DESCRIPTION Mometasone furoate monohydrate, the active component of NASONEX Nasal Spray, 50 mcg, is an anti-inflammatory corticosteroid having the chemical name, 9,21-Dichloro-118,17-dihydroxy-16cr-methyl-pregna-1,4-dien-3,20-dione 17-(2 furoate) monohydrate, and the following chemical structure:

Mometacynthac/Lo<sub>2</sub>-H<sub>2</sub>O<sub>2</sub>-H<sub>2</sub>O<sub>3</sub>-H<sub>2</sub>O<sub>4</sub>-D<sub>4</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>4</sub>-H<sub>2</sub>O<sub>4</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>4</sub>-H<sub>2</sub>O<sub>5</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<sub>2</sub>O<sub>5</sub>-H<su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CLINICAL PHARMACOLOGY NASONEX Nasal Spray, 50 mcg is a corticosteroid demonstrating anti-inflammatory properties. The precise mechanism of corticosteroid demonstrating 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 (eg., mast cells, eosinophis, neutrophis, macrophages, and lymphocytes) and mediators (eg., histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation.

In two clinical studies utilizing nasal antigen challenge, NASONEX Nasal Spray, 50 mcg decreased some markers of the early- and late-phase allergic response. These observations included decreases (so 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 NASONEX 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 eosinophila and inflammatory cell infiltration (eg. eosinophils, lymphocytes, monocytes, neutrophils, and plasma cells).

Pharmacokinetics: Absorption: Mometasone furoate monohydrate administered as a nasal spray is virtually undetectable in plasma from adult and pediatric subjects despite the use of a sensitive assay with a lower quantitation limit (LOO) of 50 pcg/mL.

Distribution: The in vitro protein binding for mometasone furoate was recorded to be 98% to 99%, in conceptration arone of 5 to 500 norlm.

quantitation limit (LOQ) of 50 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.

\*Metabolism: 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 68-hydroxy-mometasone furoate. In human liver microsomes, the formation of the metabolite is regulated by cytochrome P-450 3A4 (CYP3A4).

\*\*Elimitation: Collegation Liverapore admissipation 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

is excreted as metabolites mostly via the bile, and to a limited extent, into the urine.

Special Populations: The effects of renal impairment, hepatic impairment, age, or gender on mometasone furoate pharmacokinetics have not been adequately investigated.

Pharmacodynamics: Three clinical pharmacology studies have been conducted in humans to assess the effect of NASONEX Nasal Spray, 50 mcg at various doses on adrenal function. In one study, daily doses of 200 and 400 mcg of NASONEX Nasal Spray, 50 mcg and 10 mg of prednisone were compared to placebo in 64 patients with altergic rhinitis. Adrenal function before and after 36 consecutive days of treatment was assessed by measuring plasma cortisol levels following a 6-hour Cortrosyn (ACTH) inition and by measuring 24-hour urinary-free cortisol levels. NASONEX Nasal Spray, 50 mcg, at both the 200- and 400-mcg dose, was not associated with a statistically significant decrease in mean plasma cortisol levels post-Cortrosyn infusion or a statistically significant decrease in the 24-hour urinary-free cortisol levels compared to placebo. A statistically significant decrease in the mean plasma cortisol levels post-Cortrosyn infusion and 24-hour urinary-free cortisol levels made to the prediction of the proposition of the placebo.

A second study assessed adrenal response to NASONEX Nasal Spray, 50 mcg (400 and 1600 mcg/day), prednisone (10 mg/day), and placebo, administered for 29 days in 48 male volunteers. The 24-hour plasma cortisol area under the curve (AUC.<sub>2.0.1</sub>) during and after an 8-hour Cortrosyn infusion and 24-hour urinary-free cortisol levels were determined at baseline and after 29 days of treatment. No statistically significant differences of adrenal function were observed with NASONEX Nasal Spray, 50 mcg compared to placebo.

A third study evaluated single, rising doses of NASONEX Nasal Spray, 50 mcg compared to placebo.

adrenal function were observed with NASONEX Nasal Spray, 50 mcg compared to placebo.

A third study evaluated single, rising doses of NASONEX Nasal Spray, 50 mcg (1000, 2000, and 4000 mcg/day), orally administered mometasone furoate (2000, 4000, and 8000 mcg/day), orally administered dexamethasone (200, 400, and 800 mcg/day), and placebo (administered at the end of each series of doses) in 24 male volunteers. Dose administrations were separated by at least 72 hours. Determination of serial plasma cortisol levels at 8 μm and for the 24-hour period following each treatment were used to calculate the plasma cortisol area under the curve (AUC<sub>0.28</sub>). In addition, 24-hour urinary-free cortisol levels were collected prior to initial treatment administration and during the period immediately following each dose. No statistically significant decreases in the plasma ortisol AUC, 8 μm cortisol levels, or 24-hour urinary-free cortisol levels were observed in volunteers treated with either NASONEX Nasal Spray, 50 mcg or oral mometasone, as compared with placebo treatment. Conversely, nearly all volunteers treated with the there doses of dexamethasone demonstrated abnormal 8 μm cortisol levels (defined as a cortisol level +10 mcg/dL), reduced 24-hour plasma AUC values, and decreased 24-hour urinary-free cortisol levels, as compared to placebo treatment.

AUC values, and decreased 24-hour uninary-free cortisol levels, as compared to placebo treatment. Three clinical pharmacology studies have been conducted in pediatric patients to assess the effect of mometasone furoate nasal spray, on the adrenal function at daily doses of 50, 100, and 200 mcg vs placebo. In one study, adrenal function before and after 7 consecutive days of treatment was assessed in 48 pediatric patients with allergic rhinitis (ages 6 to 11 years) by measuring morning plasma cortisol and 24-hour uninary-free cortisol levels. Mometasone furoate nasal spray, at all three doses, was not associated with a statistically significant decrease in mean plasma cortisol levels compared to placebo. In the second study, adrenal function before and after 14 consecutive days of treatment was assessed in 48 pediatric patients (ages 3 to 5 years) with allergic rhinitis by measuring plasma cortisol levels following a 30-minute Cortrosyn infusion. Mometasone furoate nasal spray, 50 mcg, at all three doses (50, 100, and 200 mcg/day), was not associated with a statistically significant decrease in mean plasma cortisol levels post-Cortrosyn infusion compared to placebo. All patients had a normal response to Cortrosyn. In the third study, adrenal function before and after up to 42 consecutive days of once-daily treatment was assessed in 52 patients with allergic rhinitis (ages 2 to 5 years), 28 of whom received mometasone furoate nasal spray, 50 mcg per nostril (total daily dose 100 mcg), by measuring morning plasma cortisol and 24-hour urinary-free cortisol levels. Mometasone furoate nasal spray was not associated with a statistically significant decrease in mean plasma cortisol levels consecutive days of more part of the placebo. All patients had a normal response to Cortrosyn in the placebo of the placebo. All patients had a statistically significant decrease in mean plasma cortisol levels consecutive days of once-daily treatment was assessed in 52 patients which allergic rhinitis and the placebo. Clinical Studies

Mometasone furoate nasal spray was not associated with a statistically significant decrease in mean plasma cortisol levels or a statistically significant decrease in the 24-hour urinary-free cortisol levels compared to placebo.

Clinical Studies: The efficacy and safety of NASONEX Nasal Spray, 50 mg in the prophylaxis and treatment of seasonal allergic rhinitis and the treatment of perennial allergic rhinitis have been evaluated in 18 controlled trials, and one uncontrolled clinical trial, in approximately 3000 adults (agost 17 to 85 years) and adolescents (ages 12 to 16 years). This included 1757 males and 1453 females, including a total of 283 adolescents (182 boys and 101 girls) with seasonal allergic or perennial allergic rhinitis, treated with NASONEX Nasal Spray, 50 mgg at doses ranging from 50 to 800 mgg/day. The majority of patients were treated with 200 mgg/day. These trials evaluated the total nasal symptom scores that included stuffiness, rhinorrhea, Itching, and sneezing. Patients treated with NASONEX Nasal Spray, 50 mgg, 200 mgg/day had a significant decrease in total nasal symptom scores compared to placebo-treated patients. No additional benefit was observed for mometasone furoate doses greater than 200 mgg/day. Atola of 350 patients have been treated with NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 1 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for 0 year or longer. The efficacy and safety of NASONEX Nasal Spray, 50 mgg for mgg to 11 years) have been evaluated in four controlled trials. This included approximately 990 pediatric patients ages 3 to 11 years, 50 mgg in the treatment of 10 patients with seas

INDICATIONS AND USAGE NASONEX Nasal Spray, 50 mcg 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. NASONEX Nasal Spray, 50 mcg is indicated for the prophylaxis of the nasal symptoms of seasonal allergic rhinitis in adult and adolescent patients 12 years and older. In patients with a known seasonal allergen that precipitates nasal symptoms of seasonal allergic rhinitis, initiation of prophylaxis with NASONEX Nasal Spray, 50 mcg is recommended 2 to 4 weeks prior to the anticipated start of the pollen season. Safety and effectiveness of NASONEX Nasal Spray, 50 mcg in pediatric patients less than 2 years of age have not been established.

**CONTRAINDICATIONS** Hypersensitivity to any of the ingredients of this preparation contraindicates its use.

WARNINGS The replacement of a systemic corticosteroid with a topical cor WARNINGS The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency and, in addition, some patients may experience symptoms of withdrawa! ie, joint and/or muscular pain, lassitude, and depression. Careful attention must be given when patients previously treated for prolonged periods with systemic corticosteroids are transferred to topical corticosteroids, with careful monitoring for acute adrenal insufficiency in response to stress. This is particularly important in those patients who have associated ashma or other clinical conditions where too rapid a decrease in systemic corticosteroid dosing may cause a severe exacerbation of their symptoms.

If recommended doses of intransal corticosteroids are exceeded or individuals are particularly sensitive or predisposed by vitrue of recent systemic steroid therapy, symptoms of hypercorticism may occur, including very rare cases of menstraul irregularities, canceliform lesions, and cushingoid features. If such changes occur, topical corticosteroids should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

continued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

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 nonimmune 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 affects 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 globin (VZIG) 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.

PRECAUTIONS General: Intranasal corticosteroids may cause a reduction PRECAUTIONS General: intransasi conticosteriotis may cause a reduction in growth velocity when administered to pediatric patients (see PRECAU-TIONS, Pediatric Use section). In clinical studies with NASONEX Nasal Spray, 50 mog, the development of localized infections of the nose and pharynx with Candida albicars has occurred only rarely. When such an infection develops, use of NASONEX Nasal Spray, 50 mog should be discontinued and properties below the centrals between such that of the conductions are considered and provided and provi

ued and appropriate local or systemic therapy instituted, if needed.
Nasal corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculous infection of the respiratory tract, or in untreat ed fungal, bacterial, systemic viral infections, or ocular herpes simplex. Rarely, immediate hypersensitivity reactions may occur after the intranasal administration of mometasone furoate monohydrate. Extremely

Intranasal administration of momentasone furdate mononydrate. Extremely rare instances of wheezing have been reported.

Rare instances of nasal septum perforation and increased intraocular pressure have also been reported following the intranasal application of aerosolized corticosteroids. As with any long-term topical treatment of the nasal cavity, patients using NASONEX Nasal Spray, 50 mcg over several months or longer should be examined periodically for possible changes in

the nasal mucosa.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septum ulcers, nasal surgery, on nasal trauma should not use a nasal corticosteroid until healing has occurred Glaucoma and cataract formation was evaluated in one controlled study of 12 weeks' duration and one uncontrolled study of 12 months' duration in patients treated with NASONEY Nasal Spray, 50 mcg at 200 mcg/day, using intraocular pressure measurements and slit lamp examination. No significant Intracoular pressure ineasculenters and in situal repressure pressure measurements for the 141 NASONEX-treated patients. No individual NASONEX-treated patients in the 12-week study, as compared with 141 placebo-treated patients. No individual NASONEX-treated patient was noted to have developed a significant elevation in intracoular pressure or cataracts in this 12-week study. Likewise, no significant change the proposed patient was noted to have developed as implicant elevation in intracoular pressure or cataracts in this 12-week study. Likewise, no significant change from baseline was noted in the mean intraocular pressure measurements for the 139 NASONEX-treated patients in the 12-month study and again, no cataracts were detected in these patients. Nonetheless, nasal and inhaled cor-

ticosteroids have been associated with the development of glaucoma and/or cataracts. Therefore, close follow-up is warranted in patients with a change in vision and with a history of glaucoma and/or cataracts.

When nasal corticosteroids are used at excessive doses, systemic corti-

costeroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, NASONEX Nasal Spray, 50 mcg should be continued slowly, consistent with accepted procedu es for discontinuing Information for Patients: Patients being treated with NASONEX Nasal

Spray, 50 mgg should be given the following information and instructions. This information is intended to aid in the safe and effective use of this med-

**PHARMACIST** GIVE TO PATIENT Patient's Instructions for Use SHAKE WELL BEFORE EACH USE

NASONEX\* (mometasone furoate monohydrate) Nasal Spray, 50 mcg\*

Shake the bottle well before each use. Read complete instructions carefully and use only as directed.

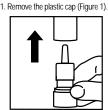


Figure 1

2. The very first time the spray is used, prime the pump by pressing downward on the shoulders of the white applicator using your forefinger and middle finger while supporting the base of the bottle with your thumb (Figure 2). Press down and release the pump ten times or until a fine spray appears. DO NOT spray into eyes. The pump is now ready to use. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by spraying two times or until a fine spray appears.



Figure 2

3. Gently blow your nose to clear the nostrils. Close one nostril. Tilt your head forward slightly and, keeping the bottle upright, carefully insert the nasal applicator into the other nostril (Figure 3). DO NOT spray directly onto nasal



Figure 3

4. For each spray, press firmly downward once on the shoulders of the white applicator using your forefinger and middle finger while sup-porting the base of the bottle with your thumb. Breathe gently inward through the nostril (Figure 4)



Figure 4

5. Then breathe out through the mouth.6. Repeat in the other nostril. 7. Wipe the nasal applicator with a clean tissue and replace the

**Pediatric Use:** Administration to young children should be aided by an adult. The **Patient's Instructions** for Use, Steps 1 to 7 should be fol-

The correct amount of medication in each spray can only be assured up to 120 sprays from the bottle even though the bottle is not completely empty. You should keep track of the number of sprays used from each bottle of NASONEX Nasal Spray, 50 mcg and discard the bottle after using 120 sprays.

Cleaning: Please see Applicator Cleaning Instructions on reverse.

Caution: NASONEX Nasal Spray, 50 mcg is formulated for once-daily dosing. You should use NASONEX Nasal Spray, 50 mcg only once daily at a regular interval. Since NASONEX Nasal Spray, 50 mcg is not intended to give rapid relief of your nasal symptoms, the prescribed dosage should not be increased by using more often than once daily in an attempt to increase its effectiveness. NASONEX Nasal Spray 50 mcg conattempt to increase its enectiveness.

NASONEX Nasal Spray, 50 mcg controls the underlying disorders responsible for your attacks so it is important that you use it regularly at the time recommended by your physician. Based on single-day studphysical is based on single-day stud-ies done in a park during pollen sea-son or in a controlled pollen expo-sure room, improvement in nasal symptoms of allergic rhinitis has been shown to occur within 11 hours after the first dose. In other studies that lasted up to 2 weeks, improvement in nasal symptoms of seasonal allergic rhinitis was shown to occur within 2 days after the first dose. The full benefit of NASONEX Medel Serve Entered is excelled. Nasal Spray, 50 mcg is usually achieved within 1 to 2 weeks.

NASONEX Nasal Spray, 50 mcg should not be sprayed into the eyes. Spraying NASONEX Nasal Spray, 50 mcg directly onto the nasal septum should be avoided.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Protect from light. When NASONEX Nasal Spray, 50 mcg is removed from its cardboard container, prolonged exposure of the product to direct light should be avoided. Brief exposure to light, as with nor-mal use, is acceptable. SHAKE WELL BEFORE EACH

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U.S. Patent No. D355,844 Rev. 6/03

ication. It is not a disclosure of all intended or possible adverse effects. Patients should use NASONEX Nasal Spray, 50 mog at regular intervals (once daily) since its effectiveness depends on regular use. Improvement in nasal symptoms of allergic rhinitis has been shown to occur within 11 hours after the first dose based on one single-dose, parallel-group study of patients in an outdoor "park" setting (park study) and one environmental exposure unit (EEU) study and within 2 days after the first dose in two randomized, double-blind, placebo-controlled, parallel-group seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks after initiation of dosing. Patients should take the medication as directed and should not increase the prescribed dosage by using it more than once a day in an attempt to increase its effectiveness. Patients should contact their physician if symptoms do not improve, or if the condition worsens. To assure proper use of this nasal spray, and to attain maximum benefit, patients should read and follow the accompanying Patient's Instructions for Use carefully. Administration to young children should be aided by an adult. Patients should be cautioned not to spray NASONEX Nasal Spray, 50 mcg into the eyes or directly onto the nasal septum.

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles, and patients should also be advised that if they are exposed, medical advice should be sought without delay.

\*\*Carcinogenesis\*\* Mutanenesis\*\* Imnairment of Entitibre\*\* in a 2-wear.

also be advised that if they are exposed, medical advice should be sought without delay.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year carcinogenicity study in Sprague Dawley rats, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 67 mcg/kg (approximately 3 and 2 times the maximum recommended daily intranasal dose in adults and children, respectively, on a mcg/m² basis). In a 19-month carcinogenicity study in Swiss CD-1 mice, mometasone furoate demonstrated no statistically significant increase in the incidence of tumors at inhalation doses up to 160 mcg/kg (approximately 3 and 2 times the maximum recommended daily intranasal dose in adults and children, respectively, on a mcg/m² basis).

Mometasone furoate increased chromosomal aberrations in an in vitro Chinese hamster ovary-cell assay, but did not increase chromosomal aberrations in an in vitro Chinese hamster lung cell assay. Mometasone furoate was not mutagenic in the Ames test or mouse-lymphoma assay, and was not clastogenic in an in vivo mouse micronucleus assay and a rat bone marrow chromosomal aberration assay or a mouse male germ-cell chromosomal aberration assay, Mometasone furoate also did not induce unscheduled DNA synthesis in vivo in rat hepatocytes.

In reproductive studies in rats, impairment of fertility was not produced by subcutaneous doses up to 15 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m² basis).

mended daily intranasal dose in adults on a mcg/m² basis).

Pregnancy: Teratogenic Effects: Pregnancy Category C: When administered to pregnant mice, rats, and rabbits, mometasone furoate increased fetal malformations. The doses that produced malformations also decreased fetal growth, as measured by lower fetal weights and/or delayed ossification. Mometasone furoate also caused dystocia and related complications when administered to rats during the end of pregnancy.

In mice, mometasone furoate caused cleft palate at subcutaneous doses of 60 mcg/kg and above (approximately equivalent to the maximum recommended daily intranasal dose in adults on a mcg/m² basis). Fetal survival was reduced at 180 mcg/kg (approximately 4 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). No toxicity was observed at 20 mcg/kg (less than the maximum recommended daily intranasal dose of adults on a mcg/m² basis). In rats, mometasone furoate produced umbilical hernia at topical dermal doses of 600 mcg/kg and above (approximately 25 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). A dose of 300 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). A dose of 300 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). The state of the maximum recommended daily intranasal dose in adults on a mcg/m² basis). No toxicity was observed at 20 mcg/kg (approximately 25 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). The dose of 300 mcg/kg and above (approximately 25 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis) produced delays in ossification, but no malformations.

300 mcg/kg (approximately 10 times the maximum recommended daily intransal dose in adults on a mcg/m² basis) produced delays in ossification, but no malformations.

In rabbits, mometasone furoate caused multiple malformations (eg. flexed front paws, galibladder agenesis, umbilical hemia, hydrocephaly) at topical dermal doses of 150 mcg/kg and above (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). In an oral study, mometasone furoate increased resorptions and caused cleft palate and/or head malformations (hydrocephaly or domed head) at 700 mcg/kg (approximately 55 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). At 2800 mcg/kg (approximately 230 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis), most litters were aborted or resorbed. No toxicity was observed at 140 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). When rats received subcutaneous doses of mometasone furoate throughout pregnancy or during the later stages of pregnancy. T5 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m² basis) caused prolonged and difficult labor and reduced the number of live births, birth weighf, and early pup survival. Similar effects were not observed at 7.5 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m² basis).

There are no adequate and well-controlled studies in pregnant women. NASONEX Nasal Spray, 50 mcg, like other corticosteroids, should be used during pregnancy only if the potential benefits justify the potential freisk to the fetus. Experience with oral corticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses suggests that rodents are more rone to testopace in effects from corticosteroids than humans. In addition,

relus. Experience with oral corticosterious since mer introduction in prat-macologic, 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 preg-nancy, most women will require a lower evogenous corticosteroid dose and many will not need corticosteroid treatment during pregnancy.

Nonteratogenic Effects: Hypoadrenalism may occur in infants born to women receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

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 NASONEX Nasal Spray, 50 mcg is administered

Pediatric Use: Controlled clinical studies have shown intranasal cortico Pediatric Use: Controlled clinical studies have shown intransal cortico-steroids may cause a reduction in growth velocity in pediatric patients. This effect has been observed in the absence of laboratory evidence of hypothal-amic-pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic conticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with intransal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with intransal corticosteroids has not been adequately studied. unknown. The potential for "catch up" growth following discontinuation of reatment with intransact corticosteroids has not been adequately studied. The growth of pediatric patients receiving intransact corticosteroids, including NASONEX Nasal Spray, 50 mcg should be monitored routinely (eg., via stadiometry). The potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of safe and effective noncorticosteroid treatment alternatives. To minimize the systemic effects of intransact corticosteroids, including NASONEX Nasal Spray, 50 mcg, each patient should be titrated to his/her lowest effective dose. Seven hundred and twenty (720) patients 3 to 11 years of age were treated with mometasone furoate nasal spray, 50 mcg (100 mcg total daily dose) in controlled clinical trials (see CLINICAL PHARMACOLOSY, Chincal Studies section). Twenty-eight (28) patients 2 to 5 years of age were treated with mometasone furoate nasal spray, 50 mcg (100 mcg total daily dose) in a controlled trial to evaluate safety (see CLINICAL PHARMACOLOGY, Pharmacokinetics section). Safety and effectiveness in children less than 2 years of age have not been established.

A clinical study has been conducted for 1 year in pediatric patients (ages 3 to 9 years) to assess the effect of NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity, No statistically significant effect on growth velocity was observed for NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity, No statistically significant effect on growth velocity was observed for NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity, No statistically significant effect on growth velocity was observed for NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity, No statistically significant effect on growth velocity was observed for NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose) on growth velocity, No statistically significant effect on growth velocity

Geriatric Use: A total of 203 patients above 64 years of age (age range 64 to 85 years) have been treated with NASONEX Nasal Spray, 50 mog for up to 3 months. The adverse reactions reported in this population were similar in type and incidence to those reported by younger patients.

(ADVERSE IREACTIONS) In controlled US and international clinical studies, a total of 3210 adult and adolescent patients ages 12 years and older received treatment with NASONEX Nasal Spray, 50 mcg at doses of 50 to 800 mcg/day. The majority of patients (n = 2103) were treated with 200 mcg/day. The majority of patients (n = 2103) were treated with 200 mcg/day. In controlled US and international studies, a total of 990 pediatric patients (ages 3 to 11 years) received treatment with NASONEX Nasal Spray, 50 mcg, at doses of 25 to 200 mcg/day. A total of 513 adult, adolescent, and pediatric patients for patients treated with NASONEX Nasal Spray, 50 mcg was comparable to patients treated with NASONEX Nasal Spray, 50 mcg was comparable to patients treated with the vehicle placebo. Also, adverse events did not differ significantly based on age, sex, or race. Three percent or less of patients in clinical trials discontinued treatment because of adverse events; this rate was similar for the vehicle and active comparators. All adverse events (regardless of relationship to treatment) reported by 5% or more of adult and adolescent patients ages 12 years and older who received NASONEX Nasal Spray, 50 mcg, 100 mcg/day in clinical trials vs placebo and that were more common with NASONEX Nasal Spray, 50 mcg than placebo, are displayed in the table below.

ADVERSE EVENTS FROM CONTROLLED CLINICAL TRIALS IN ADVERSE REACTIONS In controlled US and international clinical studies

ADVERSE EVENTS FROM CONTROLLED CLINICAL TRIALS IN SEASONAL ALLERGIC AND PERENNIAL ALLERGIC RHINITIS (PERCENT OF PATIENTS REPORTING)

	Adult and Adolescent Patients 12 years and older		Pediatric Patients Ages 3 to 11 years	
	NASONEX 200 mcg (n = 2103)	VEHICLE PLACEBO (n = 1671)	NASONEX 100 mcg (n = 374)	VEHICLE PLACEBO (n = 376)
Headache	26	22	17	18
Viral Infection	14	11	8	9
Pharyngitis	12	10	10	10
Epistaxis/Blood- Tinged Mucus	11	6	8	9
Coughing	7	6	13	15
Upper Respirato Tract Infection	ry 6	2	5	4
Dysmenorrhea	5	3	1	0
Musculoskeletal	Pain 5	3	1	1
Sinusitis	5	3	4	4
Vomiting	1	1	5	4

Sinusitis 5 3 4 4 4

Vomiting 1 1 5 5 4

Other adverse events which occurred in less than 5% but greater than or equal to 2% of mometasone furoate adult and adolescent patients (ages 12 years and older) treated with 200-mcg doses (regardless of relationship to treatment), and more frequently than in the placebo group included: arthraigla, asthma, bronchlits, chest pain, conjunctivitis, diarrhea, dyspepsia, earache, flu-like symptoms, myalgia, nausea, and rhinitis.

Other adverse events which occurred in less than 5% but greater than or equal to 2% of mometasone furoate pediatric patients ages 3 to 11 years treated with 100-mcg doses vs placebo (regardless of relationship to treatment) and more frequently than in the placebo group included: diarrhea, nasal inritation, otitis media, and wheezing.

The adverse event (regardless of relationship to treatment) reported by 5% of pediatric patients ages 2 to 5 years who received NASONEX Nasal Spray, 50 mcg, 100 mcg/day in a clinical trial vs placebo including 56 subjects (28 each NASONEX Nasal Spray, 50 mcg and placebo) and that was more common with NASONEX Nasal Spray, 50 mcg and placebo) and that was more common with NASONEX Nasal Spray, 50 mcg than placebo, included: upper respiratory tract infection (7% vs. 0%, respectively). The other adverse event which occurred in less than 5% but greater than or equal to 2% of mometasone furoate pediatric patients ages 2 to 5 years treated with 100-mcg doses vs placebo (regardless of relationship to treatment) amore frequently than in the placebo group included: skin trauma.

Rare cases of nasal ulcers and nasal and oral candidiasis were also reported in patients treated with NASONEX Nasal Spray, 50 mcg, primarily in patients treated with NASONEX Nasal Spray, 50 mcg, primarily in patients treated with NASONEX Nasal Spray, 50 mcg, primarily in patients treated for longer than 4 weeks.

In postmarketing surveillance of this product, cases of nasal burning and irritation, anaphylaxis and anagloedema, and rare cases of nasal septal

(reported very/rarely.)

OVERDOSAGE There are no data available on the effects of acute or chronic overdosage with NASONEX 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 (8 times the recommended dose of NASONEX Nasal Spray, 50 mcg) daily for 29 days, to healthy human volunteers, was well tolerated with no increased incidence of adverse events. Single intranasal doses up to 4000 mcg have been studied in human volunteers with no adverse effects reported. Single oral doses up to 8000 mcg have been studied in human volunteers with no adverse effects reported. Chronic overdosage with any corticosteroid may result in signs or symptoms of hypercorticism (see PRECAUTIONS). Acute overdosage with this dosage form is unlikely since one bottle of NASONEX Nasal Spray, 50 mcg contains approximately 8500 mcg of mometasone furroate.

DOSAGE AND ADMINISTRATION Adults and Children 12 Years of Age DUSAGE AND ADMINISTRATION Adults and children 12 Years of Age and Older: The usual recommended dose for prophylaxis and treatment of the nasal symptoms of seasonal allergic rhinitis and treatment of the nasal symptoms of perennial allergic rhinitis is two sprays (50 mcg of mometasone furrate in each spray) in each nostril once daily (fotal daily dose of 200 mcg.) In patients with a known seasonal allergen that precipitates nasal symptoms of seasonal allergic rhinitis, prophylaxis with NASONEX Nasal Spray, 50 mcg (200 mcg/day) is recommended 2 to 4 weeks prior to the anticipated start of the pollen season.

Children 2 to 11 Years of Age: The usual recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis.

Children 2 to 11 Years of Age: The usual recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic thinitis is one spray (50 mog of mometasone furoate in each spray) in each nostril once daily (total daily dose of 100 mcg).

Improvement in nasal symptoms of allergic rhinitis has been shown to
occur within 11 hours after the first dose based on one single-dose, parallel-group study of patients in an outdoor "park" setting (park study) and one
environmental exposure unit (EEU) study and within 2 days after the first
dose in two randomized, double-blind, placebo-controlled, parallel-group
seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks. Patients should use NASONEX Nasal Spray, 50 mcg only
once daily at a regular interval.

Prior to initial use of NASONEX Nasal Spray, 50 mcg, the pump must be
primed by actuating ten times or until a fine spray appears. The pump my
estored 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.

Directions for Use: Illustrated Patient's instructions for Use accompany
each package of NASONEX Nasal Spray, 50 mcg.

Directions for Cleaning: Illustrated Applicator Cleaning Instructions
accompany each package of NASONEX (Masal Spray, 50 mcg.

HOW SUPPLIED NASONEX (mometasone furoate monohydrate) Nasal

HOW SUPPLIED NASONEX (mometasone furoate monohydrate) Nasal Spray, 50 mcg is supplied in a white, high-density, polyethylene bottle fitted with a white metered-dose, manual spray pump, and teal-green cap. It contains 17 g of product formulation, 120 sprays, each delivering 50 mcg of mometasone furoate per actuation. Supplied with Patients Instructions for Use (NDC 0085-1197-01).

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Protect from light.

When NASONEX Nasal Spray, 50 mcg is removed from its cardboard container, prolonged exposure of the product to direct light should be avoided. Brief exposure to light, as with normal use, is acceptable. SHAKE WELL BEFORE EACH USE.

PHARMACIST **GIVE TO PATIENT** 

**APPLICATOR CLEANING** INSTRUCTIONS

Please see reverse for Patient's Instructions for Use.

**NASONEX**<sup>®</sup> (mometasone furoate monohydrate) Nasal Spray, 50 mcg\*

1. To clean the nasal applicator, remove the



2. Pull gently upward on the white nasal applicator so that it comes

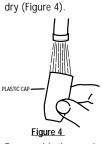


Figure 2

3. Soak the nasal applicator in cold tap water and/or rinse both ends of the nasal applicator under cold tap water and dry



4. Rinse the plastic cap under cold water and



5. Reassemble the nasal applicator being certain the pump stem is reinserted into the applicator's center hole (Figure 5).



PUMP STEM Figure 5

6. Reprime the pump by pressing downward on the shoulders of the white applicator using your forefinger and middle finger while supporting the base of the bottle with your thumb. Press down and release the pump two times or until a fine spray appears. DO NOT spray into eyes. The pump is now ready to use. The pump may be stored unused for up to 1 week without repriming. If unused for more than 1 week, reprime by spraying two times or until a fine spray appears



7. Replace the plastic cap (Figure 7).



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