline cellulose and carmellose sodium)
Glycerol
Polysorbate 80
Anhydrous citric acid
Sodium citrate
Benzalkonium chloride
Purified water

6.2. Incompatibilities

Not applicable

6.3. Shelf life

3 years
After first opening of the bottle: 2 months.

6.4. Special precautions for storage

Store below 30ºC.
Do not freeze.

6.5. Nature and contents of container

NASOALDO 50 micrograms/spray, nasal spray, suspension, comes in high-density polyethylene bottles containing 18 g (140 doses) of the product, provided with a manual spray pump and nasal applicator with attached lid.

6.6. Special precautions for disposal and other handling

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

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8 MARKETING AUTHORISATION NUMBER

07563/09627/NMR/2022

9 DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

27-07-2022

10 DATE OF REVISION OF THE TEXT

10/2017

11 DOSIMETRY (IF APPLICABLE)

Not applicable

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not applicable