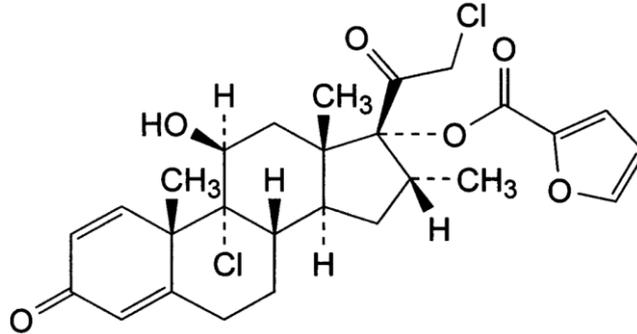


SENSEASE NASAL ALLERGY RELIEF NASAL SPRAY**NAME OF THE MEDICINE**

Mometasone furoate

Chemical Name: 9,21-dichloro-11 β -hydroxy-16 α -methyl-3,20-dioxopregna-1,4-17-yl furan-2-carboxylate

Structural Formula:



Molecular Formula: $C_{27}H_{30}Cl_2O_6$

Molecular Weight: 521.4

CAS Registry Number: 83919-23-7

DESCRIPTION

Mometasone furoate is a white or almost white powder that is practically insoluble in water, soluble in acetone and in methylene chloride, slightly soluble in ethanol (96 per cent). Sensease Nasal Allergy Relief is a white suspension.

The pKa and log P for mometasone furoate is 13.02 and 3.59 respectively. The pH of the drug product is 4.3 to 4.9.

In addition to mometasone furoate, Sensease Nasal Allergy Relief also contains citric acid monohydrate, glycerol, microcrystalline cellulose, carmellose sodium, polysorbate 80, sodium citrate, purified water and benzalkonium chloride 0.02% as preservative.

PHARMACOLOGY

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

Systemic bioavailability of mometasone furoate was investigated in 24 healthy volunteers following intranasal administration of 400 μ g of the suspension. Mometasone was detectable in plasma (at sporadic time points) in only 4 of the 24 subjects, despite the use of a sensitive assay with a limit of quantitation of 50 pg/mL. Thus, there are no relevant pharmacokinetic data for this dosage form. The study demonstrates, however, that the bioavailability of mometasone following intranasal administration is low.

Systemic effects were not detected in adults, adolescents or children following the administration of mometasone furoate aqueous nasal spray.

Mometasone furoate suspension is very poorly absorbed from the gastrointestinal tract, and the small amount that may be swallowed and absorbed undergoes extensive first-pass metabolism prior to excretion in urine and bile.

In studies utilising nasal antigen challenge, mometasone nasal spray has shown anti-inflammatory activity in both the early- and late-phase allergic responses. This has been demonstrated by decreases (vs placebo) in histamine and eosinophil activity and reductions (vs baseline) in eosinophils, neutrophils and epithelial cell adhesion proteins.

Pharmacokinetics

Sensease Nasal Allergy Relief 50 µg and the innovator exhibit similar rate and extent of absorption, and the 90% confidence intervals for the ratio of AUC_t and C_{max} were found to be between 85.4–100.6% and 95.8–110.2% respectively.

CLINICAL TRIALS

In a clinical study comparing Sensease Nasal Allergy Relief 50 µg with the US reference product, the efficacy of the two products was assessed in patients with seasonal allergic rhinitis. The assessment was based on the change in mean reflective Total Nasal Symptom Scores (TNSS, range: 0–12) from baseline after 2 weeks of drug treatment.

The results of the study showed that both mometasone nasal spray and the reference product provided significantly ($p < 0.05$) greater reduction in mean reflective TNSS than placebo. No significant difference was found between the mean change from baseline TNSS scores for the two products ($p = 0.8914$), and the actual difference in LS mean change from baseline was within $\pm 50\%$ of the drug effect size (reference TNSS minus placebo TNSS). Due to the narrow equivalence bounds in relation to the variability of the TNSS data, caused by the relatively large placebo effect, the 90% confidence interval (CI) of the difference between the two products was not completely within the equivalence bounds (-0.29, +0.29). Thus the pre-specified equivalence criteria were not met.

However, a secondary analysis showed that the ratio (%) of means (Mometasone/Reference) for the change in mean reflective TNSS was 101% and the 90% CI was 86–117%, within 80–125%. This additional analysis can be used to suggest support for clinical equivalence of the two products.

A qualitative and quantitative analysis was carried out on the US reference product and the Australian reference product and these two products were shown to be similar.

Allergic Rhinitis

An adult clinical program evaluated the efficacy and safety of mometasone in the prophylaxis and treatment of seasonal allergic rhinitis and the treatment of perennial allergic rhinitis. Five Phase I clinical studies evaluated the systemic safety and local tolerability of mometasone. Other clinical studies included:

- One Phase II dose-ranging study conducted to determine the optimum dose for the Phase III program;
- Seven Phase III studies designed to assess the safety and efficacy of mometasone in treating seasonal allergic rhinitis for 28 days (including two studies which evaluated the prophylactic efficacy of mometasone in preventing the symptoms of seasonal allergic rhinitis, and two which evaluated inflammatory response markers following nasal provocation with allergens); and,
- Five Phase III studies designed to assess the safety and efficacy of mometasone in the treatment of perennial allergic rhinitis for 12 weeks. Four studies investigated the long term safety and maintenance of therapeutic effect of mometasone over 52 weeks; one perennial allergic rhinitis study was conducted in the elderly population; and three open-label perennial allergic rhinitis studies included a "variable-dose group" in which the dose of mometasone varied from 100 to 400 µg daily depending on symptoms.

During the course of the Phase II/III clinical program, 3120 patients (12 years of age and older) were treated with mometasone nasal spray. The majority (65%) of patients was treated with 200 µg once daily. The remainder received mometasone in a dose ranging from 50 µg to 800 µg once daily. A total of 712 patients were treated with mometasone for at least 6 months and 350 patients were treated for 12 months or longer.

The results of the efficacy studies demonstrated that mometasone nasal spray 200 µg/day was consistently superior to placebo in relieving the symptoms of both seasonal allergic rhinitis and perennial allergic rhinitis and was of comparable efficacy to other commonly used topical corticosteroid sprays. In the case of seasonal allergic rhinitis it is also superior to placebo in the

prophylaxis of symptoms. In the long-term studies in perennial allergic rhinitis there was no evidence of any diminution of its efficacy over time.

After the first dose of mometasone, clinically significant improvement of symptoms was achieved within 12 hours in 28% of a group of patients (n = 190) with seasonal allergic rhinitis (median = 36 hours). However, the full benefit of treatment may not be achieved in the first 48 hours, therefore, the patient should continue regular use to achieve full therapeutic benefit.

INDICATIONS

Sensease Nasal Allergy Relief is indicated for the prophylaxis or treatment of allergic rhinitis for up to six months in adults and children 12 years of age and over.

CONTRAINDICATIONS

Sensease Nasal Allergy Relief is contraindicated for use in:

- Patients with known hypersensitivity to mometasone furoate or any of the excipients
- Severe nasal infection, especially candidiasis
- Persons with haemorrhagic diathesis or with a history of recurrent nasal bleeding.

This product should not be used for:

- Treatment longer than 6 months without the advice of a doctor or pharmacist.
- In children under 12 years of age.

PRECAUTIONS

- Mometasone nasal spray should not be used in the presence of untreated localised infection involving the nasal mucosa.
- Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal surgery or trauma should not use a nasal corticosteroid until healing has occurred.
- Mometasone furoate tended to reverse the nasal mucosa closer to a normal histological phenotype. As with any long-term treatment, patients using Mometasone Nasal Spray 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, discontinuance of mometasone nasal spray therapy or appropriate treatment may be required. Persistence of nasopharyngeal irritation may be an indication for discontinuing mometasone nasal spray.
- Mometasone nasal spray should be used with caution, if at all, in patients with active or quiescent tuberculous infections of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections or ocular herpes simplex.
- Topical corticosteroids may be absorbed in amounts that can have systemic effects. Use of excessive doses may suppress HPA function. Physicians should be alert for evidence of systemic effects, especially in chronically treated patients.
- However, there is no evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression following prolonged treatment with mometasone nasal spray. Patients who are transferred from long-term administration of systemically active corticosteroids to mometasone nasal spray require careful attention. Systemic corticosteroid withdrawal in such patients may result in adrenal insufficiency for a number of months until recovery of HPA axis function. If these patients exhibit signs and symptoms of adrenal insufficiency, systemic corticosteroid administration should be resumed and other modes of therapy and appropriate measures instituted.
- During transfer from systemic corticosteroids to mometasone nasal spray, some patients may experience symptoms of withdrawal from systemically active corticosteroids (e.g. joint and/or muscular pain, lassitude and depression initially) despite relief from nasal symptoms and will require encouragement to continue mometasone nasal spray therapy. Such transfer may also

unmask pre-existing allergic conditions such as allergic conjunctivitis and eczema, previously suppressed by systemic corticosteroid therapy.

- 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.
- Following the use of intranasal aerosolised corticosteroids, instances of nasal septum perforation or increased intraocular pressure have been reported very rarely.
- If signs or symptoms of severe bacterial infection are observed (such as fever, persistent severe unilateral facial/tooth pain, orbital or peri-orbital facial swelling, or worsening of symptoms after an initial improvement), the patient should be advised to consult their doctor immediately. If these signs and symptoms are present at the time of diagnosis, treatment with mometasone should not be initiated.
- Improvement should be seen within 7 days of starting treatment. If improvement is not seen within 7 days of continuous use, treatment should be stopped and the advice of a doctor sought. If after 7 days of continuous use, symptoms have improved but are not adequately controlled then the advice of a pharmacist or doctor should be sought.
- If signs or symptoms of eye pain and/or visual disturbance develop, treatment should be ceased and the advice of a doctor sought.

Effects on Fertility

As with other corticosteroids, at exposure levels associated with marked signs of systemic corticosteroid toxicity, mometasone furoate had progestogenic effects on the female reproductive tract and mammary glands. However, fertility was unimpaired in a reproductive toxicity study carried out in rats.

Use in Pregnancy (Category B3)¹

In animal studies, small quantities of mometasone furoate were found to cross the placenta barrier. Like other corticosteroids, at doses associated with signs of systemic toxicity, mometasone furoate reduced foetal growth and was teratogenic in mice, rats and rabbits after subcutaneous or topical application. Higher doses had progestogenic effects in pregnant rats, associated with prolonged gestation, dystocia and reduced pup survival.

There are no adequate or well-controlled studies in pregnant women. Following intranasal administration of the maximum recommended clinical dose to patients, the plasma concentrations of mometasone furoate are not measurable; thus foetal exposure is expected to be negligible and the potential for reproductive toxicity is very low.

As with other nasal corticosteroid preparations, mometasone should be used in pregnant women only if the potential benefit justifies the potential risk to the mother or foetus. Infants born of mothers who received corticosteroids during pregnancy should be observed carefully for hypoadrenalism.

Mutagenicity

Mometasone furoate is not considered to be genotoxic. There was no evidence of mutagenicity in *in vitro* tests which included tests for reverse mutation in *Salmonella typhimurium* and *Escherichia coli* and forward gene mutation in a mouse lymphoma cell line. Limited evidence of clastogenicity was obtained in Chinese Hamster ovary cells, although this finding was not confirmed in a second assay in Chinese Hamster lung cells *in vitro*, nor *in vivo* assays including a chromosomal aberration assay in mouse spermatogonia, a mouse micronucleus assay or in a rat bone marrow clastogenicity assay. Mometasone furoate did not cause DNA damage in rat liver cells.

¹ Category B3: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

Use in Lactation

After oral administration, small quantities of mometasone furoate and/or its metabolites were transferred into the milk of lactating rats. There are no data on the extent of passage of mometasone furoate and/or its metabolites into the breast milk of women using mometasone furoate nasal spray. As with other nasal corticosteroid preparation, mometasone should be used by lactating mother only if the potential benefit justifies any potential risk to the infant.

Use in Children

Sensease Nasal Allergy Relief is not recommended for children under 12 years of age.

Controlled clinical trials have shown that intranasal corticosteroids may cause a reduction in growth velocity in children. 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 children 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 children receiving intranasal corticosteroids should be monitored routinely (e.g. via stadiometry). The potential growth effects of prolonged treatment should be weighed against the clinical benefits and the availability of safe and effective non-corticosteroid alternatives. To minimise the systemic effects of intranasal corticosteroids, each patient should be titrated to his/her lowest effective dose.

However, no reduction in growth velocity was observed in a placebo-controlled clinical trial in which paediatric patients were administered mometasone nasal spray 100 µg daily for one year. The effects of treatment for periods of greater than one year have not been studied.

INTERACTIONS WITH OTHER MEDICINES

There have been no formal interaction studies performed.

ADVERSE EFFECTS

Treatment-related local adverse events reported in clinical studies include headache (8%), epistaxis (i.e. frank bleeding, blood-tinged mucus and blood flecks) (8% vs placebo 5%), nasal burning (2% vs placebo 3%), and nasal irritation (2% vs placebo 2%) and nasal ulceration, which are typically observed with the use of a corticosteroid nasal spray. Epistaxis was generally self-limiting and mild in severity, and occurred at a comparable or lower incidence compared to other active control nasal corticoids used in clinical studies (up to 15%). The incidence of all other effects was comparable with that of placebo.

In the elderly, the more common adverse events were epistaxis (12% vs placebo 5%), headache (9% vs placebo 6%) and pharyngitis (4% vs placebo 2%).

In patients treated for nasal polyposis, the overall incidence of adverse events was comparable to placebo and similar to that observed for patients with allergic rhinitis.

DOSAGE AND ADMINISTRATION

DO NOT EXCEED THE RECOMMENDED DOSAGE. FOR INTRANASAL USE ONLY.

The effect of Sensease Nasal Allergy Relief is not immediate. Full therapeutic benefit takes a few days to develop. Dosage should be administered as directed and not be taken by the patients at will for symptomatic relief.

Administration to children 12 years and over should be aided by an adult to ensure correct use.

For prophylaxis or treatment of Allergic Rhinitis in Adults and Children 12 Years of Age and Over:

In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with mometasone is recommended two to four weeks prior to the anticipated start of the pollen season.

The maximum daily dose of Sensease Nasal Allergy Relief is TWO sprays per nostril ONCE a day.

The recommended dose for prophylaxis and treatment is two sprays (50 µg/spray) in each nostril once daily (total daily dose 200 µg). Once symptoms are controlled, reducing the dose to one spray in each nostril (total daily dose 100 µg) may be effective for maintenance.

After the first dose of mometasone, clinically significant improvement of symptoms was achieved within 12 hours in 28% of a group of patients (n = 190) with seasonal allergic rhinitis (median = 36 hours). However, the full benefit of treatment may not be achieved in the first 48 hours, therefore, the patient should continue regular use to achieve full therapeutic benefit.

Instructions to patients

Shake container well before each use. **Do not** pierce the nasal applicator. After the initial priming of the Sensease Nasal Allergy Relief pump (10 actuations, until a uniform spray is observed), each actuation delivers approximately 100 µg of mometasone furoate suspension, containing 50 µg of mometasone furoate. If the spray pump has not been used for 14 days or longer, it should be reprimed with 2 actuations, until a uniform spray is observed, before the next use.

Please note that this product should be discarded 60 days after opening. The 140 dose bottle pack may supply more than 60 days treatment depending on the recommended dose. However, this product must be discarded 60 days after opening.

Cleaning your nasal spray

It is important to clean your nasal spray regularly, otherwise it may not work properly. Remove the dust cap and gently pull off the nozzle. Wash the nozzle and dust cap in warm water and then rinse under a running tap. **Do not try to unblock the nasal applicator by inserting a pin or other sharp object as this will damage the applicator and cause you not to get the right dose of medicine.** Allow to dry in a warm place. Push the nozzle back onto the bottle and replace the dust cap. The spray will need to be re-primed with 2 sprays when first used after cleaning.

OVERDOSAGE

Contact the Poisons Information Centre on 13 11 26 (Australia) for advice on the management of overdose.

Because of the low systemic bioavailability of mometasone nasal spray, overdose is unlikely to require any therapy other than observation. Treatment can be reinitiated at the usual recommended dose.

Inhalation or oral administration of excessive doses of corticosteroids may lead to suppression of hypothalamic-pituitary-adrenal (HPA) axis function.

PRESENTATION AND STORAGE CONDITIONS

Sensease Nasal Allergy Relief: metered atomising pump unit containing mometasone furoate 50 µg/actuation.

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Bottles of 65 and 140 metered doses.

Not all pack sizes may be available.

Sensease Nasal Allergy Relief is intended for nasal inhalation. Each actuated spray contains 50 µg of mometasone furoate as the active ingredient.

Store below 25°C. Do not freeze.
After opening, please discard product after 60 days.

NAME AND ADDRESS OF THE SPONSOR

Apotex Pty Ltd
16 Giffnock Ave
Macquarie Park NSW 2113

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POISON SCHEDULE OF THE MEDICINE

S2: Pharmacy Medicine.

Date of first inclusion in the ARTG: 04 November 2014