

NOSATREX

Spray

Composition

Mometasone Furoate 0.05% w/w

Action

Mechanism of Action

Mometasone Nasal Spray 50 mcg is a corticosteroid demonstrating potent anti-inflammatory properties. The precise mechanism of corticosteroid action on allergic rhinitis 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 inflammation.

In two clinical studies utilizing nasal antigen challenge, Mometasone Nasal Spray, 50 mcg decreased some markers of the early- and late-phase allergic response. These observations included decreases (vs. placebo) in histamine and eosinophil cationic protein levels, and reductions (vs. baseline) in eosinophils, neutrophils, and epithelial cell adhesion proteins. The clinical significance of these findings is not known.

The effect of Mometasone Nasal Spray, 50 mcg on nasal mucosa following 12 months of treatment was examined in 46 patients with allergic rhinitis. There was no evidence of atrophy and there was a marked reduction in intraepithelial eosinophilia and inflammatory cell infiltration (e.g., eosinophils, lymphocytes, monocytes, neutrophils, and plasma cells).

Pharmacokinetics

Absorption

Mometasone furoate monohydrate administered as a nasal spray suspension has very low bioavailability (<1%) in plasma using a sensitive assay with a lower quantitation limit (LOQ) of 0.25 pcg/mL.

Distribution

The *in vitro* protein binding for Mometasone furoate was reported to be 98% to 99% in concentration range of 5 to 500 ng/mL.

Biotransformation

Studies have shown that any portion of a Mometasone furoate dose which is swallowed and absorbed undergoes extensive metabolism to multiple metabolites. There are no major metabolites detectable in plasma. Upon *in vitro* incubation, one of the minor metabolites formed is 6 β -hydroxy-mometasone furoate. In human liver microsomes, the formation of the metabolite is regulated by cytochrome P-450 3A4 (CYP3A4).

Elimination

Following intravenous administration, the effective plasma elimination half-life of Mometasone furoate is 5.8 hours. Any absorbed drug is excreted as metabolites mostly via the bile, and to a limited extent, into the urine.

Specific Populations

Hepatic Impairment

Administration of a single inhaled dose of 400 mcg Mometasone furoate to subjects with mild (n=4), moderate (n=4), and severe (n=4) hepatic impairment resulted in only 1 or 2 subjects in each group having detectable peak plasma concentrations of Mometasone furoate (ranging from 50 to 105 pcg/mL). The observed peak plasma concentrations appear to increase with severity of hepatic impairment, however, the numbers of detectable levels were few.

Renal Impairment

The effects of renal impairment on Mometasone furoate pharmacokinetics have not been adequately investigated.

Pediatric

Mometasone furoate pharmacokinetics have not been investigated in the pediatric population.

Gender

The effects of gender on Mometasone furoate pharmacokinetics have not been adequately investigated.

Race

The effects of race on Mometasone furoate pharmacokinetics have not been adequately investigated.

Indication

Treatment Of Allergic Rhinitis

NOSATREX[®] Nasal Spray is indicated for the treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis, in adults and pediatric patients 2 years of age and older.

Treatment Of Nasal Congestion Associated With Seasonal Allergic Rhinitis

NOSATREX Nasal Spray is indicated for the relief of nasal congestion associated with seasonal allergic rhinitis, in adults and pediatric patients 2 years of age and older.

Prophylaxis Of Seasonal Allergic Rhinitis

NOSATREX Nasal Spray is indicated for the prophylaxis of the nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years and older.

Treatment Of Nasal Polyps

NOSATREX Nasal Spray is indicated for the treatment of nasal polyps in patients 18 years of age and older.

Warnings and Precautions

Local Nasal Effects

Epistaxis

In clinical studies, epistaxis was observed more frequently in patients with allergic rhinitis with MOMETASONE Nasal Spray than those who received placebo .

Candida Infection

In clinical studies with MOMETASONE Nasal Spray 50 mcg, the development of localized infections of the nose and pharynx with *Candida albicans* has occurred. When such an infection develops, use of MOMETASONE Nasal Spray 50 mcg should be discontinued and appropriate local or systemic therapy instituted, if needed.

Nasal Septum Perforation

Instances of nasal septum perforation have been reported following the intranasal application of corticosteroids. As with any long-term topical treatment of the nasal cavity, patients using MOMETASONE Nasal Spray 50 mcg over several months or longer should be examined periodically for possible changes in the nasal mucosa.

Impaired Wound Healing

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septum 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.

Hypersensitivity Reactions

Hypersensitivity reactions including instances of wheezing may occur after the intranasal administration of Mometasone furoate monohydrate. Discontinue MOMETASONE Nasal Spray if such reactions occur.

Immunosuppression

Persons who are on drugs which 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 non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, 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. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

Corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculous infection of the respiratory tract, or in untreated fungal, bacterial, systemic viral infections, or ocular herpes simplex because of the potential for worsening of these infections.

Hypothalamic-Pituitary-Adrenal Axis Effect

Hypercorticism And Adrenal Suppression

When intranasal steroids are used at higher than recommended dosages or in susceptible individuals at recommended dosages, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of MOMETASONE Nasal Spray should be discontinued slowly, consistent with accepted procedures for discontinuing oral corticosteroid therapy.

Effect On Growth

Corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Monitor the growth routinely of pediatric patients receiving MOMETASONE Nasal Spray. To minimize the systemic effects of intranasal corticosteroids, including MOMETASONE Nasal Spray, titrate each patient's dose to the lowest dosage that effectively controls his/her symptoms .

Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. MOMETASONE Nasal Spray 50 mcg, like other corticosteroids, should be used during pregnancy only if the potential benefits justify the potential risk to the fetus. Experience with oral corticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses suggests that rodents are more prone to teratogenic effects from corticosteroids than humans. In addition, because there is a natural increase in corticosteroid production during pregnancy, most women will require a lower exogenous corticosteroid dose and many will not need corticosteroid treatment during pregnancy.

Nursing Mothers

It is not known if Mometasone furoate is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be used when MOMETASONE Nasal Spray, 50 mcg is administered to nursing women.

Pediatric Use

The safety and effectiveness of MOMETASONE Nasal Spray 50 mcg for allergic rhinitis in children 12 years of age and older have been established. Use of MOMETASONE Nasal Spray 50 mcg for allergic rhinitis in pediatric patients 2 to 11 years of age is supported by safety and efficacy data from clinical studies. Seven hundred and twenty (720) patients 3 to 11 years of age with allergic rhinitis were treated with Mometasone furoate nasal spray 50 mcg (100 mcg total daily dose) in controlled clinical trials. Twenty-eight (28) patients 2 to 5 years of age with allergic rhinitis were treated with

Mometasone furoate nasal spray 50 mcg (100 mcg total daily dose) in a controlled trial to evaluate safety. Safety and effectiveness of MOMETASONE Nasal Spray 50 mcg for allergic rhinitis in children less than 2 years of age have not been established.

Adverse Reactions

Systemic and local corticosteroid use may result in the following:

- Epistaxis, ulcerations, *Candida albicans* infection, impaired wound healing.
- Cataracts and glaucoma
- Immunosuppression
- Hypothalamic-pituitary-adrenal (HPA) axis effects, including growth reduction.

Post-Marketing Experience

The following adverse reactions have been identified during the post-marketing period for MOMETASONE Nasal Spray 50 mcg: nasal burning and irritation, anaphylaxis and angioedema, disturbances in taste and smell and nasal septal perforation. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Drug Interactions

Inhibitors Of Cytochrome P450 3A4

Studies have shown that Mometasone furoate is primarily and extensively metabolized in the liver of all species investigated and undergoes extensive metabolism to multiple metabolites. *In vitro* studies have confirmed the primary role of cytochrome CYP 3A4 in the metabolism of this compound. Co-administration with ketoconazole, a potent CYP 3A4 inhibitor, may increase the plasma concentrations of Mometasone furoate

Contraindications

Contraindicated in patients with known hypersensitivity to Mometasone furoate .

Dosage & Administration

Administer NOSATREX Nasal Spray 50 mcg by the intranasal route only. Prior to initial use of NOSATREX Nasal Spray, 50 mcg, the pump must be primed by actuating ten times or until a fine spray appears. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by actuating two times, or until a fine spray appears.

Treatment Of Allergic Rhinitis

Adults And Adolescents 12 Years Of Age And Older:

The recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis is 2 sprays (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg).

Children 2 To 11 Years Of Age:

The recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis is 1 spray (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 100 mcg).

Treatment Of Nasal Congestion Associated With Seasonal Allergic Rhinitis

Adults And Adolescents 12 Years Of Age And Older:

The recommended dose for treatment of nasal congestion associated with seasonal allergic rhinitis is two sprays (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg).

Children 2 To 11 Years Of Age:

The recommended dose for treatment of nasal congestion associated with seasonal allergic rhinitis is one spray (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 100 mcg).

Prophylaxis Of Seasonal Allergic Rhinitis

Adults And Adolescents 12 Years Of Age And Older:

The recommended dose for prophylaxis treatment of nasal symptoms of seasonal allergic rhinitis is 2 sprays (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg).

In patients with a known seasonal allergen that precipitates nasal symptoms of seasonal allergic rhinitis, prophylaxis with NOSATREX Nasal Spray (200 mcg/day) is recommended 2 to 4 weeks prior to the anticipated start of the pollen season.

Treatment Of Nasal Polyps

Adults 18 Years Of Age And Older:

The recommended dose for the treatment of nasal polyps is 2 sprays (50 mcg of Mometasone furoate in each spray) in each nostril twice daily (total daily dose of 400 mcg). A dose of 2 sprays (50 mcg of Mometasone furoate in each spray) in each nostril once daily (total daily dose of 200 mcg) is also effective in some patients.

Overdose

There are no data available on the effects of acute or chronic overdose with MOMETASONE Nasal Spray 50 mcg. Because of low systemic bioavailability, and an absence of acute drug-related systemic findings in clinical studies, overdose is unlikely to require any therapy other than observation. Intranasal administration of 1600 mcg (4 times the recommended dose of MOMETASONE Nasal Spray 50 mcg for the treatment of nasal polyps in patients 18 years of age and older) daily for 29 days, to healthy human volunteers, showed no increased incidence of adverse events. Single intranasal doses up to 4000 mcg and oral inhalation doses up to 8000 mcg have been studied in human volunteers with no adverse effects reported. Chronic over dosage with any corticosteroid may result in signs or symptoms of hypercorticism. Acute overdosage with this dosage form is unlikely since one bottle of MOMETASONE Nasal Spray 50 mcg contains approximately 8500 mcg of Mometasone furoate.

Presentation**Nosatrex Spray**

Microdoser bottle 100 Metered Actuations