DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

DEC 8 2000

Mary Jane Nehring
Director, Marketed Products Support
Worldwide Regulatory Affairs
Schering Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033

NDA #20-762
Nasonex® (mometasone furoate monohydrate) Nasal Spray
MACMIS # 9001

Dear Ms. Nehring:

This letter concerns Schering Corporation's (Schering) dissemination of promotional materials for Nasonex (mometasone furoate monohydrate) Nasal Spray. Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials that contain false or misleading presentations, in violation of the Federal Food, Drug, and Cosmetic Act and implementing regulations. The specific materials are identified as physician letter NX0895, sales aids NX0747 and NX0876. Our specific objections follow.

Unsupported Claims of Superiority

Promotional material is false or misleading if it contains a drug comparison that represents or suggests that a drug is safer or more effective than another drug when such has not been demonstrated by substantial evidence.

Your letter and sales aids contain two graphical presentations comparing mometasone furoate (Nasonex) with fluticasone propionate (FP) and placebo. One presentation is that of a bar graph depicting that more patients had complete or marked relief with Nasonex than with FP. The other graph shows that more patients had total nasal symptoms improve with Nasonex than with FP. These presentations are misleading because they suggest that Nasonex is more effective than FP when such has not been demonstrated by substantial evidence. In this case, your presentations are based on selected secondary endpoints from a study by Mandl, et al., referenced as "*Comparison of Once-Daily Mometasone Furoate (Nasonex®) and Fluticasone Propionate Aqueous Nasal Sprays for the Treatment of Perennial Rhinitis*", Annals of Allergy, Asthma, & Immunology,

79:370-379, 1997. The primary objective of the study was to compare the effectiveness and tolerability of Nasonex to placebo and to FP. The primary efficacy variable was the change from baseline in total AM plus PM nasal symptom score over the first 15 days of treatment based on patient diaries. For the primary efficacy variable, Nasonex was no different from FP. Thus, your suggestion that Nasonex is superior to FP is misleading.

DDMAC is concerned that, in spite of past regulatory action concerning similar violative superiority presentations based on the Mandl Study (untitled letter dated June 24, 1998), Schering continues to misleadingly suggest that Nasonex is clinically superior to FP.

Minimization of Risk Information and Lack of Fair Balance

Promotional material is false, lacking in fair balance, or otherwise misleading if it fails to provide sufficient emphasis for information relating to risks associated with the use of the product. Risk information should be presented with a prominence and readability reasonably comparable with the presentation of information relating to the effectiveness of the drug.

Nasonex's approved product labeling (PI) contains important risk information relating to the possibility of the occurrence of adrenal insufficiency if a topical corticosteroid is used to replace a systemic corticosteroid. This information appears in the WARNINGS section of the PI. In sales aid NX0876 this warning appears once, in small type on the back page. The placement and prominence of this risk information minimizes its importance. Furthermore, the presentation of the adverse event information is also not presented with a prominence and readability reasonably comparable to the presentation of efficacy claims, taking into account all techniques apt to achieve emphasis.

Requested Action

Schering should immediately discontinue these and all other promotional materials for Nasonex that contain the same or similar violations. We request that Schering respond, in writing, with its intent to comply with the above. This response should list similarly violative materials with a description of the method for discontinuation and the discontinuation date. DDMAC should receive this response by December 22, 2000.

If you have any questions or comments, you may contact me by facsimile at 301-594-6759 or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Room 17B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondences regarding this particular matter, please refer to MACMIS # 9001 in addition to the NDA number.

Sincerely,

/S/

Laurie Lenkel, R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

Schering®

Schering Laboratories

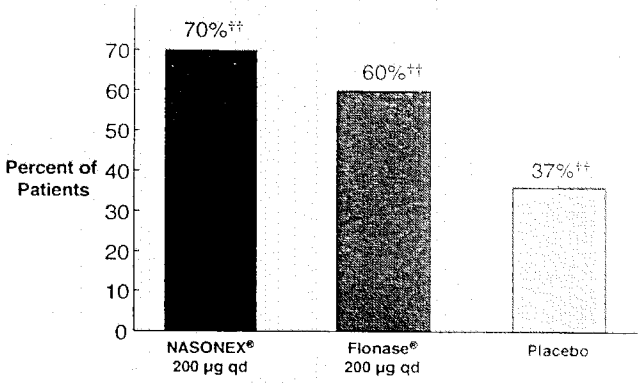
Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033-0530
Telephone (908) 298-4000

John Q. Sample, MD
123 Any Street
Suite 456
Anytown, US 12345

Dear Doctor Sample:

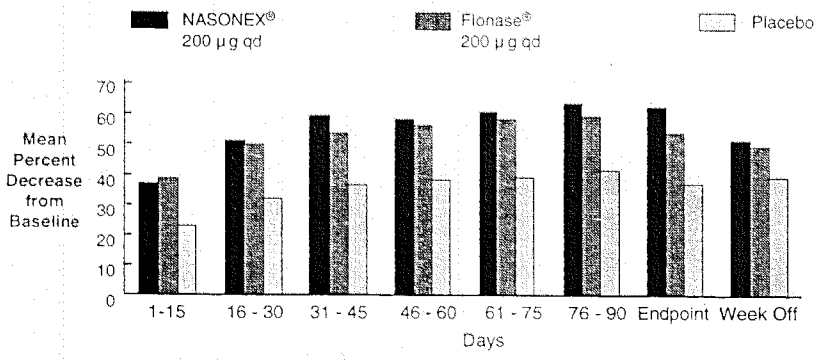
NASONEX® (mometasone furoate monohydrate) Nasal Spray, 50 mcg* can provide significant relief to your patients with perennial nasal allergy symptoms. A large clinical trial demonstrated the effectiveness of NASONEX® in the treatment of the nasal symptoms of perennial rhinitis.†

Patients With Complete or Marked Relief



††$P<0.01$ at all time points for NASONEX® & Flonase® relative to placebo.

Patient Evaluation of Total Nasal Symptoms



$P<0.01$ at all time points for NASONEX® & Flonase® relative to placebo.

Both NASONEX® and Flonase (fluticasone propionate) were superior to placebo in relieving nasal symptoms. NASONEX® was safe and well tolerated for the treatment of perennial rhinitis.

In clinical trials, using the recommended dose, the overall incidence of adverse events was comparable to vehicle placebo. The most commonly reported adverse events, not necessarily drug related, were, for NASONEX® and vehicle placebo, respectively: headache (17-26% vs 18-22%), viral infection (8-14% vs 9-11%), pharyngitis (10-12% vs 10%), epistaxis/blood-tinged mucus (8-11% vs 6-9%), and coughing (7-13% vs 6-15%).

WARNING: The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency.

As a leader in worldwide research and development of allergy products, we at Schering hope you will keep NASONEX® in mind when you consider prescribing a nasal corticosteroid spray for your patients with nasal allergies. Please see full Prescribing Information.

Sincerely,

Jason Spitz
Marketing Director, NASONEX®

*calculated on the anhydrous basis.

†Randomized, double-blind, placebo-controlled, multicenter study of 550 patients with perennial allergic rhinitis. Patients were treated for 12 weeks with either 200 mcg NASONEX® (2 sprays per nostril, once daily), 200 mcg fluticasone propionate (2 sprays per nostril, once daily), or placebo.

Flonase is a registered trademark of Glaxo Wellcome Inc.

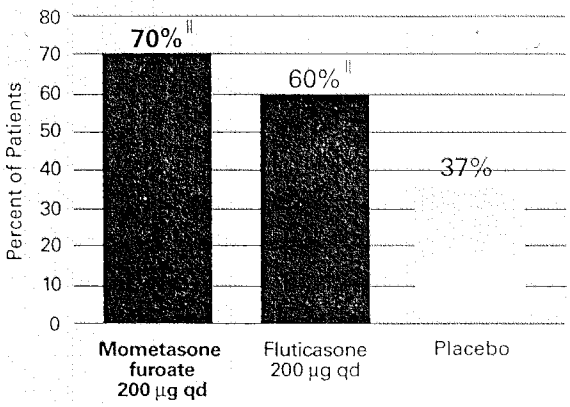
NX0895/24507904 10/00

FOR TREATMENT OF THE NASAL SYMPTOMS OF ALLERGIC RHINITIS

GROWING CONFIDENCE with Efficacy

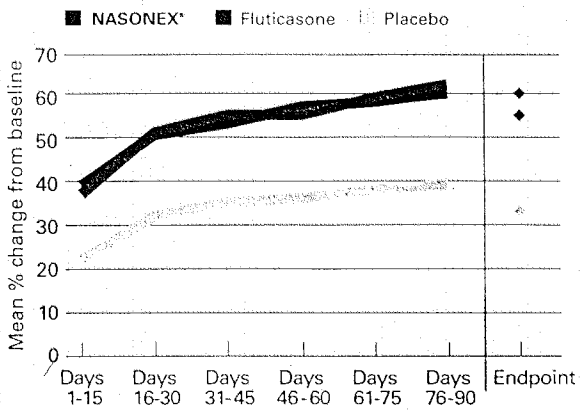
NASONEX® provides effective control of nasal allergy symptoms *in adults*[1†]

Patients with complete or marked relief as evaluated by physician



‖*P*<0.01 vs placebo

Patient evaluation of total nasal symptoms



P<0.01 at all timepoints for NASONEX® & Fluticasone relative to placebo

Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

SEE IMPORTANT SAFETY INFORMATION ON BACK COVER.

†Randomized, double-blind, placebo-controlled, multicenter study of 550 patients with perennial allergic rhinitis. Patients were treated for 12 weeks with either 200 µg NASONEX® (2 sprays per nostril, once daily), 200 µg fluticasone propionate (2 sprays per nostril, once daily), or placebo.

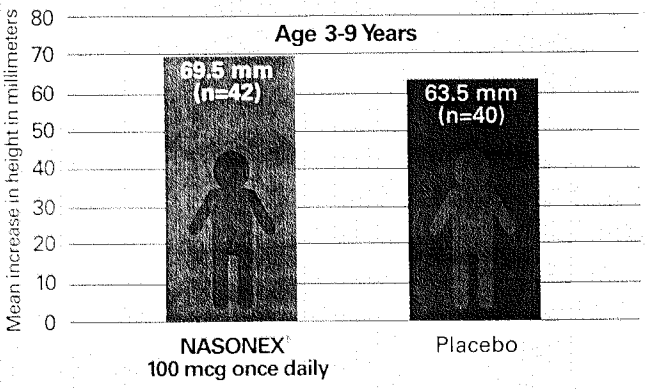
THE ONLY INTRANASAL STEROID FOR KIDS AS YOUNG AS 3 YEARS

GROWING CONFIDENCE in Pediatric Use

NASONEX®: No growth suppression in a 1-year, long-term study

- No impairment of growth in 98 children 3-9 years old with perennial allergic rhinitis[2†]
- Rate of growth of NASONEX® 100 mcg-treated patients (n=49) similar at all time points to placebo-treated patients (n=49) after 1 year

Mean increase in height over 1 year[2]



Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

Note: Controlled clinical studies have shown intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. The growth of pediatric patients receiving intranasal corticosteroids, including NASONEX® Nasal Spray, 50 mcg, should be monitored routinely (eg, via stadiometry). The potential of NASONEX® to cause growth suppression in susceptible patients or when given at higher doses cannot be ruled out.

†Randomized, placebo-controlled, double-blind, multicenter study assessed pediatric growth in 98 patients, 3-9 years of age, with perennial allergic rhinitis. Patients were treated for 1 year with either 100 mcg of NASONEX® (n=49) (1 spray per nostril, once daily) or placebo (n=49). Thirty-eight patients participated in the cosyntropin stimulation portion of the study for 1 year. No HPA-axis suppression was detected, and no impairment of growth was seen in NASONEX®-treated patients, as measured by stadiometer at baseline and at weeks 4, 8, 12, 26, 39, and 52.

NEGLIGIBLE SYSTEMIC ABSORPTION

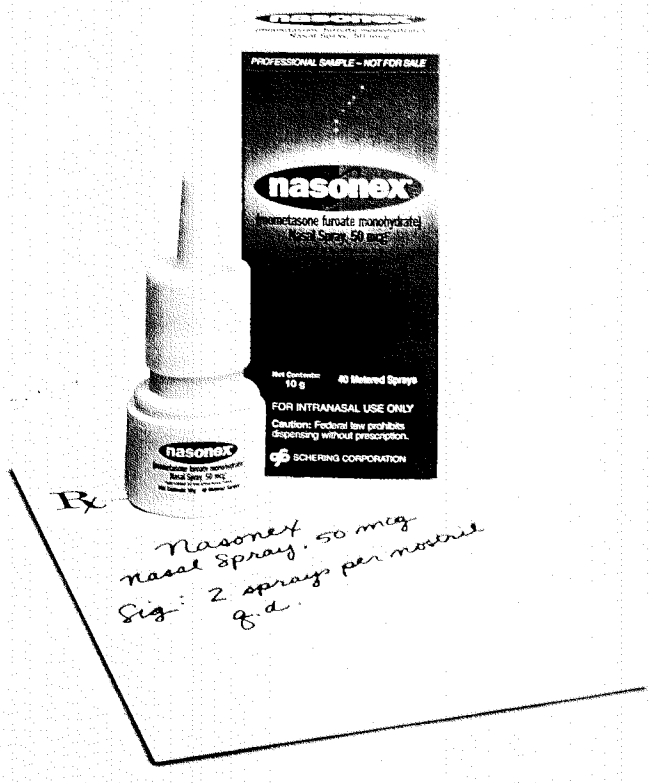
- Plasma concentrations virtually undetectable
- NASONEX® absolute bioavailability is ≤0.1%

Note: The clinical relevance of these data in the treatment of allergic rhinitis is not known.

NO HPA-AXIS SUPPRESSION

in clinical studies *in adults* with:

- Single rising doses of oral mometasone furoate up to **40 times** the recommended intranasal dose in healthy male volunteers[§]
- Single rising doses of up to **20 times** the recommended dose administered intranasally (200 mcg once daily) in healthy male volunteers[§]
- **8 times** the recommended dose after intranasal administration for 29 days in healthy male volunteers[‖]



Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

[§] A study evaluating single rising doses of NASONEX® (1000, 2000, 4000 mcg/day) and oral mometasone furoate (2000, 4000, 8000 mcg/day) showed no statistically significant decreases in plasma cortisol AUC, 8 AM cortisol, or 24-hour urinary-free cortisol levels vs placebo (n=24 healthy male volunteers).

[‖] A study evaluating the adrenal response of NASONEX® (400 and 1600 mcg/day) administered for 29 days showed no statistically significant differences in 24-hour plasma cortisol $AUC_{0\text{-}24}$, during and after an 8-hour Cortrosyn infusion, and 24-hour urinary-free cortisol levels compared to placebo (n=48 healthy male volunteers).

THE ONLY INTRANASAL STEROID FOR KIDS AS YOUNG AS 3 YEARS

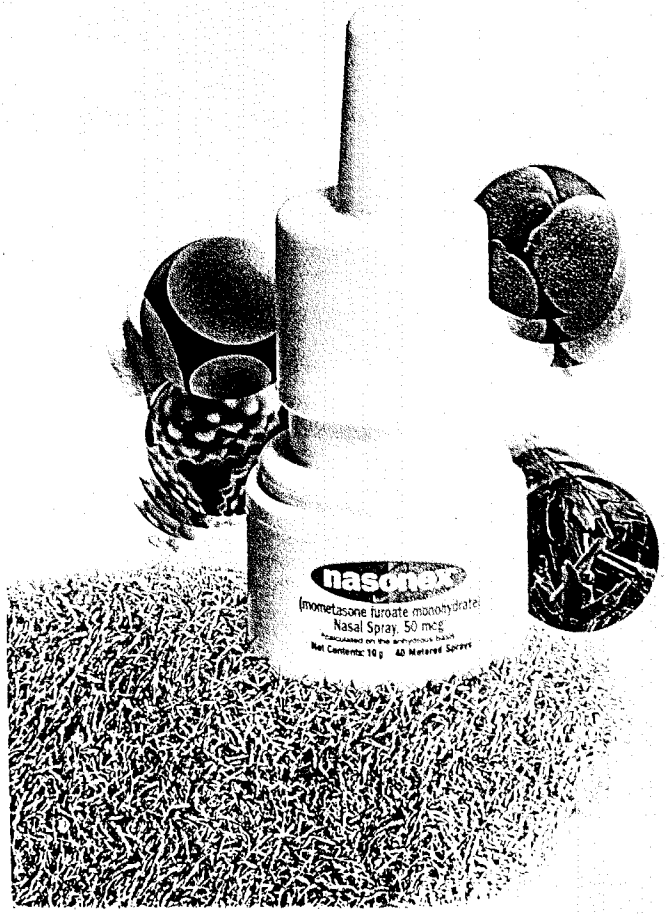
GROWING CONFIDENCE in NASONEX®

NASONEX® is the *only* available prescription nasal allergy spray with moisturizing glycerin†

NASONEX®	Flonase	Nasacort/ Nasacort AQ	Nasarel	Rhinocort/ Rhinocort Aqua	VANCENASE
YES	NO	NO	NO	NO	NO

In clinical trials, using the recommended dose, the overall incidence of adverse events was comparable to vehicle placebo. The most commonly reported adverse events, not necessarily drug related, were, for NASONEX® and vehicle placebo, respectively: headache (17-26% vs 18-22%), viral infection (8-14% vs 9-11%), pharyngitis (10-12% vs 10%), epistaxis/blood-tinged mucus (8-11% vs 6-9%), and coughing (7-13% vs 6-15%).

WARNING: The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency.



Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

†According to respective manufacturers' prescribing information.

Flonase (fluticasone propionate) is a registered trademark of Glaxo Wellcome Inc. Nasacort and Nasacort AQ are registered trademarks of Aventis Pharma. Nasarel (flunisolide) is a registered trademark of Dura Pharmaceuticals. Rhinocort and Rhinocort Aqua are registered trademarks of AstraZeneca. VANCENASE (beclomethasone dipropionate) is a registered trademark of Schering Corporation.

References: 1. Mandl MB, Nolop K, Lutsky BN, et al. Comparison of once-daily mometasone furoate (NASONEX®) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. *Ann Allergy Asthma Immunol.* 1997;79:370-378. **2.** Schenkel EJ, Skoner DP, Bronsky EA, et al. Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. *Pediatrics* [serial online]. February 1, 2000.

FOR DEMONSTRATION PURPOSES ONLY.
NOT TO BE LEFT WITH PHYSICIAN.
FURNISH FULL PRESCRIBING INFORMATION.

Schering®

ONLY NASONEX® IS FOR KIDS AS YOUNG AS 3 YEARS

For treatment of the nasal symptoms of allergic rhinitis with intranasal steroids

GROWING CONFIDENCE in NASONEX®

NASONEX® is the *only* available prescription nasal allergy spray with moisturizing glycerin†

NASONEX®	YES
Flonase	NO
Nasacort/ Nasacort AQ	NO
Nasarel	NO
Rhinocort/ Rhinocort Aqua	NO
Vancenase	NO

Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

†According to respective manufacturers' prescribing information.

Flonase (fluticasone propionate) is a registered trademark of Glaxo Wellcome Inc. Nasacort and Nasacort AQ are registered trademarks of Rhône-Poulenc Rorer. Nasarel (flunisolide) is a registered trademark of Dura Pharmaceuticals. Rhinocort and Rhinocort Aqua are registered trademarks of Astra Zeneca. Vancenase (beclomethasone dipropionate) is a registered trademark of Schering Corporation.

GROWING CONFIDENCE with Prophylaxis

NASONEX® is the *only* available nasal steroid indicated for prophylaxis of seasonal allergic rhinitis in adults and children 12 years and older

- NASONEX® can prevent most seasonal nasal allergy symptoms from ever starting
- Initiation of prophylaxis with NASONEX® is recommended 2 to 4 weeks prior to the anticipated start of the pollen season
- NASONEX® offers almost 3 times as many minimal symptom days† versus placebo[1‡]

Note: Controlled clinical studies have shown intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. The growth of pediatric patients receiving intranasal corticosteroids, including NASONEX® Nasal Spray, 50 mcg, should be monitored routinely (eg, via stadiometry). The potential of NASONEX® to cause growth suppression in susceptible patients or when given at higher doses cannot be ruled out.

WARNING: The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied by signs of adrenal insufficiency.

† Four nasal symptoms (rhinorrhea, nasal stuffiness/congestion, nasal itching, and sneezing) were scored on a 4-point scale from 0 to 3. Total nasal symptom score was calculated as the sums of these, so that it could range from 0 to 12. A nonminimal symptom day first occurred when diary morning and evening total nasal symptom score was ≥3.

‡ Multicenter, double-blind, randomized placebo-controlled, parallel-group. 330 patients ≥12 years old (efficacy population), ≥2-year history of moderate to severe allergic rhinitis. 3 groups, 8-week course, MFNS 200 mcg qd (n=114), BDP 168 mcg bid (n=112), placebo (n=104). Treatment began 4 weeks before estimated ragweed season. Primary comparison was between NASONEX® and placebo.

Reference: 1. Graft D, Aaronson D, Chervinsky P, et al. A placebo- and active-controlled randomized trial of prophylactic treatment of seasonal allergic rhinitis with mometasone furoate aqueous nasal spray. *J Allergy Clin Immunol.* 1996;98:724-731.

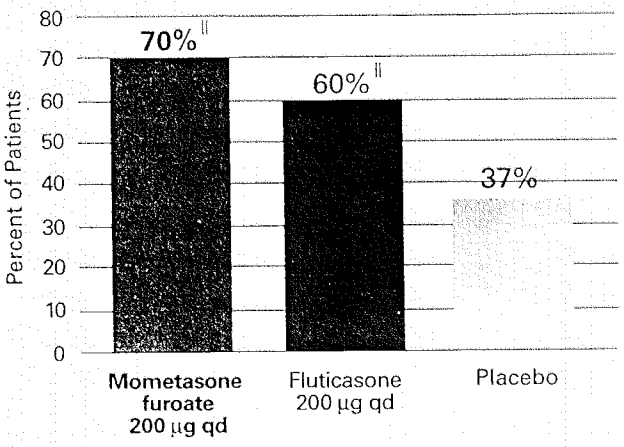
THE ONLY INTRANASAL STEROID FOR KIDS AS YOUNG AS 3 YEARS

GROWING CONFIDENCE

All Year Long

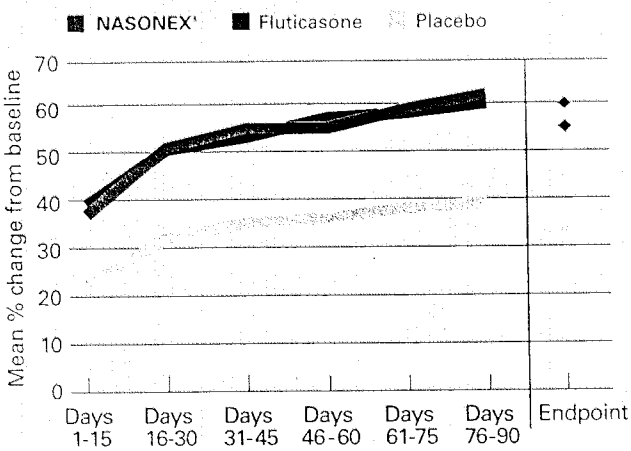
NASONEX® provides effective control of nasal allergy symptoms[1§]

Patients with complete or marked relief as evaluated by physician



‖P<0.01 vs placebo

Patient evaluation of total nasal symptoms



P<0.01 at all timepoints for NASONEX® & Fluticasone relative to placebo

NASONEX® Nasal Spray, 50 mcg, is indicated for treatment of the nasal symptoms of perennial allergic rhinitis in patients 3 years and older.

In clinical trials, using the recommended dose, the overall incidence of adverse events was comparable to vehicle placebo. The most commonly reported adverse events, not necessarily drug related, were, for NASONEX® and vehicle placebo, respectively: headache (17-26% vs 18-22%), viral infection (8-14% vs 9-11%), pharyngitis (10-12% vs 10%), epistaxis/blood-tinged mucus (8-11% vs 6-9%), and coughing (7-13% vs 6-15%).

Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

§ Randomized, double-blind, placebo-controlled, multicenter study of 550 patients with perennial allergic rhinitis. Patients were treated for 12 weeks with either 200 µg NASONEX® (2 sprays per nostril, once daily), 200 µg fluticasone propionate (2 sprays per nostril, once daily), or placebo.

Reference: 1. Mandl MB, Nolop K, Lutsky BN, et al. Comparison of once-daily mometasone furoate (NASONEX®) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. *Ann Allergy Asthma Immunol.* 1997;79:370-378.

NEGLIGIBLE SYSTEMIC ABSORPTION

- Plasma concentrations virtually undetectable
- NASONEX® absolute bioavailability is ≤0.1%

Note: The clinical relevance of these data in the treatment of allergic rhinitis is not known.

NO HPA-AXIS SUPPRESSION

No HPA-axis suppression detected in clinical studies with:

- Single rising doses of oral mometasone furoate up to **40 times** the recommended intranasal dose in healthy male volunteers†
- Single rising doses of up to **20 times** the recommended dose administered intranasally (200 mcg once daily) in healthy male volunteers†
- **8 times** the recommended dose after intranasal administration for 29 days in healthy male volunteers‡

†A study evaluating single rising doses of NASONEX® (1000, 2000, 4000 mcg/day) and oral mometasone furoate (2000, 4000, 8000 mcg/day) showed no statistically significant decreases in plasma cortisol AUC, 8 AM cortisol, or 24-hour urinary-free cortisol levels vs placebo (n=24 healthy male volunteers).

‡A study evaluating the adrenal response of NASONEX® (400 and 1600 mcg/day) administered for 29 days showed no statistically significant differences in 24-hour plasma cortisol $AUC_{0\text{-}24}$, during and after an 8-hour Cortrosyn infusion, and 24-hour urinary-free cortisol levels compared to placebo (n=48 healthy male volunteers).

THE ONLY INTRANASAL STEROID FOR KIDS AS YOUNG AS 3 YEARS

GROWING CONFIDENCE

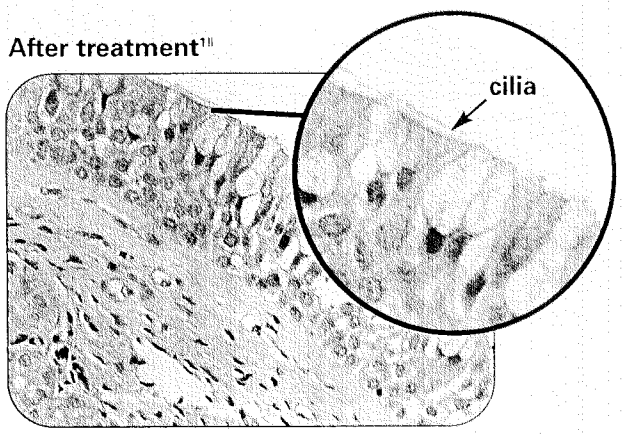
in Anti-inflammatory Action

NASONEX® has proven anti-inflammatory effect on the nasal mucosa

After 12 months of treatment with NASONEX®[1§]:

- No evidence of nasal atrophy
- Marked reduction in intraepithelial eosinophilia and other mucosal inflammatory cell infiltration in NASONEX® patients (n=46)
- No decrease in percentage of ciliated columnar epithelium

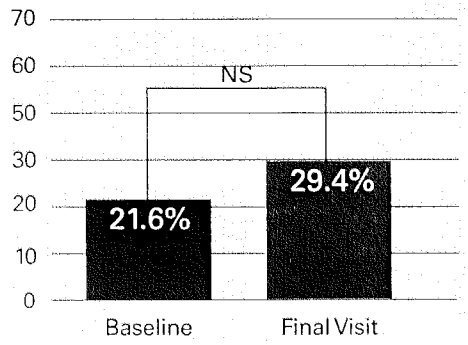
After treatment[1‖]



Biopsy demonstrates a marked reduction in intraepithelial eosinophilia and other inflammatory cell infiltration (eosinophils, monocytes, neutrophils, and plasma cells).

Note: The clinical relevance of these data in the treatment of allergic rhinitis is not known.

Percent of ciliated columnar epithelium in patients with perennial rhinitis.



No decrease in percentage of ciliated columnar epithelium at final visit.

[§]Multicenter, 12-month, uncontrolled study of patients with perennial allergic rhinitis. A total of 69 patients received 2 sprays of NASONEX® per nostril each day for a total of 200 mcg. Nasal biopsies were taken prior to and on completion of treatment. The biopsies of 46 patients were suitable for paired, blinded analysis. A group of 24 normal subjects not receiving the steroid medication or a vehicle control were included to assess the biopsy sampling technique.

[‖]Unretouched nasal biopsy pictures of a representative patient treated with NASONEX®.

Reference: 1. Minshall E, Ghaffar O, Cameron L, et al. Assessment by nasal biopsy of long-term use of mometasone furoate aqueous nasal spray (NASONEX®) in the treatment of perennial rhinitis. *Otolaryngol Head Neck Surg.* 1998;118:648-654.

Please see enclosed full Prescribing Information.

Once-a-day

nasonex®

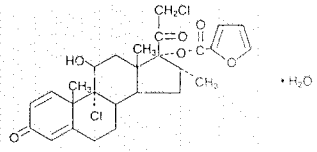
(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

NASONEX®
(mometasone furoate monohydrate)
Nasal Spray, 50 mcg*
FOR INTRANASAL USE ONLY

*calculated on the anhydrous basis

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-11β, 17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2 furoate) monohydrate, and the following chemical structure:



Mometasone furoate monohydrate is a white powder, with an empirical formula of $C_{27}H_{30}Cl_2O_6 \cdot H_2O$, and a molecular weight of 539.45. It is practically insoluble in water; slightly soluble in methanol, ethanol, and isopropanol; soluble in acetone and chloroform; and freely soluble in tetrahydrofuran. Its partition coefficient between octanol and water is greater than 5000.

NASONEX Nasal Spray, 50 mcg is a metered-dose, manual pump spray unit containing an aqueous suspension of mometasone furoate monohydrate equivalent to 0.05% w/w mometasone furoate calculated on the anhydrous basis; in an aqueous medium containing glycerin, microcrystalline cellulose and carboxymethylcellulose sodium, sodium citrate, 0.25% w/w phenylethyl alcohol, citric acid, benzalkonium chloride, and polysorbate 80. The pH is between 4.3 and 4.9.

After initial priming (10 actuations), each actuation of the pump delivers a metered spray containing 100 mg of suspension containing mometasone furoate monohydrate equivalent to 50 mcg of mometasone furoate calculated on the anhydrous basis. Each bottle of NASONEX Nasal Spray, 50 mcg provides 120 sprays.

CLINICAL PHARMACOLOGY NASONEX Nasal Spray, 50 mcg is a 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, eosinophils, neutrophils, 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 (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 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 eosinophilia 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 (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 6β-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.

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 allergic rhinitis. Adrenal function before and after 36 consecutive days of treatment was assessed by measuring plasma cortisol levels following a 6-hour Cortrosyn (ACTH) infusion 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 was detected in the prednisone treatment group compared to 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 ($AUC_{0\text{-}24}$), 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 (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 AM and for the 24-hour period following each treatment were used to calculate the plasma cortisol area under the curve ($AUC_{0\text{-}24}$). 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 cortisol AUC, 8 AM 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 three doses of dexamethasone demonstrated abnormal 8 AM 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.

Two 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 urinary-free cortisol levels. Mometasone furoate nasal spray, at all three doses, 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. 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.

Clinical Studies: The efficacy and safety of NASONEX Nasal Spray, 50 mcg 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 (ages 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 mcg at doses ranging from 50 to 800 mcg/day. The majority of patients were treated with 200 mcg/day. These trials evaluated the total nasal symptom scores that included stuffiness, rhinorrhea, itching, and sneezing. Patients treated with NASONEX Nasal Spray, 50 mcg, 200 mcg/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 mcg/day. A total of 350 patients have been treated with NASONEX Nasal Spray, 50 mcg for 1 year or longer.

The efficacy and safety of NASONEX Nasal Spray, 50 mcg in the treatment of seasonal allergic and perennial allergic rhinitis in pediatric patients (ages 3 to 11 years) have been evaluated in four controlled trials. This included approximately 990 pediatric patients ages 3 to 11 years (606 males and 384 females) with seasonal allergic or perennial allergic rhinitis treated with mometasone furoate nasal spray at doses ranging from 25 to 200 mcg/day. Pediatric patients treated with NASONEX Nasal Spray, 50 mcg (100 mcg total daily dose, 374 patients) had a significant decrease in total nasal symptom (congestion, rhinorrhea, itching, and sneezing) scores, compared to placebo-treated patients. No additional benefit was observed for the 200-mcg mometasone furoate total daily dose in pediatric patients (ages 3 to 11 years). A total of 163 pediatric patients have been treated for 1 year.

In patients with seasonal allergic rhinitis, NASONEX Nasal Spray, 50 mcg, demonstrated improvement in nasal symptoms (vs placebo) 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 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.

Prophylaxis of seasonal allergic rhinitis for patients 12 years of age and older with NASONEX Nasal Spray, 50 mcg, given at a dose of 200 mcg/day, was evaluated in two clinical studies in 284 patients. These studies were designed such that patients received 4 weeks of prophylaxis with NASONEX Nasal Spray, 50 mcg prior to the anticipated onset of the pollen season; however, some patients received only 2 to 3 weeks of prophylaxis. Patients receiving 2 to 4 weeks of prophylaxis with NASONEX Nasal Spray, 50 mcg demonstrated a statistically significantly smaller mean increase in total nasal symptom scores with onset of the pollen season as compared to placebo patients.

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 3 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 3 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 corticosteroid can be accompanied by signs of adrenal insufficiency and, in addition, some patients may experience symptoms of withdrawal; 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 asthma 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 intranasal corticosteroids are exceeded or if individuals are particularly sensitive or predisposed by virtue of recent systemic steroid therapy, symptoms of hypercorticism may occur, including very rare cases of menstrual irregularities, acneiform lesions, and cushingoid features. If such changes occur, topical corticosteroids should be discontinued 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. 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.

PRECAUTIONS General: Intranasal corticosteroids may cause a reduction in growth velocity when administered to pediatric patients (see **PRECAUTIONS, Pediatric Use** section). In clinical studies with NASONEX Nasal Spray, 50 mcg, the development of localized infections of the nose and pharynx with *Candida albicans* has occurred only rarely. When such an infection develops, use of NASONEX Nasal Spray, 50 mcg should be discontinued 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 untreated fungal, bacterial, systemic viral infections, or ocular herpes simplex.

Rarely, immediate hypersensitivity reactions may occur after the intranasal administration of mometasone furoate monohydrate. Extreme 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, or 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 NASONEX Nasal Spray, 50 mcg at 200 mcg/day, using intraocular pressure measurements and slit lamp examination. No significant change from baseline was noted in the mean intraocular pressure measurements for the 141 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 intraocular 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 corticosteroids 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 corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, NASONEX Nasal Spray, 50 mcg should be discontinued slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

Information for Patients: Patients being treated with NASONEX Nasal Spray, 50 mcg should be given the following information and instructions. This information is intended to aid in the safe and

effective use of this medication. It is not a disclosure of all intended or possible adverse effects. Patients should use NASONEX Nasal Spray, 50 mcg 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.

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, Mutagenesis, Impairment of Fertility: In a 2-year carcinogenicity study of Sprague Dawley rats, mometasone furoate demonstrated no statistically significant increase 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 of 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 4 and 3 times the maximum recommended daily intranasal dose in adults and children, respectively, on a mcg/m² basis).

At cytotoxic doses, mometasone furoate produced an increase in chromosome aberrations *in vitro* in Chinese hamster ovary-cell cultures in the nonactivation phase, but not in the presence of rat liver S9 fraction. Mometasone furoate was not mutagenic in the mouse-lymphoma assay and the *Salmonella/E. coli*/mammalian microsome mutation assay, a Chinese hamster lung cell (CHL) chromosomal-aberrations assay, an *in vivo* mouse bone-marrow erythrocyte-micronucleus assay, a rat bone-marrow clastogenicity assay, and the mouse male germ-cell clastogenicity 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). However, mometasone furoate caused prolonged gestation, prolonged and difficult labor, reduced offspring survival, and reduced maternal body weight gain at a dose of 15 mcg/kg.

Pregnancy: ***Teratogenic Effects: Pregnancy Category C:*** Mometasone furoate caused cleft palate in mice at subcutaneous doses of 60 mcg/kg and above (approximately 2 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). Offspring survival was reduced in the 180-mcg/kg group (approximately 4 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). No such effects were observed at 20 mcg/kg (less than the maximum recommended daily intranasal dose in adults on a mcg/m² basis).

In rabbits, mometasone furoate caused flexed front paws at a topical dermal dose of 150 mcg/kg (approximately 14 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis).

In rats, mometasone furoate produced umbilical hernia, cleft palate, and delayed ossification at a topical dermal dose of 600 mcg/kg (approximately 30 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis). At 1200 mcg/kg (approximately 60 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis), microphthalmia, umbilical hernias, and delayed ossification were observed in rat pups.

In these developmental studies, there were also reductions in maternal body weight gain and effects on fetal growth (lower fetal body weights and/or delayed ossification) in mice (60 and 180 mcg/kg), rabbits (150 mcg/kg), and rats (600 mcg/kg).

In an oral developmental study in rabbits, at 700 mcg/kg, (approximately 70 times the maximum recommended daily intranasal dose in adults on a mcg/m² basis), increased incidences of resorptions and malformations, including cleft palate and/or head malformations (hydrocephaly or domed head) were observed. Pregnancy failure was observed in most rabbits at 2800 mcg/kg (approximately 270 times 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 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.

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 to nursing women.

Pediatric Use: Controlled clinical studies have shown intranasal corticosteroids may cause a reduction in growth velocity in pediatric patients. This effect has been observed in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The long-term effects of this reduction in growth velocity associated with intranasal corticosteroids, including the impact on final adult height, are unknown. The potential for "catch up" growth following discontinuation of treatment with intranasal corticosteroids has not been adequately studied. The growth of pediatric patients receiving intranasal 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 intranasal 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. Safety and effectiveness in children less than 3 years of age have not been established.

A clinical study has been conducted for one 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 compared to placebo. No evidence of clinically relevant HPA axis suppression was observed following a 30-minute Cosyntropin infusion.

The potential of NASONEX Nasal Spray to cause growth suppression in susceptible patients or when given at higher doses cannot be ruled out.

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 mcg 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 REACTIONS In controlled US and International clinical studies, a total of 3210 adult and adolescent patients aged 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. In controlled US and International studies, a total of 990 pediatric patients (ages 3 to 11 years) received treatment with NASONEX, 50 mcg, at doses of 25 to 200 mcg/day. The majority of pediatric patients (720) were treated with 100 mcg/day. A total of 513 adult, adolescent, and pediatric patients have been treated for 1 year or longer. The overall incidence of adverse events for 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 aged 12 years and older who received NASONEX Nasal Spray, 50 mcg, 200 mcg/day and by pediatric patients ages 3 to 11 years 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 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 Respiratory Tract Infection	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

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

Other adverse events which occurred in less than 5% but greater or equal to 2% of mometasone furoate pediatric patients aged 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 irritation, otitis media, and wheezing.

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 for longer than 4 weeks.

In postmarketing surveillance of this product, cases of nasal burning and irritation and rare cases of nasal septal perforation have been reported.

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 furoate.

DOSAGE 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 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 NASONEX Nasal Spray, 50 mcg (200 mcg/day) is recommended 2 to 4 weeks prior to the anticipated start of the pollen season.

Children 3 to 11 Years of Age: The usual recommended dose for treatment of the nasal symptoms of seasonal allergic and perennial allergic rhinitis is one spray (50 mcg 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 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.

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

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 Patient's Instructions for Use (NDC 0085-1197-01).

Store between 2° and 25°C (36° and 77°F). 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.

Schering®

Schering Corporation
Kenilworth, NJ 07033 USA

Rev. 12/99

20109858T

For treatment of the nasal symptoms of allergic rhinitis with intranasal steroids

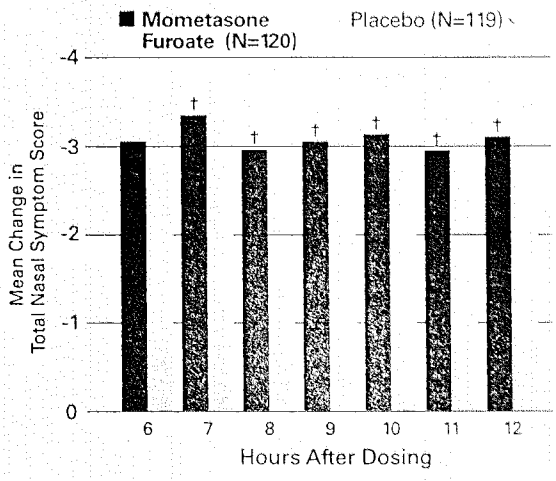
GROWING CONFIDENCE in Fast Relief

NASONEX® has onset of action within 11 hours in adults and children 12 years and older

- NASONEX® delivers fast relief

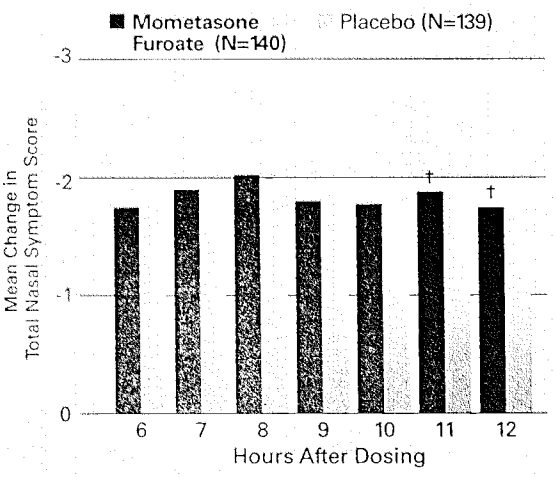
Rapid onset of action was proven in two studies, in two different environments—a "park" setting and an environmental exposure unit.†‡ Maximum relief achieved within 1 to 2 weeks.[1-2]

"Park" Study

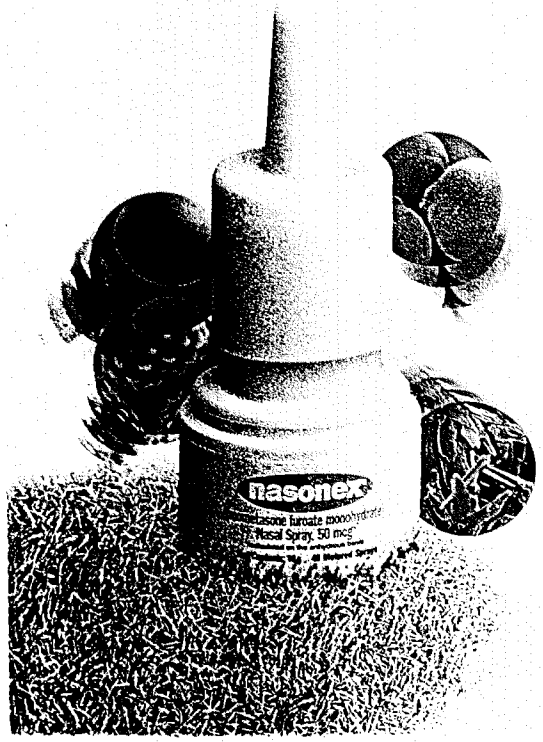


†Statistically significant difference between groups ($P<0.05$)

Environmental Exposure Unit



†Statistically significant difference between groups ($P<0.05$)



Once-a-day

nasonex®

(mometasone furoate monohydrate) Nasal Spray, 50 mcg*

*calculated on the anhydrous basis

†Randomized, double-blind, placebo-controlled, one-day outdoor park study of patients with symptoms of seasonal allergic rhinitis. One group received a single dose of NASONEX® 200 µg (n=120) or placebo (n=119).

‡Double-blind, placebo-controlled, randomized, single-dose, parallel-group comparison conducted at an environmental control unit with 279 patients treated with NASONEX® 200 µg or placebo.

References: 1. Data on file, Schering Corporation. 2. Berkowitz RB, Roberson S, Zora J, et al. Mometasone furoate nasal spray is rapidly effective in the treatment of seasonal allergic rhinitis in an outdoor (park) acute exposure setting. *Allergy and Asthma Proc.* 1999;20:167-172.

Please see enclosed full Prescribing Information.