

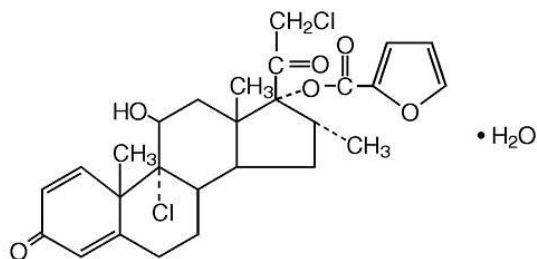
1 **NASONEX®**
2 **(mometasone furoate monohydrate)**
3 **Nasal Spray, 50 mcg***

**PRODUCT
INFORMATION**

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5 **FOR INTRANASAL USE ONLY**
6 ***calculated on the anhydrous basis**

7
8 **DESCRIPTION** Mometasone furoate monohydrate, the active component of
9 NASONEX Nasal Spray, 50 mcg, is an anti-inflammatory corticosteroid having the
10 chemical name, 9,21-Dichloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-
11 dione 17-(2 furoate) monohydrate, and the following chemical structure:

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17 Mometasone furoate monohydrate is a white powder, with an empirical
18 formula of $C_{27}H_{30}Cl_2O_6 \cdot H_2O$, and a molecular weight of 539.45. It is practically
19 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.

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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, citric acid, benzalkonium chloride, and polysorbate 80. The pH is between 4.3 and 4.9.

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

31

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

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

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

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

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

55 **Metabolism:** Studies have shown that any portion of a mometasone furoate
56 dose which is swallowed and absorbed undergoes extensive metabolism to multiple

57 metabolites. There are no major metabolites detectable in plasma. Upon in vitro
58 incubation, one of the minor metabolites formed is 6 β -hydroxy-mometasone furoate.
59 In human liver microsomes, the formation of the metabolite is regulated by
60 cytochrome P-450 3A4 (CYP3A4).

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

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

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

80 A second study assessed adrenal response to NASONEX Nasal Spray, 50
81 mcg (400 and 1600 mcg/day), prednisone (10 mg/day), and placebo, administered
82 for 29 days in 48 male volunteers. The 24-hour plasma cortisol area under the curve
83 (AUC₀₋₂₄), during and after an 8-hour Cortrosyn infusion and 24-hour urinary-free
84 cortisol levels were determined at baseline and after 29 days of treatment. No
85 statistically significant differences of adrenal function were observed with NASONEX
86 Nasal Spray, 50 mcg compared to placebo.

87 A third study evaluated single, rising doses of NASONEX Nasal Spray, 50
88 mcg (1000, 2000, and 4000 mcg/day), orally administered mometasone furoate
89 (2000, 4000, and 8000 mcg/day), orally administered dexamethasone (200, 400,
90 and 800 mcg/day), and placebo (administered at the end of each series of doses) in
91 24 male volunteers. Dose administrations were separated by at least 72 hours.
92 Determination of serial plasma cortisol levels at 8 AM and for the 24-hour period
93 following each treatment were used to calculate the plasma cortisol area under the
94 curve (AUC₀₋₂₄). In addition, 24-hour urinary-free cortisol levels were collected prior
95 to initial treatment administration and during the period immediately following each
96 dose. No statistically significant decreases in the plasma cortisol AUC, 8 AM cortisol
97 levels, or 24-hour urinary-free cortisol levels were observed in volunteers treated
98 with either NASONEX Nasal Spray, 50 mcg or oral mometasone, as compared with
99 placebo treatment. Conversely, nearly all volunteers treated with the three doses of
100 dexamethasone demonstrated abnormal 8 AM cortisol levels (defined as a cortisol
101 level <10 mcg/dL), reduced 24-hour plasma AUC values, and decreased 24-hour
102 urinary-free cortisol levels, as compared to placebo treatment.

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

118 the third study, adrenal function before and after up to 42 consecutive days of once-
119 daily treatment was assessed in 52 patients with allergic rhinitis (ages 2 to 5 years),
120 28 of whom received mometasone furoate nasal spray, 50 mcg per nostril (total daily
121 dose 100 mcg), by measuring morning plasma cortisol and 24-hour urinary-free
122 cortisol levels. Mometasone furoate nasal spray was not associated with a
123 statistically significant decrease in mean plasma cortisol levels or a statistically
124 significant decrease in the 24-hour urinary-free cortisol levels compared to placebo.

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

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

148 for the 200-mcg mometasone furoate total daily dose in pediatric patients (ages 3 to
149 11 years). A total of 163 pediatric patients have been treated for 1 year.

150 In patients with seasonal allergic rhinitis, NASONEX Nasal Spray, 50 mcg,
151 demonstrated improvement in nasal symptoms (vs placebo) within 11 hours after the
152 first dose based on one single-dose, parallel-group study of patients in an outdoor
153 “park” setting (park study) and one environmental exposure unit (EEU) study, and
154 within 2 days in two randomized, double-blind, placebo-controlled, parallel-group
155 seasonal allergic rhinitis studies. Maximum benefit is usually achieved within 1 to 2
156 weeks after initiation of dosing.

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

166

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

177

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

180

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

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

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

209

210 **PRECAUTIONS General:** Intranasal corticosteroids may cause a reduction in
211 growth velocity when administered to pediatric patients (see **PRECAUTIONS,**
212 **Pediatric Use** section). In clinical studies with NASONEX Nasal Spray, 50 mcg, the
213 development of localized infections of the nose and pharynx with *Candida albicans*
214 has occurred only rarely. When such an infection develops, use of NASONEX Nasal
215 Spray, 50 mcg should be discontinued and appropriate local or systemic therapy
216 instituted, if needed.

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

220 Rarely, immediate hypersensitivity reactions may occur after the intranasal
221 administration of mometasone furoate monohydrate. Extremely rare instances of
222 wheezing have been reported.

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

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

231 Glaucoma and cataract formation was evaluated in one controlled study of 12
232 weeks' duration and one uncontrolled study of 12 months' duration in patients
233 treated with NASONEX Nasal Spray, 50 mcg at 200 mcg/day, using intraocular
234 pressure measurements and slit lamp examination. No significant change from
235 baseline was noted in the mean intraocular pressure measurements for the 141
236 NASONEX-treated patients in the 12-week study, as compared with 141 placebo-
237 treated patients. No individual NASONEX-treated patient was noted to have
238 developed a significant elevation in intraocular pressure or cataracts in this 12-week
239 study. Likewise, no significant change from baseline was noted in the mean

240 intraocular pressure measurements for the 139 NASONEX-treated patients in the
241 12-month study and again, no cataracts were detected in these patients.
242 Nonetheless, nasal and inhaled corticosteroids have been associated with the
243 development of glaucoma and/or cataracts. Therefore, close follow-up is warranted
244 in patients with a change in vision and with a history of glaucoma and/or cataracts.

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

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

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

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

272 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 2-year
273 carcinogenicity study in Sprague Dawley rats, mometasone furoate demonstrated no
274 statistically significant increase in the incidence of tumors at inhalation doses up to
275 67 mcg/kg (approximately 3 and 2 times the maximum recommended daily
276 intranasal dose in adults and children, respectively, on a mcg/m² basis). In a 19-
277 month carcinogenicity study in Swiss CD-1 mice, mometasone furoate demonstrated
278 no statistically significant increase in the incidence of tumors at inhalation doses up
279 to 160 mcg/kg (approximately 3 and 2 times the maximum recommended daily
280 intranasal dose in adults and children, respectively, on a mcg/m² basis).

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

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

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

298 In mice, mometasone furoate caused cleft palate at subcutaneous doses of
299 60 mcg/kg and above (approximately equivalent to the maximum recommended

300 daily intranasal dose in adults on a mcg/m² basis). Fetal survival was reduced at 180
301 mcg/kg (approximately 4 times the maximum recommended daily intranasal dose in
302 adults on a mcg/m² basis). No toxicity was observed at 20 mcg/kg (less than the
303 maximum recommended daily intranasal dose in adults on a mcg/m² basis).

304 In rats, mometasone furoate produced umbilical hernia at topical dermal
305 doses of 600 mcg/kg and above (approximately 25 times the maximum
306 recommended daily intranasal dose in adults on a mcg/m² basis). A dose of 300
307 mcg/kg (approximately 10 times the maximum recommended daily intranasal dose
308 in adults on a mcg/m² basis) produced delays in ossification, but no malformations.

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

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

326 There are no adequate and well-controlled studies in pregnant women.
327 NASONEX Nasal Spray, 50 mcg, like other corticosteroids, should be used during
328 pregnancy only if the potential benefits justify the potential risk to the fetus.
329 Experience with oral corticosteroids since their introduction in pharmacologic, as
330 opposed to physiologic, doses suggests that rodents are more prone to teratogenic

331 effects from corticosteroids than humans. In addition, because there is a natural
332 increase in corticosteroid production during pregnancy, most women will require a
333 lower exogenous corticosteroid dose and many will not need corticosteroid treatment
334 during pregnancy.

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

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

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

358 Seven hundred and twenty (720) patients 3 to 11 years of age were treated with
359 mometasone furoate nasal spray, 50 mcg (100 mcg total daily dose) in controlled
360 clinical trials (see **CLINICAL PHARMACOLOGY, Clinical Studies** section).
361 Twenty-eight (28) patients 2 to 5 years of age were treated with mometasone furoate

362 nasal spray, 50 mcg (100 mcg total daily dose) in a controlled trial to evaluate safety
363 (see **CLINICAL PHARMACOLOGY, Pharmacokinetics** section). Safety and
364 effectiveness in children less than 2 years of age have not been established.

365 A clinical study has been conducted for 1 year in pediatric patients (ages 3 to
366 9 years) to assess the effect of NASONEX Nasal Spray, 50 mcg (100 mcg total daily
367 dose) on growth velocity. No statistically significant effect on growth velocity was
368 observed for NASONEX Nasal Spray, 50 mcg compared to placebo. No evidence of
369 clinically relevant HPA axis suppression was observed following a 30-minute
370 cosyntropin infusion.

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

374 **Geriatric Use:** A total of 203 patients above 64 years of age (age range 64 to
375 85 years) have been treated with NASONEX Nasal Spray, 50 mcg for up to 3
376 months. The adverse reactions reported in this population were similar in type and
377 incidence to those reported by younger patients.

378

379 **ADVERSE REACTIONS** In controlled US and international clinical studies, a total of
380 3210 adult and adolescent patients ages 12 years and older received treatment with
381 NASONEX Nasal Spray, 50 mcg at doses of 50 to 800 mcg/day. The majority of
382 patients (n = 2103) were treated with 200 mcg/day. In controlled US and
383 international studies, a total of 990 pediatric patients (ages 3 to 11 years) received
384 treatment with NASONEX Nasal Spray, 50 mcg, at doses of 25 to 200 mcg/day. The
385 majority of pediatric patients (720) were treated with 100 mcg/day. A total of 513
386 adult, adolescent, and pediatric patients have been treated for 1 year or longer. The
387 overall incidence of adverse events for patients treated with NASONEX Nasal Spray,
388 50 mcg was comparable to patients treated with the vehicle placebo. Also, adverse
389 events did not differ significantly based on age, sex, or race. Three percent or less of
390 patients in clinical trials discontinued treatment because of adverse events; this rate
391 was similar for the vehicle and active comparators.

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

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

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

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

429 frequently than in the placebo group included: diarrhea, nasal irritation, otitis media,
430 and wheezing.

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

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

443 In postmarketing surveillance of this product, cases of nasal burning and
444 irritation, anaphylaxis and angioedema, and rare cases of nasal septal perforation
445 have been reported. Disturbances of taste and smell have been reported very
446 rarely.

447

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

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

462

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

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

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

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

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

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

489

490 **Directions for Cleaning:** Illustrated **Applicator Cleaning Instructions**
491 accompany each package of NASONEX Nasal Spray, 50 mcg.

492

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

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

500

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

504

505 **SHAKE WELL BEFORE EACH USE.**

506

507 *Schering®*

508 Schering Corporation

509 Kenilworth, NJ 07033 USA

510

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514

515 XXXXXXXXT

516

517 **PHARMACIST**

518 **Pull to Remove**

519 **GIVE TO PATIENT**

520 **Patient's Instructions for Use**

521 **SHAKE WELL BEFORE EACH USE**

522

523 **NASONEX®**

524 **(mometasone furoate monohydrate)**

525 **Nasal Spray, 50 mcg***

526 *calculated on the anhydrous basis

527

528 **Shake the bottle well before each use. Read complete instructions carefully**

529 **and use only as directed.**

530

531 1. Remove the plastic cap (Figure 1).

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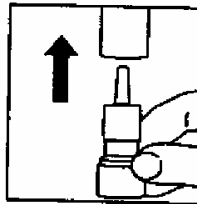


Figure 1

536 2. The very first time the spray is used, prime the pump by pressing downward

537 on the shoulders of the white applicator using your forefinger and middle finger while

538 supporting the base of the bottle with your thumb (Figure 2). Press down and

539 release the pump ten times or until a fine spray appears. DO NOT spray into eyes.

540 The pump is now ready to use. The pump may be stored unused for up to 1 week

541 without repriming. If unused for more than 1 week, reprime by spraying two times or

542 until a fine spray appears.

543

544



Figure 2

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

549

550

551

552



Figure 3

553

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

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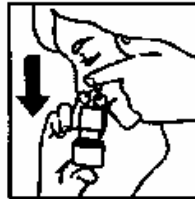


Figure 4

561

562 5. Then breathe out through the mouth.

563 6. Repeat in the other nostril.

564 7. Wipe the nasal applicator with a clean tissue and replace the plastic cap.

565

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

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

568

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

573

574 **Cleaning:** Please see **Applicator Cleaning Instructions** on reverse.

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

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

588

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

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

592

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

595

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

599

600 **SHAKE WELL BEFORE EACH USE.**

601

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608 U.S. Patent No. D355,844

609 Rev. XX/XX

610 **PHARMACIST**

611 **GIVE TO PATIENT**

612 **APPLICATOR CLEANING INSTRUCTIONS**

613

614 **Please see reverse for Patient's Instructions for Use**

615

616 **NASONEX®**

617 **(mometasone furoate monohydrate)**

618 **Nasal Spray, 50 mcg***

619 *calculated on the anhydrous basis

620

621 1. To clean the nasal applicator, remove the plastic cap (Figure 1).

622

623

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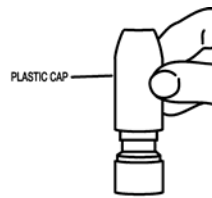


Figure 1

627 2. Pull gently upward on the white nasal applicator so that it comes free (Figure 2).

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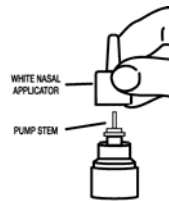


Figure 2

633 3. Soak the nasal applicator in cold tap water and/or rinse both ends of the nasal
634 applicator under cold tap water and dry. (Figure 3).

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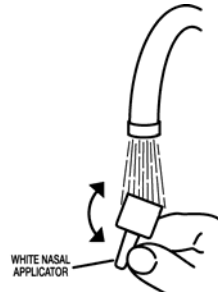


Figure 3

641 4. Rinse the plastic cap under cold water and dry (Figure 4).

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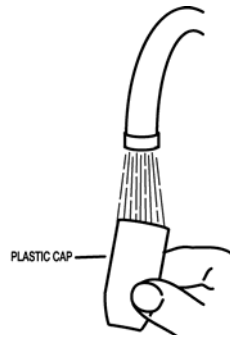


Figure 4

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

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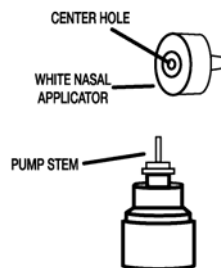


Figure 5

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

662

663

664

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668



Figure 6

669 7. Replace the plastic cap (Figure 7).

670

671

672

673

674

675



Figure 7

676

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683 Rev. XX/XX