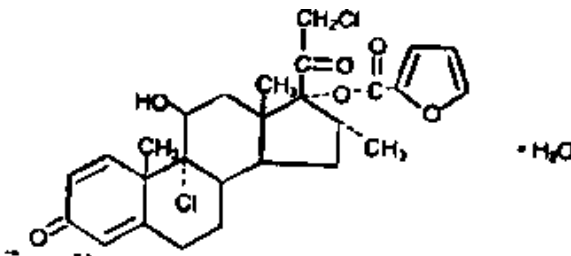


**PRODUCT
INFORMATION****NASONEX®****(mometasone furoate monohydrate)****Nasal Spray, 50 mcg*****FOR INTRANASAL USE ONLY**

*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-11 β ,17-dihydroxy-16 α -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

31 monohydrate equivalent to 50 mcg of mometasone furoate calculated on the
32 anhydrous basis. Each bottle of NASONEX Nasal Spray, 50 mcg provides 120
33 sprays.

34

35 **CLINICAL PHARMACOLOGY** NASONEX Nasal Spray, 50 mcg is a corticosteroid
36 demonstrating anti-inflammatory properties. The precise mechanism of
37 corticosteroid action on allergic rhinitis is not known. Corticosteroids have been
38 shown to have a wide range of effects on multiple cell types (eg, mast cells,
39 eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (eg,
40 histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation.

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

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

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

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

58 **Metabolism:** Studies have shown that any portion of a mometasone furoate
59 dose which is swallowed and absorbed undergoes extensive metabolism to multiple
60 metabolites. There are no major metabolites detectable in plasma. Upon in vitro
61 incubation, one of the minor metabolites formed is 6 β -hydroxy-mometasone furoate.

62 In human liver microsomes, the formation of the metabolite is regulated by
63 cytochrome P-450 3A4 (CYP3A4).

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

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

70 **Pharmacodynamics:** Three clinical pharmacology studies have been
71 conducted in humans to assess the effect of NASONEX Nasal Spray, 50 mcg at
72 various doses on adrenal function. In one study, daily doses of 200 and 400 mcg of
73 NASONEX Nasal Spray, 50 mcg and 10 mg of prednisone were compared to
74 placebo in 64 patients with allergic rhinitis. Adrenal function before and after 36
75 consecutive days of treatment was assessed by measuring plasma cortisol levels
76 following a 6-hour Cortrosyn (ACTH) infusion and by measuring 24-hour urinary-free
77 cortisol levels. NASONEX Nasal Spray, 50 mcg, at both the 200- and 400-mcg dose,
78 was not associated with a statistically significant decrease in mean plasma cortisol
79 levels post-Cortrosyn infusion or a statistically significant decrease in the 24-hour
80 urinary-free cortisol levels compared to placebo. A statistically significant decrease
81 in the mean plasma cortisol levels post-Cortrosyn infusion and 24-hour urinary-free
82 cortisol levels was detected in the prednisone treatment group compared to placebo.

83 A second study assessed adrenal response to NASONEX Nasal Spray, 50
84 mcg (400 and 1600 mcg/day), prednisone (10 mg/day), and placebo, administered
85 for 29 days in 48 male volunteers. The 24-hour plasma cortisol area under the curve
86 (AUC_{0-24}), during and after an 8-hour Cortrosyn infusion and 24-hour urinary-free
87 cortisol levels were determined at baseline and after 29 days of treatment. No
88 statistically significant differences of adrenal function were observed with NASONEX
89 Nasal Spray, 50 mcg compared to placebo.

90 A third study evaluated single, rising doses of NASONEX Nasal Spray, 50
91 mcg (1000, 2000, and 4000 mcg/day), orally administered mometasone furoate
92 (2000, 4000, and 8000 mcg/day), orally administered dexamethasone (200, 400,

93 and 800 mcg/day), and placebo (administered at the end of each series of doses) in
94 24 male volunteers. Dose administrations were separated by at least 72 hours.
95 Determination of serial plasma cortisol levels at 8 am and for the 24-hour period
96 following each treatment were used to calculate the plasma cortisol area under the
97 curve (AUC₀₋₂₄). In addition, 24-hour urinary-free cortisol levels were collected prior
98 to initial treatment administration and during the period immediately following each
99 dose. No statistically significant decreases in the plasma cortisol AUC, 8 AM cortisol
100 levels, or 24-hour urinary-free cortisol levels were observed in volunteers treated
101 with either NASONEX Nasal Spray, 50 mcg or oral mometasone, as compared with
102 placebo treatment. Conversely, nearly all volunteers treated with the three doses of
103 dexamethasone demonstrated abnormal 8 am cortisol levels (defined as a cortisol
104 level <10 mcg/dL), reduced 24-hour plasma AUC values, and decreased 24-hour
105 urinary-free cortisol levels, as compared to placebo treatment.

106 Three clinical pharmacology studies have been conducted in pediatric
107 patients to assess the effect of mometasone furoate nasal spray, on the adrenal
108 function at daily doses of 50, 100, and 200 mcg vs placebo. In one study, adrenal
109 function before and after 7 consecutive days of treatment was assessed in 48
110 pediatric patients with allergic rhinitis (ages 6 to 11 years) by measuring morning
111 plasma cortisol and 24-hour urinary-free cortisol levels. Mometasone furoate nasal
112 spray, at all three doses, was not associated with a statistically significant decrease
113 in mean plasma cortisol levels or a statistically significant decrease in the 24-hour
114 urinary-free cortisol levels compared to placebo. In the second study, adrenal
115 function before and after 14 consecutive days of treatment was assessed in 48
116 pediatric patients (ages 3 to 5 years) with allergic rhinitis by measuring plasma
117 cortisol levels following a 30-minute Cortrosyn infusion. Mometasone furoate nasal
118 spray, 50 mcg, at all three doses (50, 100, and 200 mcg/day), was not associated
119 with a statistically significant decrease in mean plasma cortisol levels post-Cortrosyn
120 infusion compared to placebo. All patients had a normal response to Cortrosyn. In
121 the third study, adrenal function before and after up to 42 consecutive days of once-
122 daily treatment was assessed in 52 patients with allergic rhinitis (ages 2 to 5 years),
123 28 of whom received mometasone furoate nasal spray, 50 mcg per nostril (total daily

124 dose 100 mcg), by measuring morning plasma cortisol and 24-hour urinary-free
125 cortisol levels. Mometasone furoate nasal spray was not associated with a
126 statistically significant decrease in mean plasma cortisol levels or a statistically
127 significant decrease in the 24-hour urinary-free cortisol levels compared to placebo.

128 **Clinical Studies:** The efficacy and safety of NASONEX Nasal Spray, 50 mcg
129 in the prophylaxis and treatment of seasonal allergic rhinitis and the treatment of
130 perennial allergic rhinitis have been evaluated in 18 controlled trials, and one
131 uncontrolled clinical trial, in approximately 3000 adults (ages 17 to 85 years) and
132 adolescents (ages 12 to 16 years). This included 1757 males and 1453 females,
133 including a total of 283 adolescents (182 boys and 101 girls) with seasonal allergic
134 or perennial allergic rhinitis, treated with NASONEX Nasal Spray, 50 mcg at doses
135 ranging from 50 to 800 mcg/day. The majority of patients were treated with 200
136 mcg/day. These trials evaluated the total nasal symptom scores that included
137 stuffiness, rhinorrhea, itching, and sneezing. Patients treated with NASONEX Nasal
138 Spray, 50 mcg, 200 mcg/day had a significant decrease in total nasal symptom
139 scores compared to placebo-treated patients. No additional benefit was observed for
140 mometasone furoate doses greater than 200 mcg/day. A total of 350 patients have
141 been treated with NASONEX Nasal Spray, 50 mcg for 1 year or longer.

142 The efficacy and safety of NASONEX Nasal Spray, 50 mcg in the treatment of
143 seasonal allergic and perennial allergic rhinitis in pediatric patients (ages 3 to 11
144 years) have been evaluated in four controlled trials. This included approximately 990
145 pediatric patients ages 3 to 11 years (606 males and 384 females) with seasonal
146 allergic or perennial allergic rhinitis treated with mometasone furoate nasal spray at
147 doses ranging from 25 to 200 mcg/day. Pediatric patients treated with NASONEX
148 Nasal Spray, 50 mcg (100 mcg total daily dose, 374 patients) had a significant
149 decrease in total nasal symptom (congestion, rhinorrhea, itching, and sneezing)
150 scores, compared to placebo-treated patients. No additional benefit was observed
151 for the 200-mcg mometasone furoate total daily dose in pediatric patients (ages 3 to
152 11 years). A total of 163 pediatric patients have been treated for 1 year.

153 In patients with seasonal allergic rhinitis, NASONEX Nasal Spray, 50 mcg,
154 demonstrated improvement in nasal symptoms (vs placebo) within 11 hours after the

155 first dose based on one single-dose, parallel-group study of patients in an outdoor
156 “park” setting (park study) and one environmental exposure unit (EEU) study, and
157 within 2 days in two randomized, double-blind, placebo-controlled, parallel-group
158 seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2
159 weeks after initiation of dosing.

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

169

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

180

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

183

184 **WARNINGS** The replacement of a systemic corticosteroid with a topical
185 corticosteroid can be accompanied by signs of adrenal insufficiency and, in addition,

186 some patients may experience symptoms of withdrawal; ie, joint and/or muscular
187 pain, lassitude, and depression. Careful attention must be given when patients
188 previously treated for prolonged periods with systemic corticosteroids are transferred
189 to topical corticosteroids, with careful monitoring for acute adrenal insufficiency in
190 response to stress. This is particularly important in those patients who have
191 associated asthma or other clinical conditions where too rapid a decrease in
192 systemic corticosteroid dosing may cause a severe exacerbation of their symptoms.

193 If recommended doses of intranasal corticosteroids are exceeded or if
194 individuals are particularly sensitive or predisposed by virtue of recent systemic
195 steroid therapy, symptoms of hypercorticism may occur, including very rare cases of
196 menstrual irregularities, acneiform lesions, and cushingoid features. If such changes
197 occur, topical corticosteroids should be discontinued slowly, consistent with
198 accepted procedures for discontinuing oral steroid therapy.

199 Persons who are on drugs which suppress the immune system are more
200 susceptible to infections than healthy individuals. Chickenpox and measles, for
201 example, can have a more serious or even fatal course in nonimmune children or
202 adults on corticosteroids. In such children or adults who have not had these
203 diseases, particular care should be taken to avoid exposure. How the dose, route,
204 and duration of corticosteroid administration affects the risk of developing a
205 disseminated infection is not known. The contribution of the underlying disease
206 and/or prior corticosteroid treatment to the risk is also not known. If exposed to
207 chickenpox, prophylaxis with varicella zoster immune globin (VZIG) may be
208 indicated. If exposed to measles, prophylaxis with pooled intramuscular
209 immunoglobulin (IG) may be indicated. (See the respective package inserts for
210 complete VZIG and IG prescribing information.) If chickenpox develops, treatment
211 with antiviral agents may be considered.

212

213 **PRECAUTIONS General:** Intranasal corticosteroids may cause a reduction in
214 growth velocity when administered to pediatric patients (see **PRECAUTIONS,**
215 **Pediatric Use** section). In clinical studies with NASONEX Nasal Spray, 50 mcg, the
216 development of localized infections of the nose and pharynx with *Candida albicans*

217 has occurred only rarely. When such an infection develops, use of NASONEX Nasal
218 Spray, 50 mcg should be discontinued and appropriate local or systemic therapy
219 instituted, if needed.

220 Nasal corticosteroids should be used with caution, if at all, in patients with
221 active or quiescent tuberculous infection of the respiratory tract, or in untreated
222 fungal, bacterial, systemic viral infections, or ocular herpes simplex.

223 Rarely, immediate hypersensitivity reactions may occur after the intranasal
224 administration of mometasone furoate monohydrate. Extreme rare instances of
225 wheezing have been reported.

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

231 Because of the inhibitory effect of corticosteroids on wound healing, patients
232 who have experienced recent nasal septum ulcers, nasal surgery, or nasal trauma
233 should not use a nasal corticosteroid until healing has occurred.

234 Glaucoma and cataract formation was evaluated in one controlled study of 12
235 weeks' duration and one uncontrolled study of 12 months' duration in patients
236 treated with NASONEX Nasal Spray, 50 mcg at 200 mcg/day, using intraocular
237 pressure measurements and slit lamp examination. No significant change from
238 baseline was noted in the mean intraocular pressure measurements for the 141
239 NASONEX-treated patients in the 12-week study, as compared with 141 placebo-
240 treated patients. No individual NASONEX-treated patient was noted to have
241 developed a significant elevation in intraocular pressure or cataracts in this 12-week
242 study. Likewise, no significant change from baseline was noted in the mean
243 intraocular pressure measurements for the 139 NASONEX-treated patients in the
244 12-month study and again, no cataracts were detected in these patients.
245 Nonetheless, nasal and inhaled corticosteroids have been associated with the
246 development of glaucoma and/or cataracts. Therefore, close follow-up is warranted
247 in patients with a change in vision and with a history of glaucoma and/or cataracts.

248 When nasal corticosteroids are used at excessive doses, systemic
249 corticosteroid effects such as hypercorticism and adrenal suppression may appear.
250 If such changes occur, NASONEX Nasal Spray, 50 mcg should be discontinued
251 slowly, consistent with accepted procedures for discontinuing oral steroid therapy.

252 **Information for Patients:** Patients being treated with NASONEX Nasal
253 Spray, 50 mcg should be given the following information and instructions. This
254 information is intended to aid in the safe and effective use of this medication. It is not
255 a disclosure of all intended or possible adverse effects. Patients should use
256 NASONEX Nasal Spray, 50 mcg at regular intervals (once daily) since its
257 effectiveness depends on regular use. Improvement in nasal symptoms of allergic
258 rhinitis has been shown to occur within 11 hours after the first dose based on one
259 single-dose, parallel-group study of patients in an outdoor “park” setting (park study)
260 and one environmental exposure unit (EEU) study and within 2 days after the first
261 dose in two randomized, double-blind, placebo-controlled, parallel-group seasonal
262 allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2 weeks
263 after initiation of dosing. Patients should take the medication as directed and should
264 not increase the prescribed dosage by using it more than once a day in an attempt
265 to increase its effectiveness. Patients should contact their physician if symptoms do
266 not improve, or if the condition worsens. To assure proper use of this nasal spray,
267 and to attain maximum benefit, patients should read and follow the accompanying
268 Patient’s Instructions for Use carefully. Administration to young children should be
269 aided by an adult.

270 Patients should be cautioned not to spray NASONEX Nasal Spray, 50 mcg
271 into the eyes or directly onto the nasal septum.

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

275 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year
276 carcinogenicity study in Sprague Dawley rats, mometasone furoate demonstrated
277 no statistically significant increase in the incidence of tumors at inhalation doses up
278 to 67 mcg/kg (approximately 3 and 2 times the maximum recommended daily

279 intranasal dose in adults and children, respectively, on a mcg/m² basis). In a 19-
280 month carcinogenicity study in Swiss CD-1 mice, mometasone furoate demonstrated
281 no statistically significant increase in the incidence of tumors at inhalation doses up
282 to 160 mcg/kg (approximately 3 and 2 times the maximum recommended daily
283 intranasal dose in adults and children, respectively, on a mcg/m² basis).

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

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

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

300 In mice, mometasone furoate caused cleft palate at subcutaneous doses of
301 60 mcg/kg and above (approximately equivalent to the maximum recommended
302 daily intranasal dose in adults on a mcg/m² basis). Fetal survival was reduced at
303 180 mcg/kg (approximately 4 times the maximum recommended daily intranasal
304 dose in adults on a mcg/m² basis). No toxicity was observed at 20 mcg/kg (less than
305 the maximum recommended daily intranasal dose in adults on a mcg/m² basis).

306 In rats, mometasone furoate produced umbilical hernia at topical dermal
307 doses of 600 mcg/kg and above (approximately 25 times the maximum
308 recommended daily intranasal dose in adults on a mcg/m² basis). A dose of 300

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

311 In rabbits, mometasone furoate caused multiple malformations (e.g., flexed
312 front paws, gallbladder agenesis, umbilical hernia, hydrocephaly) at topical dermal
313 doses of 150 mcg/kg and above (approximately 10 times the maximum
314 recommended daily intranasal dose in adults on a mcg/m² basis). In an oral study,
315 mometasone furoate increased resorptions and caused cleft palate and/or head
316 malformations (hydrocephaly or domed head) at 700 mcg/kg (approximately 55
317 times the maximum recommended daily intranasal dose in adults on a mcg/m²
318 basis). At 2800 mcg/kg (approximately 230 times the maximum recommended daily
319 intranasal dose in adults on a mcg/m² basis), most litters were aborted or resorbed.
320 No toxicity was observed at 140 mcg/kg (approximately 10 times the maximum
321 recommended daily intranasal dose in adults on a mcg/m² basis).

322 When rats received subcutaneous doses of mometasone furoate throughout
323 pregnancy or during the later stages of pregnancy, 15 mcg/kg (less than the
324 maximum recommended daily intranasal dose in adults on a mcg/m² basis) caused
325 prolonged and difficult labor and reduced the number of live births, birth weight and
326 early pup survival. Similar effects were not observed at 7.5 mcg/kg (less than the
327 maximum recommended daily intranasal dose in adults on a mcg/m² basis).

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

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

340 **Nursing Mothers:** It is not known if mometasone furoate is excreted in
341 human milk. Because other corticosteroids are excreted in human milk, caution
342 should be used when NASONEX Nasal Spray, 50 mcg is administered to nursing
343 women.

344 **Pediatric Use:** Controlled clinical studies have shown intranasal
345 corticosteroids may cause a reduction in growth velocity in pediatric patients. This
346 effect has been observed in the absence of laboratory evidence of hypothalamic-
347 pituitary-adrenal (HPA) axis suppression, suggesting that growth velocity is a more
348 sensitive indicator of systemic corticosteroid exposure in pediatric patients than
349 some commonly used tests of HPA axis function. The long-term effects of this
350 reduction in growth velocity associated with intranasal corticosteroids, including the
351 impact on final adult height, are unknown. The potential for “catch up” growth
352 following discontinuation of treatment with intranasal corticosteroids has not been
353 adequately studied. The growth of pediatric patients receiving intranasal
354 corticosteroids, including NASONEX Nasal Spray, 50 mcg should be monitored
355 routinely (eg, via stadiometry). The potential growth effects of prolonged treatment
356 should be weighed against clinical benefits obtained and the availability of safe and
357 effective noncorticosteroid treatment alternatives. To minimize the systemic effects
358 of intranasal corticosteroids, including NASONEX Nasal Spray, 50 mcg, each patient
359 should be titrated to his/her lowest effective dose.

360 Seven hundred and twenty (720) patients 3 to 11 years of age were treated with
361 mometasone furoate nasal spray, 50 mcg (100 mcg total daily dose) in controlled
362 clinical trials (see **CLINICAL PHARMACOLOGY, Clinical Studies** section).
363 Twenty-eight (28) patients 2 to 5 years of age were treated with mometasone furoate
364 nasal spray, 50 mcg (100 mcg total daily dose) in a controlled trial to evaluate safety
365 (see **CLINICAL PHARMACOLOGY, Pharmacokinetics** section). Safety and
366 effectiveness in children less than 2 years of age have not been established.

367 A clinical study has been conducted for 1 year in pediatric patients (ages 3 to
368 9 years) to assess the effect of NASONEX Nasal Spray, 50 mcg (100 mcg total daily
369 dose) on growth velocity. No statistically significant effect on growth velocity was
370 observed for NASONEX Nasal Spray, 50 mcg compared to placebo. No evidence of

371 clinically relevant HPA axis suppression was observed following a 30-minute
372 Cosyntropin infusion.

373 The potential of NASONEX Nasal Spray, 50 mcg to cause growth
374 suppression in susceptible patients or when given at higher doses cannot be ruled
375 out.

376 **Geriatric Use:** A total of 203 patients above 64 years of age (age range 64 to
377 85 years) have been treated with NASONEX Nasal Spray, 50 mcg for up to 3
378 months. The adverse reactions reported in this population were similar in type and
379 incidence to those reported by younger patients.

380

381 **ADVERSE REACTIONS** In controlled US and International clinical studies, a total
382 of 3210 adult and adolescent patients aged 12 years and older received treatment
383 with NASONEX Nasal Spray, 50 mcg at doses of 50 to 800 mcg/day. The majority of
384 patients (n = 2103) were treated with 200 mcg/day. In controlled US and
385 International studies, a total of 990 pediatric patients (ages 3 to 11 years) received
386 treatment with NASONEX Nasal Spray, 50 mcg, at doses of 25 to 200 mcg/day. The
387 majority of pediatric patients (720) were treated with 100 mcg/day. A total of 513
388 adult, adolescent, and pediatric patients have been treated for 1 year or longer. The
389 overall incidence of adverse events for patients treated with NASONEX Nasal Spray,
390 50 mcg was comparable to patients treated with the vehicle placebo. Also, adverse
391 events did not differ significantly based on age, sex, or race. Three percent or less of
392 patients in clinical trials discontinued treatment because of adverse events; this rate
393 was similar for the vehicle and active comparators.

394 All adverse events (regardless of relationship to treatment) reported by 5% or
395 more of adult and adolescent patients ages 12 years and older who received
396 NASONEX Nasal Spray, 50 mcg, 200 mcg/day and by pediatric patients ages 3 to
397 11 years who received NASONEX Nasal Spray, 50 mcg, 100 mcg/day in clinical
398 trials vs placebo and that were more common with NASONEX Nasal Spray, 50 mcg
399 than placebo, are displayed in the table below.

400

401 **ADVERSE EVENTS FROM CONTROLLED CLINICAL TRIALS IN SEASONAL ALLERGIC**
 402 **AND PERENNIAL ALLERGIC RHINITIS**
 403 **(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)
411 Headache	26	22	17	18
412 Viral Infection	14	11	8	9
413 Pharyngitis	12	10	10	10
414 Epistaxis/Blood-Tinged Mucus	11	6	8	9
415 Coughing	7	6	13	15
416 Upper Respiratory Tract Infection	6	2	5	4
417 Dysmenorrhea	5	3	1	0
418 Musculoskeletal Pain	5	3	1	1
419 Sinusitis	5	3	4	4
420 Vomiting	1	1	5	4

421

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

428 Other adverse events which occurred in less than 5% but greater or equal to
 429 2% of mometasone furoate pediatric patients ages 3 to 11 years treated with 100-
 430 mcg doses vs placebo (regardless of relationship to treatment) and more frequently

431 than in the placebo group included: diarrhea, nasal irritation, otitis media, and
432 wheezing.

433 The adverse event (regardless of relationship to treatment) reported by 5% of
434 pediatric patients ages 2 to 5 years who received NASONEX Nasal Spray, 50 mcg,
435 100 mcg/day in a clinical trial vs placebo including 56 subjects (28 each Nasonex
436 and placebo) and that was more common with NASONEX Nasal Spray, 50 mcg than
437 placebo, included: upper respiratory tract infection (7% vs 0%, respectively). The
438 other adverse event which occurred in less than 5% but greater than or equal to 2%
439 of mometasone furoate pediatric patients ages 2 to 5 years treated with 100 mcg
440 doses vs placebo (regardless of relationship to treatment) and more frequently than
441 in the placebo group included: skin trauma.

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

445 In postmarketing surveillance of this product, cases of nasal burning and
446 irritation, anaphylaxis and angioedema, and rare cases of nasal septal perforation
447 have been reported.

448

449 **OVERDOSAGE** There are no data available on the effects of acute or chronic
450 overdosage with NASONEX Nasal Spray, 50 mcg. Because of low systemic
451 bioavailability, and an absence of acute drug-related systemic findings in clinical
452 studies, overdose is unlikely to require any therapy other than observation.
453 Intranasal administration of 1600 mcg (8 times the recommended dose of
454 NASONEX Nasal Spray, 50 mcg) daily for 29 days, to healthy human volunteers,
455 was well tolerated with no increased incidence of adverse events. Single intranasal
456 doses up to 4000 mcg have been studied in human volunteers with no adverse
457 effects reported. Single oral doses up to 8000 mcg have been studied in human
458 volunteers with no adverse effects reported. Chronic overdosage with any
459 corticosteroid may result in signs or symptoms of hypercorticism (see
460 **PRECAUTIONS**). Acute overdosage with this dosage form is unlikely since one

461 bottle of NASONEX Nasal Spray, 50 mcg contains approximately 8500 mcg of
462 mometasone furoate.

463

464 **DOSAGE AND ADMINISTRATION Adults and Children 12 Years of Age and**
465 **Older:** The usual recommended dose for prophylaxis and treatment of the nasal
466 symptoms of seasonal allergic rhinitis and treatment of the nasal symptoms of
467 perennial allergic rhinitis is two sprays (50 mcg of mometasone furoate in each
468 spray) in each nostril once daily (total daily dose of 200 mcg).

469 In patients with a known seasonal allergen that precipitates nasal symptoms
470 of seasonal allergic rhinitis, prophylaxis with NASONEX Nasal Spray, 50 mcg (200
471 mcg/day) is recommended 2 to 4 weeks prior to the anticipated start of the pollen
472 season.

473 **Children 2 to 11 Years of Age:** The usual recommended dose for treatment
474 of the nasal symptoms of seasonal allergic and perennial allergic rhinitis is one spray
475 (50 mcg of mometasone furoate in each spray) in each nostril once daily (total daily
476 dose of 100 mcg).

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

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

488 **Directions for Use:** Illustrated Patient’s Instructions for Use accompany each
489 package of NASONEX Nasal Spray, 50 mcg.

490

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

496 **Store between 2° and 25°C (36° and 77°F). Protect from light.**

497 **When NASONEX Nasal Spray, 50 mcg is removed from its cardboard**
498 **container, prolonged exposure of the product to direct light should be**
499 **avoided. Brief exposure to light, as with normal use, is acceptable.**

500

501 **SHAKE WELL BEFORE EACH USE.**

502

503 *SP* Schering Corporation

504 Kenilworth, NJ 07033 USA

505

506

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509

510 XXXXXXXXT

511

512 **PHARMACIST**

513 TEAR AT PERFORATION

514 GIVE TO PATIENT

515 **Patient's Instructions for Use**

516 SHAKE WELL BEFORE EACH USE

517

518 **NASONEX®**

519 **(mometasone furoate monohydrate)**

520 **Nasal Spray, 50 mcg***

521 *calculated on the anhydrous basis

522

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

525

526 1. Remove the teal-green plastic cap (Figure 1).

527

528

529

530

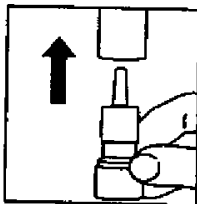


Figure 1

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

538

539

540

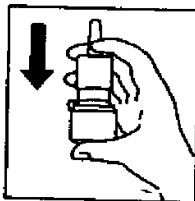


Figure 2

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

544

545

546

547



Figure 3

548

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

552

553

554

555



Figure 4

556

557 5. Then breathe out through the mouth.

558 6. Repeat in the other nostril.

559 7. Replace the plastic cap.

560

561 **Pediatric Use:** Administration to young children should be aided by an adult. The

562 **Patient's Instructions for Use,** Steps 1 to 7 should be followed.

563

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

568

569 **Cleaning:** To clean the nasal applicator, remove the plastic cap and pull gently
570 upward on the white nasal applicator so that it comes free. Wash the applicator and
571 cap under a cold water tap. Dry and replace the nasal applicator followed by the
572 plastic cap.

573

574 **Caution:** NASONEX Nasal Spray, 50 mcg is formulated for once-daily dosing. You
575 should use NASONEX Nasal Spray, 50 mcg only once daily at a regular interval.
576 Since NASONEX Nasal Spray, 50 mcg is not intended to give rapid relief of your
577 nasal symptoms, the prescribed dosage should not be increased by using more
578 often than once daily in an attempt to increase its effectiveness. NASONEX Nasal
579 Spray, 50 mcg controls the underlying disorders responsible for your attacks so it is
580 important that you use it regularly at the time recommended by your physician.

581 Based on single-day

582 studies done in a park during pollen season or in a controlled pollen exposure room,
583 improvement in nasal symptoms of allergic rhinitis has been shown to occur within
584 11 hours after the first dose. In other studies that lasted up to 2 weeks, improvement
585 in nasal symptoms of seasonal allergic rhinitis was shown to occur within 2 days
586 after the first dose. The full benefit of NASONEX Nasal Spray, 50 mcg is usually
587 achieved within 1 to 2 weeks.

588 NASONEX Nasal Spray, 50 mcg should not be sprayed into the eyes.

589 Spraying NASONEX Nasal Spray, 50 mcg directly onto the nasal septum should be
590 avoided.

591

592 **Store between 2° and 25°C (36° and 77°F). Protect from light.**

593

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595 **container, prolonged exposure of the product to direct light should be**
596 **avoided. Brief exposure to light, as with normal use, is acceptable.**

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/s/

Robert Meyer

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