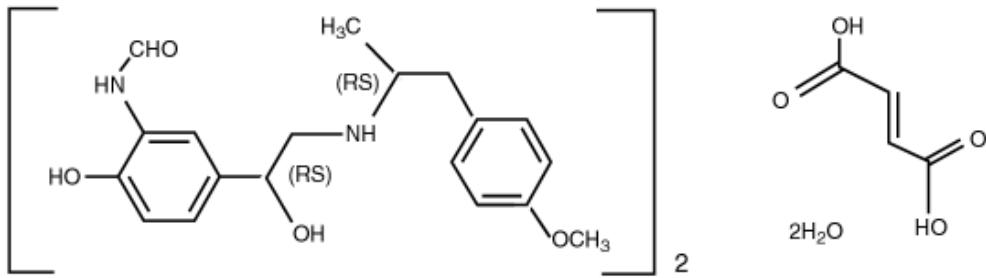


1 **DESCRIPTION**

2 FORADIL® AEROLIZER™ consists of a capsule dosage form containing a dry powder
3 formulation of Foradil (formoterol fumarate) intended for oral inhalation only with the
4 Aerolizer™ Inhaler.

5 Each clear, hard gelatin capsule contains a dry powder blend of 12 mcg of formoterol
6 fumarate and 25 mg of lactose as a carrier.

7 The active component of Foradil is formoterol fumarate, a racemate. Formoterol
8 fumarate is a selective beta₂-adrenergic bronchodilator. Its chemical name is (\pm)-2-hydroxy-5-
9 [(1RS)-1-hydroxy-2-[(1RS)-2-(4-methoxyphenyl)-1-methylethyl]-amino]ethyl]formanilide
10 fumarate dihydrate; its structural formula is



11
12
13 Formoterol fumarate has a molecular weight of 840.9, and its empirical formula is
14 (C₁₉H₂₄N₂O₄)₂•C₄H₄O₄•2H₂O. Formoterol fumarate is a white to yellowish crystalline
15 powder, which is freely soluble in glacial acetic acid, soluble in methanol, sparingly soluble in
16 ethanol and isopropanol, slightly soluble in water, and practically insoluble in acetone, ethyl
17 acetate, and diethyl ether.

18 The Aerolizer Inhaler is a plastic device used for inhaling Foradil. The amount of drug
19 delivered to the lung will depend on patient factors, such as inspiratory flow rate and
20 inspiratory time. Under standardized in vitro testing at a fixed flow rate of 60 L/min for
21 2 seconds, the Aerolizer Inhaler delivered 10 mcg of formoterol fumarate from the
22 mouthpiece. Peak inspiratory flow rates (PIFR) achievable through the Aerolizer Inhaler were
23 evaluated in 33 adult and adolescent patients and 32 pediatric patients with mild-to-moderate
24 asthma. Mean PIFR was 117.82 L/min (range 34-188 L/min) for adult and adolescent patients,
25 and 99.66 L/min (range 43-187 L/min) for pediatric patients. Approximately ninety percent of
26 each population studied generated a PIFR through the device exceeding 60 L/min.

27 To use the delivery system, a Foradil capsule is placed in the well of the Aerolizer
28 Inhaler, and the capsule is pierced by pressing and releasing the buttons on the side of the
29 device. The formoterol fumarate formulation is dispersed into the air stream when the patient
30 inhales rapidly and deeply through the mouthpiece.

31 **CLINICAL PHARMACOLOGY**

32 **Mechanism of Action**

33 Formoterol fumarate is a long-acting selective beta₂-adrenergic receptor agonist
34 (beta₂-agonist). Inhaled formoterol fumarate acts locally in the lung as a bronchodilator. In

35 vitro studies have shown that formoterol has more than 200-fold greater agonist activity at
36 beta₂-receptors than at beta₁-receptors. Although beta₂-receptors are the predominant
37 adrenergic receptors in bronchial smooth muscle and beta₁-receptors are the predominant
38 receptors in the heart, there are also beta₂-receptors in the human heart comprising 10%-50%
39 of the total beta-adrenergic receptors. The precise function of these receptors has not been
40 established, but they raise the possibility that even highly selective beta₂-agonists may have
41 cardiac effects.

42 The pharmacologic effects of beta₂-adrenoceptor agonist drugs, including formoterol,
43 are at least in part attributable to stimulation of intracellular adenyl cyclase, the enzyme that
44 catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3', 5'-adenosine
45 monophosphate (cyclic AMP). Increased cyclic AMP levels cause relaxation of bronchial
46 smooth muscle and inhibition of release of mediators of immediate hypersensitivity from
47 cells, especially from mast cells.

48 In vitro tests show that formoterol is an inhibitor of the release of mast cell mediators,
49 such as histamine and leukotrienes, from the human lung. Formoterol also inhibits histamine-
50 induced plasma albumin extravasation in anesthetized guinea pigs and inhibits allergen-
51 induced eosinophil influx in dogs with airway hyper-responsiveness. The relevance of these
52 in vitro and animal findings to humans is unknown.

53 **Animal Pharmacology**

54 Studies in laboratory animals (minipigs, rodents, and dogs) have demonstrated the occurrence
55 of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis)
56 when beta-agonists and methylxanthines are administered concurrently. The clinical
57 significance of these findings is unknown.

58 **Pharmacokinetics**

59 Information on the pharmacokinetics of formoterol in plasma has been obtained in healthy
60 subjects by oral inhalation of doses higher than the recommended range and in COPD patients
61 after oral inhalation of doses at and above the therapeutic dose. Urinary excretion of
62 unchanged formoterol was used as an indirect measure of systemic exposure. Plasma drug
63 disposition data parallel urinary excretion, and the elimination half-lives calculated for urine
64 and plasma are similar.

65 **Absorption**

66 Following inhalation of a single 120 mcg dose of formoterol fumarate by 12 healthy subjects,
67 formoterol was rapidly absorbed into plasma, reaching a maximum drug concentration of
68 92 pg/mL within 5 minutes of dosing. In COPD patients treated for 12 weeks with formoterol
69 fumarate 12 or 24 mcg b.i.d., the mean plasma concentrations of formoterol ranged between
70 4.0 and 8.8 pg/mL and 8.0 and 17.3 pg/mL, respectively, at 10 min, 2 h and 6 h post
71 inhalation.

72 Following inhalation of 12 to 96 mcg of formoterol fumarate by 10 healthy males,
73 urinary excretion of both (R,R)- and (S,S)-enantiomers of formoterol increased proportionally

74 to the dose. Thus, absorption of formoterol following inhalation appeared linear over the dose
75 range studied.

76 In a study in patients with asthma, when formoterol 12 or 24 mcg twice daily was
77 given by oral inhalation for 4 weeks or 12 weeks, the accumulation index, based on the
78 urinary excretion of unchanged formoterol ranged from 1.63 to 2.08 in comparison with the
79 first dose. For COPD patients, when formoterol 12 or 24 mcg twice daily was given by oral
80 inhalation for 12 weeks, the accumulation index, based on the urinary excretion of unchanged
81 formoterol was 1.19 - 1.38. This suggests some accumulation of formoterol in plasma with
82 multiple dosing. The excreted amounts of formoterol at steady-state were close to those
83 predicted based on single-dose kinetics. As with many drug products for oral inhalation,
84 it is likely that the majority of the inhaled formoterol fumarate delivered is swallowed and
85 then absorbed from the gastrointestinal tract.

86 **Distribution**

87 The binding of formoterol to human plasma proteins in vitro was 61%-64% at concentrations
88 from 0.1 to 100 ng/mL. Binding to human serum albumin in vitro was 31%-38% over a range
89 of 5 to 500 ng/mL. The concentrations of formoterol used to assess the plasma protein binding
90 were higher than those achieved in plasma following inhalation of a single 120 mcg dose.

91 **Metabolism**

92 Formoterol is metabolized primarily by direct glucuronidation at either the phenolic or
93 aliphatic hydroxyl group and O-demethylation followed by glucuronide conjugation at either
94 phenolic hydroxyl groups. Minor pathways involve sulfate conjugation of formoterol and
95 deformylation followed by sulfate conjugation. The most prominent pathway involves direct
96 conjugation at the phenolic hydroxyl group. The second major pathway involves O-
97 demethylation followed by conjugation at the phenolic 2'-hydroxyl group. Four cytochrome
98 P450 isozymes (CYP2D6, CYP2C19, CYP2C9 and CYP2A6) are involved in the O-
99 demethylation of formoterol. Formoterol did not inhibit CYP450 enzymes at therapeutically
100 relevant concentrations. Some patients may be deficient in CYP 2D6 or 2C19 or both.
101 Whether a deficiency in one or both of these isozymes results in elevated systemic exposure to
102 formoterol or systemic adverse effects has not been adequately explored.

103 **Excretion**

104 Following oral administration of 80 mcg of radiolabeled formoterol fumarate to 2 healthy
105 subjects, 59%-62% of the radioactivity was eliminated in the urine and 32%-34% in the feces
106 over a period of 104 hours. Renal clearance of formoterol from blood in these subjects was
107 about 150 mL/min. Following inhalation of a 12 mcg or 24 mcg dose by 16 patients with
108 asthma, about 10% and 15%-18% of the total dose was excreted in the urine as unchanged
109 formoterol and direct conjugates of formoterol, respectively. Following inhalation of 12 mcg
110 or 24 mcg dose by 18 patients with COPD the corresponding values were 7% and 6-9% of the
111 dose, respectively.

112 Based on plasma concentrations measured following inhalation of a single 120 mcg
113 dose by 12 healthy subjects, the mean terminal elimination half-life was determined to be 10

114 hours. From urinary excretion rates measured in these subjects, the mean terminal elimination
115 half-lives for the (R,R)- and (S,S)-enantiomers were determined to be 13.9 and 12.3 hours,
116 respectively. The (R,R)- and (S,S)-enantiomers represented about 40% and 60% of unchanged
117 drug excreted in the urine, respectively, following single inhaled doses between 12 and
118 120 mcg in healthy volunteers and single and repeated doses of 12 and 24 mcg in patients
119 with asthma. Thus, the relative proportion of the two enantiomers remained constant over the
120 dose range studied and there was no evidence of relative accumulation of one enantiomer over
121 the other after repeated dosing.

122 ***Special Populations***

123 *Gender:* After correction for body weight, formoterol pharmacokinetics did not differ
124 significantly between males and females.

125 *Geriatric and Pediatric:* The pharmacokinetics of formoterol have not been studied in the
126 elderly population, and limited data are available in pediatric patients.

127 In a study of children with asthma who were 5 to 12 years of age, when formoterol
128 fumarate 12 or 24 mcg was given twice daily by oral inhalation for 12 weeks, the
129 accumulation index ranged from 1.18 to 1.84 based on urinary excretion of unchanged
130 formoterol. Hence, the accumulation in children did not exceed that in adults, where the
131 accumulation index ranged from 1.63 to 2.08 (see above). Approximately 6% and 6.5% to 9%
132 of the dose was recovered in the urine of the children as unchanged and conjugated
133 formoterol, respectively.

134

135 *Hepatic/Renal Impairment:* The pharmacokinetics of formoterol have not been studied in
136 subjects with hepatic or renal impairment.

137 ***Pharmacodynamics***

138 ***Systemic Safety and Pharmacokinetic/Pharmacodynamic Relationships***

139 The major adverse effects of inhaled beta₂-agonists occur as a result of excessive activation of
140 the systemic beta-adrenergic receptors. The most common adverse effects in adults and
141 adolescents include skeletal muscle tremor and cramps, insomnia, tachycardia, decreases in
142 plasma potassium, and increases in plasma glucose.

143 Pharmacokinetic/pharmacodynamic (PK/PD) relationships between heart rate, ECG
144 parameters, and serum potassium levels and the urinary excretion of formoterol were
145 evaluated in 10 healthy male volunteers (25 to 45 years of age) following inhalation of single
146 doses containing 12, 24, 48, or 96 mcg of formoterol fumarate. There was a linear relationship
147 between urinary formoterol excretion and decreases in serum potassium, increases in plasma
148 glucose, and increases in heart rate.

149 In a second study, PK/PD relationships between plasma formoterol levels and pulse
150 rate, ECG parameters, and plasma potassium levels were evaluated in 12 healthy volunteers
151 following inhalation of a single 120 mcg dose of formoterol fumarate (10 times the

152 recommended clinical dose). Reductions of plasma potassium concentration were observed in
153 all subjects. Maximum reductions from baseline ranged from 0.55 to 1.52 mmol/L with a
154 median maximum reduction of 1.01 mmol/L. The formoterol plasma concentration was highly
155 correlated with the reduction in plasma potassium concentration. Generally, the maximum
156 effect on plasma potassium was noted 1 to 3 hours after peak formoterol plasma
157 concentrations were achieved. A mean maximum increase of pulse rate of 26 bpm was
158 observed 6 hours post dose. The maximum increase of mean corrected QT interval (QTc) was
159 25 msec when calculated using Bazett's correction and was 8 msec when calculated using
160 Fredericia's correction. The QTc returned to baseline within 12-24 hours post-dose.
161 Formoterol plasma concentrations were weakly correlated with pulse rate and increase of QTc
162 duration. The effects on plasma potassium, pulse rate, and QTc interval are known
163 pharmacological effects of this class of study drug and were not unexpected at the very high
164 formoterol dose (120 mcg single dose, 10 times the recommended single dose) tested in this
165 study. These effects were well-tolerated by the healthy volunteers.

166 The electrocardiographic and cardiovascular effects of FORADIL AEROLIZER were
167 compared with those of albuterol and placebo in two pivotal 12-week double-blind studies of
168 patients with asthma. A subset of patients underwent continuous electrocardiographic
169 monitoring during three 24-hour periods. No important differences in ventricular or
170 supraventricular ectopy between treatment groups were observed. In these two studies, the
171 total number of patients with asthma exposed to any dose of FORADIL AEROLIZER who
172 had continuous electrocardiographic monitoring was about 200.

173 Continuous electrocardiographic monitoring was not included in the clinical studies of
174 FORADIL AEROLIZER that were performed in COPD patients. The electrocardiographic
175 effects of FORADIL AEROLIZER were evaluated versus placebo in a 12-month pivotal
176 double-blind study of patients with COPD. An analysis of ECG intervals was performed for
177 patients who participated at study sites in the United States, including 46 patients treated with
178 FORADIL AEROLIZER 12 mcg twice daily, and 50 patients treated with FORADIL
179 AEROLIZER 24 mcg twice daily. ECGs were performed pre-dose, and at 5-15 minutes and 2
180 hours post-dose at study baseline and after 3, 6 and 12 months of treatment. The results
181 showed that there was no clinically meaningful acute or chronic effect on ECG intervals,
182 including QTc, resulting from treatment with FORADIL AEROLIZER.

183 **Tachyphylaxis/Tolerance**

184 In a clinical study in 19 adult patients with mild asthma, the bronchoprotective effect of
185 formoterol, as assessed by methacholine challenge, was studied following an initial dose of
186 24 mcg (twice the recommended dose) and after 2 weeks of 24 mcg twice daily. Tolerance to
187 the bronchoprotective effects of formoterol was observed as evidenced by a diminished
188 bronchoprotective effect on FEV₁ after 2 weeks of dosing, with loss of protection at the end of
189 the 12 hour dosing period.

190 Rebound bronchial hyper-responsiveness after cessation of chronic formoterol therapy
191 has not been observed.

192 In three large clinical trials in patients with asthma, while efficacy of formoterol
193 versus placebo was maintained, a slightly reduced bronchodilatory response (as measured by

194 12-hour FEV₁ AUC) was observed within the formoterol arms over time, particularly with the
195 24 mcg twice daily dose (twice the daily recommended dose). A similarly reduced FEV₁ AUC
196 over time was also noted in the albuterol treatment arms (180 mcg four times daily by
197 metered-dose inhaler).

198 CLINICAL TRIALS

199 Adolescent and Adult Asthma Trials

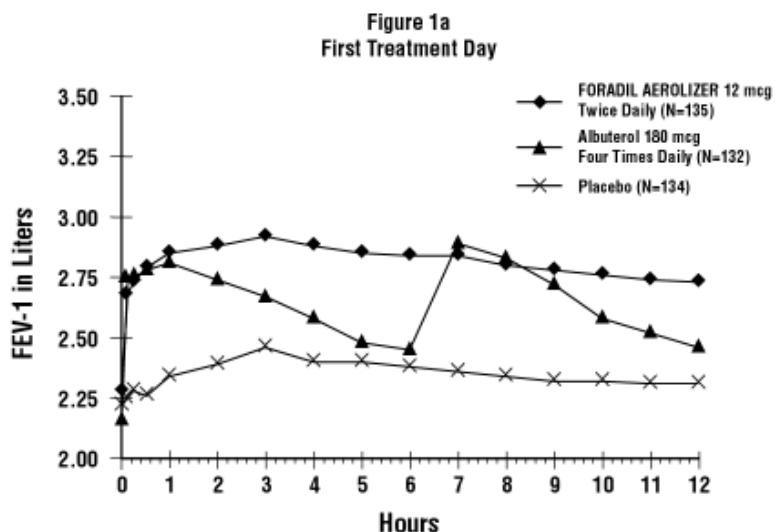
200 In a placebo-controlled, single-dose clinical trial, the onset of bronchodilation (defined as a
201 15% or greater increase from baseline in FEV₁) was similar for FORADIL AEROLIZER and
202 albuterol 180 mcg by metered-dose inhaler.

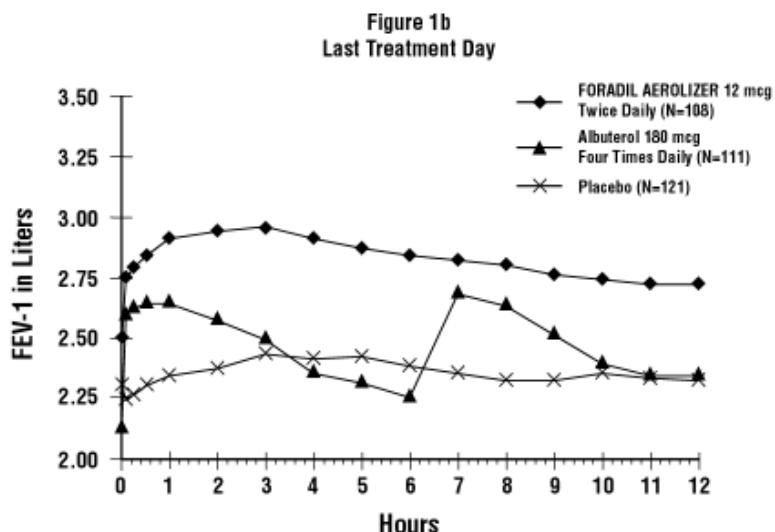
203 In single-dose and multiple-dose clinical trials, the maximum improvement in FEV₁
204 for FORADIL AEROLIZER 12 mcg generally occurred within 1 to 3 hours, and an increase
205 in FEV₁ above baseline was observed for 12 hours in most patients.

206 FORADIL AEROLIZER was compared to albuterol 180 mcg four times daily by
207 metered-dose inhaler, and placebo in a total of 1095 adult and adolescent patients 12 years of
208 age and above with mild-to-moderate asthma (defined as FEV₁ 40%-80% of the patient's
209 predicted normal value) who participated in two pivotal, 12-week, multi-center, randomized,
210 double-blind, parallel group studies.

211 The results of both studies showed that FORADIL AEROLIZER 12 mcg twice daily
212 resulted in significantly greater post-dose bronchodilation (as measured by serial FEV₁ for
213 12 hours post-dose) throughout the 12-week treatment period. Mean FEV₁ measurements
214 from both studies are shown below for the first and last treatment days (see Figures 1 and 2).

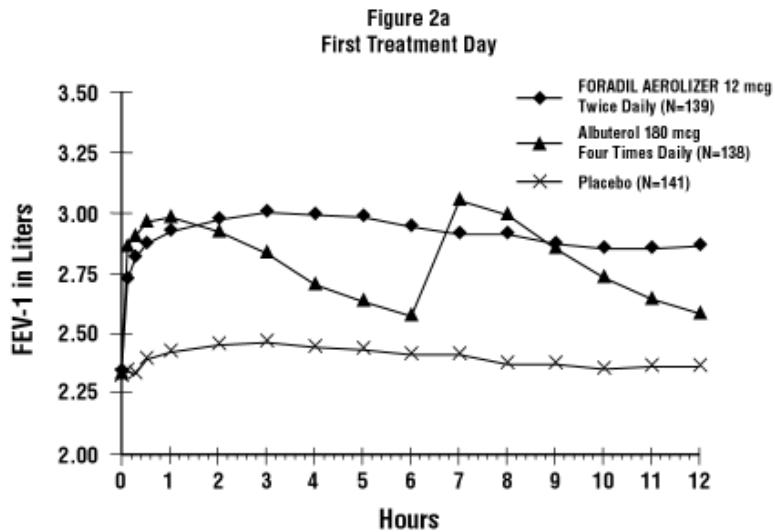
215 Figures 1a and 1b: Mean FEV₁ from Clinical Trial A



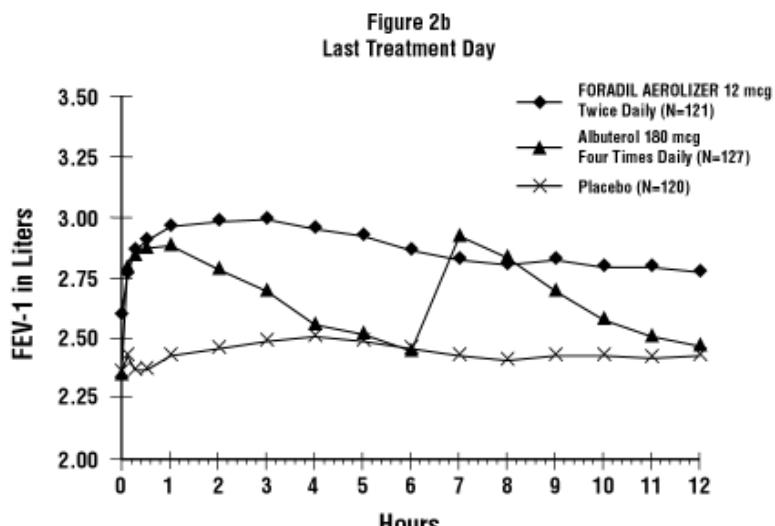


217

218 Figures 2a and 2b: Mean FEV₁ from Clinical Trial B



219



220

221 Compared with placebo and albuterol, patients treated with FORADIL AEROLIZER
222 12 mcg demonstrated improvement in many secondary efficacy endpoints, including
223 improved combined and nocturnal asthma symptom scores, fewer nighttime awakenings,
224 fewer nights in which patients used rescue medication, and higher morning and evening peak
225 flow rates.

226 **Pediatric Asthma Trial**

227 A 12-month, multi-center, randomized, double-blind, parallel-group, study compared
228 FORADIL AEROLIZER and placebo in a total of 518 children with asthma (ages 5-12 years)
229 who required daily bronchodilators and anti-inflammatory treatment. Efficacy was evaluated
230 on the first day of treatment, at Week 12, and at the end of treatment.

231 FORADIL AEROLIZER 12 mcg twice daily demonstrated a greater 12-hour FEV₁
232 AUC compared to placebo on the first day of treatment, after twelve weeks of treatment, and
233 after one year of treatment.

234 **Adolescent and Adult Exercise-Induced Bronchospasm Trials**

235 The effect of FORADIL AEROLIZER on exercise-induced bronchospasm (defined as >20%
236 fall in FEV₁) was examined in two randomized, single-dose, double-blind, crossover studies
237 in a total of 38 patients 13 to 41 years of age with exercise-induced bronchospasm. Exercise
238 challenge testing was conducted 15 minutes, and 4, 8, and 12 hours following administration
239 of a single dose of study drug (FORADIL AEROLIZER 12 mcg, albuterol 180 mcg by
240 metered-dose inhaler, or placebo) on separate test days. FORADIL AEROLIZER 12 mcg and
241 albuterol 180 mcg were each superior to placebo for FEV₁ measurements obtained 15 minutes
242 after study drug administration. FORADIL AEROLIZER 12 mcg maintained superiority over
243 placebo at 4, 8, and 12 hours after administration. The efficacy of FORADIL AEROLIZER in
244 the prevention of exercise-induced bronchospasm when dosed on a regular twice daily
245 regimen has not been studied.

246 **Adult COPD Trials**

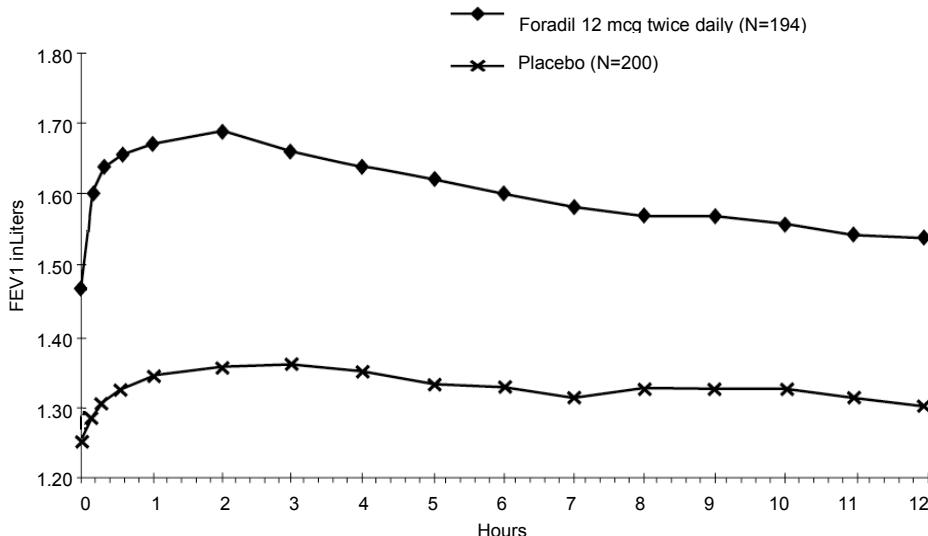
247 In multiple-dose clinical trials in patients with COPD, FORADIL AEROLIZER 12 mcg was
248 shown to provide ~~rapid~~-onset of significant bronchodilation (defined as 15% or greater
249 increase from baseline in FEV₁), ~~reached~~ within 5 minutes of oral inhalation) after the first
250 dose. Bronchodilation was maintained for at least 12 hours.

251 FORADIL AEROLIZER was studied in two pivotal, double-blind, placebo-controlled,
252 randomized, multi-center, parallel-group trials in a total of 1634 adult patients (age range: 34-
253 88 years; mean age: 63 years) with COPD who had a mean FEV₁ that was 46% of predicted.
254 The diagnosis of COPD was based upon a prior clinical diagnosis of COPD, a smoking
255 history (greater than 10 pack-years), age (at least 40 years), spirometry results
256 (prebronchodilator baseline FEV₁ less than 70% of the predicted value, and at least 0.75 liters,
257 with the FEV₁/VC being less than 88% for men and less than 89% for women), and symptom
258 score (greater than zero on at least four of the seven days prior to randomization). These
259 studies included approximately equal numbers of patients with and without baseline
260 bronchodilator reversibility, defined as a 15% or greater increase FEV₁ after inhalation of 200
261 mcg of albuterol sulfate. A total of 405 patients received FORADIL AEROLIZER 12 mcg,
262 administered twice daily. Each trial compared FORADIL AEROLIZER 12 mcg twice daily
263 and FORADIL AEROLIZER 24 mcg twice daily with placebo and an active control drug.
264 The active control drug was ipratropium bromide in COPD Trial A, and slow-release
265 theophylline in COPD Trial B (the theophylline arm in this study was open-label). The
266 treatment period was 12 weeks in COPD Trial A, and 12 months in COPD Trial B.

267 The results showed that FORADIL AEROLIZER 12 mcg twice daily resulted in significantly
268 greater post-dose bronchodilation (as measured by serial FEV₁ for 12 hours post-dose; the
269 primary efficacy analysis) compared to placebo when evaluated after 12 weeks of treatment in
270 both trials, and after 12 months of treatment in the 12-month trial (COPD Trial B). Compared
271 to FORADIL AEROLIZER 12 mcg twice daily, FORADIL AEROLIZER 24 mcg twice daily
272 did not provide any additional benefit on a variety of endpoints including FEV₁.

273 Mean FEV₁ measurements after 12 weeks of treatment for one of the two major efficacy
274 studies ~~is are~~ shown in the figure below.

275 Figure 3

276 Mean FEV₁ after 12 Weeks of treatment from COPD Trial A

277

278 FORADIL AEROLIZER 12 mcg twice daily was statistically superior to placebo at all post-
279 dose timepoints tested (from 5 minutes to 12 hours post-dose) throughout the 12-week (COPD
280 Trial A) and 12-month (COPD Trial B) treatment periods.

281 In both pivotal trials compared with placebo, patients treated with FORADIL
282 AEROLIZER 12 mcg demonstrated improved morning pre-medication peak expiratory flow
283 rates and took fewer puffs of rescue albuterol.

284 INDICATIONS AND USAGE

285 FORADIL AEROLIZER is indicated for long-term, twice-daily (morning and evening)
286 administration in the maintenance treatment of asthma and in the prevention of bronchospasm
287 in adults and children 5 years of age and older with reversible obstructive airways disease,
288 including patients with symptoms of nocturnal asthma, who require regular treatment with
289 inhaled, short-acting, beta₂-agonists. It is not indicated for patients whose asthma can be
290 managed by occasional use of inhaled, short-acting, beta₂-agonists.

291 FORADIL AEROLIZER is also indicated for the acute prevention of exercise-induced
292 bronchospasm (EIB) in adults and children 12 years of age and older, when administered on
293 an occasional, as needed basis.

294 FORADIL AEROLIZER can be used to treat asthma concomitantly with short-acting
295 beta₂-agonists, inhaled or systemic corticosteroids, and theophylline therapy (see
296 PRECAUTIONS, Drug Interactions). A satisfactory clinical response to FORADIL
297 AEROLIZER does not eliminate the need for continued treatment with an anti-inflammatory
298 agent.

299 FORADIL AEROLIZER is indicated for the long-term, twice daily (morning and
300 evening) administration in the maintenance treatment of bronchoconstriction in patients with
301 Chronic Obstructive Pulmonary Disease including chronic bronchitis and emphysema.

302 **CONTRAINDICATIONS**

303 Foradil (formoterol fumarate) is contraindicated in patients with a history of hypersensitivity
304 to formoterol fumarate or to any components of this product.

305 **WARNINGS**

306 **IMPORTANT INFORMATION: FORADIL AEROLIZER SHOULD NOT BE
307 INITIATED IN PATIENTS WITH SIGNIFICANTLY WORSENING OR ACUTELY
308 DETERIORATING ASTHMA, WHICH MAY BE A LIFE-THREATENING
309 CONDITION.** The use of FORADIL AEROLIZER in this setting is inappropriate.

310 **FORADIL AEROLIZER IS NOT A SUBSTITUTE FOR INHALED OR ORAL
311 CORTICOSTEROIDS.** Corticosteroids should not be stopped or reduced at the time
312 FORADIL AEROLIZER is initiated. (See PRECAUTIONS, Information for Patients
313 and the accompanying Patient Instructions For Use.)

314 When beginning treatment with FORADIL AEROLIZER, patients who have
315 been taking inhaled, short-acting beta₂-agonists on a regular basis (e.g., four times a day)
316 should be instructed to discontinue the regular use of these drugs and use them only for
317 symptomatic relief of acute asthma symptoms (see PRECAUTIONS, Information for
318 Patients).

319 **Paradoxical Bronchospasm**

320 As with other inhaled beta₂-agonists, formoterol can produce paradoxical bronchospasm, that
321 may be life-threatening. If paradoxical bronchospasm occurs, FORADIL AEROLIZER should
322 be discontinued immediately and alternative therapy instituted.

323 **Deterioration of Asthma**

324 Asthma may deteriorate acutely over a period of hours or chronically over several days or
325 longer. If the usual dose of FORADIL AEROLIZER no longer controls the symptoms of
326 bronchoconstriction, and the patient's inhaled, short-acting beta₂-agonist becomes less
327 effective or the patient needs more inhalation of short-acting beta₂-agonist than usual, these
328 may be markers of deterioration of asthma. In this setting, a re-evaluation of the patient and
329 the asthma treatment regimen should be undertaken at once, giving special consideration to
330 the possible need for anti-inflammatory treatment, e.g., corticosteroids. Increasing the daily
331 dosage of FORADIL AEROLIZER beyond the recommended dose in this situation is not
332 appropriate. FORADIL AEROLIZER should not be used more frequently than twice daily
333 (morning and evening) at the recommended dose.

334 **Use of Anti-inflammatory Agents**

335 The use of beta₂-agonists alone may not be adequate to control asthma in many patients. Early
336 consideration should be given to adding anti-inflammatory agents, e.g., corticosteroids. There
337 are no data demonstrating that Foradil has any clinical anti-inflammatory effect and therefore
338 it cannot be expected to take the place of corticosteroids. Patients who already require oral or
339 inhaled corticosteroids for treatment of asthma should be continued on this type of treatment
340 even if they feel better as a result of initiating or increasing the dose of FORADIL
341 AEROLIZER. Any change in corticosteroid dosage, in particular a reduction, should be made
342 ONLY after clinical evaluation (see PRECAUTIONS, Information for Patients).

343 **Cardiovascular Effects**

344 Formoterol fumarate, like other beta₂-agonists, can produce a clinically significant
345 cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure,
346 and/or symptoms. Although such effects are uncommon after administration of FORADIL
347 AEROLIZER at recommended doses, if they occur, the drug may need to be discontinued. In
348 addition, beta-agonists have been reported to produce ECG changes, such as flattening of the
349 T wave, prolongation of the QTc interval, and ST segment depression. The clinical
350 significance of these findings is unknown. Therefore, formoterol fumarate, like other
351 sympathomimetic amines, should be used with caution in patients with cardiovascular
352 disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension
353 (see PRECAUTIONS, General).

354 **Immediate Hypersensitivity Reactions**

355 Immediate hypersensitivity reactions may occur after administration of FORADIL
356 AEROLIZER, as demonstrated by cases of anaphylactic reactions, urticaria, angioedema,
357 rash, and bronchospasm.

358 **Do Not Exceed Recommended Dose**

359 Fatalities have been reported in association with excessive use of inhaled sympathomimetic
360 drugs in patients with asthma. The exact cause of death is unknown, but cardiac arrest
361 following an unexpected development of a severe acute asthmatic crisis and subsequent
362 hypoxia is suspected.

363 **PRECAUTIONS**

364 **General**

365 FORADIL AEROLIZER should not be used to treat acute symptoms of asthma. FORADIL
366 AEROLIZER has not been studied in the relief of acute asthma symptoms and extra doses
367 should not be used for that purpose. When prescribing FORADIL AEROLIZER, the
368 physician should also provide the patient with an inhaled, short-acting beta₂-agonist for
369 treatment of symptoms that occur acutely, despite regular twice-daily (morning and evening)
370 use of FORADIL AEROLIZER. Patients should also be cautioned that increasing inhaled

371 beta₂-agonist use is a signal of deteriorating asthma. (See Information for Patients and the
372 accompanying Patient Instructions For Use.)

373 Formoterol fumarate, like other sympathomimetic amines, should be used with caution
374 in patients with cardiovascular disorders, especially coronary insufficiency, cardiac
375 arrhythmias, and hypertension; in patients with convulsive disorders or thyrotoxicosis; and in
376 patients who are unusually responsive to sympathomimetic amines. Clinically significant
377 changes in systolic and/or diastolic blood pressure, pulse rate and electrocardiograms have
378 been seen infrequently in individual patients in controlled clinical studies with formoterol.
379 Doses of the related beta₂-agonist albuterol, when administered intravenously, have been
380 reported to aggravate preexisting diabetes mellitus and ketoacidosis.

381 Beta-agonist medications may produce significant hypokalemia in some patients,
382 possibly through intracellular shunting, which has the potential to produce adverse
383 cardiovascular effects. The decrease in serum potassium is usually transient, not requiring
384 supplementation.

385 Clinically significant changes in blood glucose and/or serum potassium were
386 infrequent during clinical studies with long-term administration of FORADIL AEROLIZER
387 at the recommended dose.

388 Foradil® capsules should ONLY be used with the Aerolizer™ Inhaler and SHOULD
389 NOT be taken orally.

390 Foradil® capsules should always be stored in the blister, and only removed
391 IMMEDIATELY before use.

392 **Information for Patients**

393 It is important that patients understand how to use the Aerolizer Inhaler appropriately and how
394 it should be used in relation to other asthma medications they are taking (see the
395 accompanying Patient Instructions For Use).

396 The active ingredient of Foradil (formoterol fumarate) is a long-acting, bronchodilator
397 used for the treatment of asthma, including nocturnal asthma, and for the prevention of
398 exercise-induced bronchospasm. FORADIL AEROLIZER provides bronchodilation for up to
399 12 hours. Patients should be advised not to increase the dose or frequency of FORADIL
400 AEROLIZER without consulting the prescribing physician. Patients should be warned not to
401 stop or reduce concomitant asthma therapy without medical advice.

402 FORADIL AEROLIZER is not indicated to relieve acute asthma symptoms and extra
403 doses should not be used for that purpose. Acute symptoms should be treated with an inhaled,
404 short-acting, beta₂-agonist (the health-care provider should prescribe the patient with such
405 medication and instruct the patient in how it should be used). Patients should be instructed to
406 seek medical attention if their symptoms worsen, if FORADIL AEROLIZER treatment
407 becomes less effective, or if they need more inhalations of a short-acting beta₂-agonist than
408 usual. Patients should not inhale more than the contents of the prescribed number of capsules
409 at any one time. The daily dosage of FORADIL AEROLIZER should not exceed one capsule
410 twice daily (24 mcg total daily dose).

411 When FORADIL AEROLIZER is used for the prevention of EIB, the contents of one
412 capsule should be taken at least 15 minutes prior to exercise. Additional doses of FORADIL
413 AEROLIZER should not be used for 12 hours. Prevention of EIB has not been studied in
414 patients who are receiving chronic FORADIL AEROLIZER administration twice daily and
415 these patients should not use additional FORADIL AEROLIZER for prevention of EIB.

416 FORADIL AEROLIZER should not be used as a substitute for oral or inhaled
417 corticosteroids. The dosage of these medications should not be changed and they should not
418 be stopped without consulting the physician, even if the patient feels better after initiating
419 treatment with FORADIL AEROLIZER.

420 Patients should be informed that treatment with beta₂-agonists may lead to adverse
421 events which include palpitations, chest pain, rapid heart rate, tremor or nervousness. Patients
422 should be informed never to use FORADIL AEROLIZER with a spacer and never to exhale
423 into the device.

424 Patients should avoid exposing the Foradil capsules to moisture and should handle the
425 capsules with dry hands. The Aerolizer™ Inhaler should never be washed and should be kept
426 dry. The patient should always use the new Aerolizer Inhaler that comes with each refill.

427 Women should be advised to contact their physician if they become pregnant or if they
428 are nursing.

429 Patients should be told that in rare cases, the gelatin capsule might break into small
430 pieces. These pieces should be retained by the screen built into the Aerolizer Inhaler.
431 However, it remains possible that rarely, tiny pieces of gelatin might reach the mouth or throat
432 after inhalation. The capsule is less likely to shatter when pierced if: storage conditions are
433 strictly followed, capsules are removed from the blister immediately before use, and the
434 capsules are only pierced once.

435 **Drug Interactions**

436 If additional adrenergic drugs are to be administered by any route, they should be used with
437 caution because the pharmacologically predictable sympathetic effects of formoterol may be
438 potentiated.

439 Concomitant treatment with xanthine derivatives, steroids, or diuretics may potentiate
440 any hypokalemic effect of adrenergic agonists.

441 The ECG changes and/or hypokalemia that may result from the administration of
442 non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened
443 by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded.
444 Although the clinical significance of these effects is not known, caution is advised in the
445 co-administration of beta-agonist with non-potassium sparing diuretics.

446 Formoterol, as with other beta₂-agonists, should be administered with extreme caution
447 to patients being treated with monamine oxidase inhibitors, tricyclic antidepressants, or drugs
448 known to prolong the QTc interval because the action of adrenergic agonists on the
449 cardiovascular system may be potentiated by these agents. Drugs that are known to prolong
450 the QTc interval have an increased risk of ventricular arrhythmias.

451 Beta-adrenergic receptor antagonists (beta-blockers) and formoterol may inhibit the
452 effect of each other when administered concurrently. Beta-blockers not only block the
453 therapeutic effects of beta-agonists, such as formoterol, but may produce severe
454 bronchospasm in asthmatic patients. Therefore, patients with asthma should not normally be
455 treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after
456 myocardial infarction, there may be no acceptable alternatives to the use of beta-blockers in
457 patients with asthma. In this setting, cardioselective beta-blockers could be considered,
458 although they should be administered with caution.

459 **Carcinogenesis, Mutagenesis, Impairment of Fertility**

460 The carcinogenic potential of formoterol fumarate has been evaluated in 2-year drinking water
461 and dietary studies in both rats and mice. In rats, the incidence of ovarian leiomyomas was
462 increased at doses of 15 mg/kg and above in the drinking water study and at 20 mg/kg in the
463 dietary study, but not at dietary doses up to 5 mg/kg (AUC exposure approximately 450 times
464 human exposure at the maximum recommended daily inhalation dose). In the dietary study,
465 the incidence of benign ovarian theca-cell tumors was increased at doses of 0.5 mg/kg and
466 above (AUC exposure at the low dose of 0.5 mg/kg was approximately 45 times human
467 exposure at the maximum recommended daily inhalation dose). This finding was not observed
468 in the drinking water study, nor was it seen in mice (see below).

469 In mice, the incidence of adrenal subcapsular adenomas and carcinomas was increased
470 in males at doses of 69 mg/kg and above in the drinking water study, but not at doses up to
471 50 mg/kg (AUC exposure approximately 590 times human exposure at the maximum
472 recommended daily inhalation dose) in the dietary study. The incidence of hepatocarcinomas
473 was increased in the dietary study at doses of 20 and 50 mg/kg in females and 50 mg/kg in
474 males, but not at doses up to 5 mg/kg in either males or females (AUC exposure
475 approximately 60 times human exposure at the maximum recommended daily inhalation
476 dose). Also in the dietary study, the incidence of uterine leiomyomas and leiomyosarcomas
477 was increased at doses of 2 mg/kg and above (AUC exposure at the low dose of 2 mg/kg was
478 approximately 25 times human exposure at the maximum recommended daily inhalation
479 dose). Increases in leiomyomas of the rodent female genital tract have been similarly
480 demonstrated with other beta-agonist drugs.

481 Formoterol fumarate was not mutagenic or clastogenic in the following tests:
482 mutagenicity tests in bacterial and mammalian cells, chromosomal analyses in mammalian
483 cells, unscheduled DNA synthesis repair tests in rat hepatocytes and human fibroblasts,
484 transformation assay in mammalian fibroblasts and micronucleus tests in mice and rats.

485 Reproduction studies in rats revealed no impairment of fertility at oral doses up to
486 3 mg/kg (approximately 1000 times the maximum recommended daily inhalation dose in
487 humans on a mg/m² basis).

488 **Pregnancy, Teratogenic Effects, Pregnancy Category C**

489 Formoterol fumarate has been shown to cause stillbirth and neonatal mortality at oral doses of
490 6 mg/kg (approximately 2000 times the maximum recommended daily inhalation dose in
491 humans on a mg/m² basis) and above in rats receiving the drug during the late stage of

492 pregnancy. These effects, however, were not produced at a dose of 0.2 mg/kg (approximately
493 70 times the maximum recommended daily inhalation dose in humans on a mg/m² basis).
494 When given to rats throughout organogenesis, oral doses of 0.2 mg/kg and above delayed
495 ossification of the fetus, and doses of 6 mg/kg and above decreased fetal weight. Formoterol
496 fumarate did not cause malformations in rats or rabbits following oral administration. Because
497 there are no adequate and well-controlled studies in pregnant women, FORADIL
498 AEROLIZER should be used during pregnancy only if the potential benefit justifies the
499 potential risk to the fetus.

500 **Use in Labor and Delivery**

501 Formoterol fumarate has been shown to cause stillbirth and neonatal mortality at oral doses of
502 6 mg/kg (approximately 2000 times the maximum recommended daily inhalation dose in
503 humans on a mg/m² basis) and above in rats receiving the drug for several days at the end of
504 pregnancy. These effects were not produced at a dose of 0.2 mg/kg (approximately 70 times
505 the maximum recommended daily inhalation dose in humans on a mg/m² basis). There are no
506 adequate and well-controlled human studies that have investigated the effects of FORADIL
507 AEROLIZER during labor and delivery.

508 Because beta-agonists may potentially interfere with uterine contractility, FORADIL
509 AEROLIZER should be used during labor only if the potential benefit justifies the potential
510 risk.

511 **Nursing Mothers**

512 In reproductive studies in rats, formoterol was excreted in the milk. It is not known whether
513 formoterol is excreted in human milk, but because many drugs are excreted in human milk,
514 caution should be exercised if FORADIL AEROLIZER is administered to nursing women.
515 There are no well-controlled human studies of the use of FORADIL AEROLIZER in nursing
516 mothers.

517 **Pediatric Use**

518 **Asthma**

519 A total of 776 children 5 years of age and older with asthma were studied in three
520 multiple-dose controlled clinical trials. Of the 512 children who received formoterol, 508
521 were 5-12 years of age, and approximately one third were 5-8 years of age.

522 **Exercise Induced Bronchoconstriction**

523 A total of 20 adolescent patients, 12-16 years of age, were studied in three well-controlled
524 single-dose clinical trials.

525 The safety and effectiveness of FORADIL AEROLIZER in pediatric patients below
526 5 years of age has not been established. (See CLINICAL TRIALS, Pediatric Asthma Trial,
527 and ADVERSE REACTIONS, Experience in Pediatric, Adolescent and Adult Patients.)

528 Geriatric Use

529 Of the total number of patients who received FORADIL AEROLIZER in adolescent and adult
530 chronic dosing asthma clinical trials, 318 were 65 years of age or older and 39 were 75 years
531 of age and older. Of the 811 patients who received FORADIL AEROLIZER in two pivotal
532 multiple-dose controlled clinical studies in patients with COPD, 395 (48.7%) were 65 years of
533 age or older while 62 (7.6%) were 75 years of age or older. No overall differences in safety or
534 effectiveness were observed between these subjects and younger subjects. A slightly higher
535 frequency of chest infection was reported in the 39 asthma patients 75 years of age and older,
536 although a causal relationship with Foradil has not been established. Other reported clinical
537 experience has not identified differences in responses between the elderly and younger adult
538 patients, but greater sensitivity of some older individuals cannot be ruled out. (See
539 PRECAUTIONS, Drug Interactions.)

540 ADVERSE REACTIONS

541 Adverse reactions to Foradil are similar in nature to other selective beta₂-adrenoceptor
542 agonists; e.g., angina, hypertension or hypotension, tachycardia, arrhythmias, nervousness,
543 headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise,
544 hypokalemia, hyperglycemia, metabolic acidosis and insomnia.

545 Experience in Pediatric, Adolescent and Adult Patients with Asthma

546 Of the 5,824 patients in multiple-dose controlled clinical trials, 1,985 were treated with
547 FORADIL AEROLIZER at the recommended dose of 12 mcg twice daily. The following
548 table shows adverse events where the frequency was greater than or equal to 1% in the Foradil
549 twice daily group and where the rates in the Foradil group exceeded placebo. Three adverse
550 events showed dose ordering among tested doses of 6, 12 and 24 mcg administered twice
551 daily: tremor, dizziness and dysphonia.

NUMBER AND FREQUENCY OF ADVERSE EXPERIENCES IN PATIENTS 5 YEARS OF AGE AND OLDER FROM MULTIPLE-DOSE CONTROLLED CLINICAL TRIALS

555 Adverse Event		556 Foradil Aerolizer 12 mcg twice daily		557 Placebo	
		n	(%)	n	(%)
558 Total Patients		1985	(100)	969	(100)
559 Infection viral		341	(17.2)	166	(17.1)
560 Bronchitis		92	(4.6)	42	(4.3)
561 Chest infection		54	(2.7)	4	(0.4)
562 Dyspnea		42	(2.1)	16	(1.7)
563 Chest pain		37	(1.9)	13	(1.3)
564 Tremor		37	(1.9)	4	(0.4)
565 Dizziness		31	(1.6)	15	(1.5)
566 Insomnia		29	(1.5)	8	(0.8)
567 Tonsilitis		23	(1.2)	7	(0.7)
568 Rash		22	(1.1)	7	(0.7)
569 Dysphonia		19	(1.0)	9	(0.9)

570 **Experience in Children with Asthma**

571 The safety of FORADIL AEROLIZER compared to placebo was investigated in one large,
572 multicenter, randomized, double-blind clinical trial in 518 children with asthma (ages 5-12
573 years) in need of daily bronchodilators and anti-inflammatory treatment. The numbers and
574 percent of patients who reported adverse events were comparable in the 12 mcg twice daily
575 and placebo groups. In general, the pattern of the adverse events observed in children differed
576 from the usual pattern seen in adults. The adverse events that were more frequent in the
577 formoterol group than in the placebo group reflected infection/inflammation (viral infection,
578 rhinitis, tonsilitis, gastroenteritis) or abdominal complaints (abdominal pain, nausea,
579 dyspepsia).

580 **Experience in Adult Patients with COPD**

581 Of the 1634 patients in two pivotal multiple dose Chronic Obstructive Pulmonary Disease
582 (COPD) controlled trials, 405 were treated with FORADIL AEROLIZER 12 mcg twice daily.
583 The numbers and percent of patients who reported adverse events were comparable in the 12
584 mcg twice daily and placebo groups. Adverse events (AE's) experienced were similar to
585 those seen in asthmatic patients, but with a higher incidence of COPD-related AE's in both
586 placebo and formoterol treated patients.

587 The following table shows adverse events where the frequency was greater than or
588 equal to 1% in the FORADIL AEROLIZER group and where the rates in the FORADIL
589 AEROLIZER group exceeded placebo. The two clinical trials included doses of 12 mcg and
590 24 mcg, administered twice daily. Seven adverse events showed dose ordering among tested
591 doses of 12 and 24 mcg administered twice daily; pharyngitis, fever, muscle cramps,
592 increased sputum, dysphonia, myalgia, and tremor.

593

NUMBER AND FREQUENCY OF ADVERSE EXPERIENCES IN ADULT COPD PATIENTS TREATED IN MULTIPLE-DOSE CONTROLLED CLINICAL TRIALS		
Adverse event	FORADIL AEROLIZER 12mcg twice daily n (%)	Placebo n (%)
Total patients	405 (100)	420 (100)
Upper respiratory tract infection	30 (7.4)	24 (5.7)
Pain back	17 (4.2)	17 (4.0)
Pharyngitis	14 (3.5)	10 (2.4)
Pain chest	13 (3.2)	9 (2.1)
Sinusitis	11 (2.7)	7 (1.7)
Fever	9 (2.2)	6 (1.4)
Cramps leg	7 (1.7)	2 (0.5)
Cramps muscle	7 (1.7)	0
Anxiety	6 (1.5)	5 (1.2)
Pruritis	6 (1.5)	4 (1.0)
Sputum increased	6 (1.5)	5 (1.2)
Mouth dry	5 (1.2)	4 (1.0)
Trauma	5 (1.2)	0

594 Overall, the frequency of all cardiovascular adverse events in the two pivotal studies
595 was low and comparable to placebo (6.4% for FORADIL AEROLIZER 12 mcg twice daily,
596 and 6.0% for placebo). There were no frequently-occurring specific cardiovascular adverse
597 events for FORADIL AEROLIZER (frequency greater than or equal to 1% and greater than
598 placebo).

599 Post Marketing Experience

600 In extensive worldwide marketing experience with Foradil, serious exacerbations of asthma,
601 including some that have been fatal, have been reported. While most of these cases have been
602 in patients with severe or acutely deteriorating asthma (see WARNINGS), a few have
603 occurred in patients with less severe asthma. The contribution of Foradil to these cases could
604 not be determined.

605 Rare reports of anaphylactic reactions, including severe hypotension and angioedema,
606 have also been received in association with the use of formoterol fumarate inhalation powder.

607 DRUG ABUSE AND DEPENDENCE

608 There was no evidence in clinical trials of drug dependence with the use of Foradil.

609 **OVERDOSAGE**

610 The expected signs and symptoms with overdosage of FORADIL AEROLIZER are those of
611 excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the signs
612 and symptoms listed under ADVERSE REACTIONS, e.g., angina, hypertension or
613 hypotension, tachycardia, with rates up to 200 beats/min., arrhythmias, nervousness,
614 headache, tremor, seizures, muscle cramps, dry mouth, palpitation, nausea, dizziness, fatigue,
615 malaise, hypokalemia, hyperglycemia, and insomnia. Metabolic acidosis may also occur. As
616 with all inhaled sympathomimetic medications, cardiac arrest and even death may be
617 associated with an overdose of FORADIL AEROLIZER.

618 Treatment of overdosage consists of discontinuation of FORADIL AEROLIZER
619 together with institution of appropriate symptomatic and/or supportive therapy. The judicious
620 use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such
621 medication can produce bronchospasm. There is insufficient evidence to determine if dialysis
622 is beneficial for overdosage of FORADIL AEROLIZER. Cardiac monitoring is recommended
623 in cases of overdosage.

624 The minimum acute lethal inhalation dose of formoterol fumarate in rats is 156 mg/kg;
625 (approximately 53,000 and 25,000 times the maximum recommended daily inhalation dose in
626 adults and children, respectively, on a mg/m² basis). The median lethal oral doses in Chinese
627 hamsters, rats, and mice provide even higher multiples of the maximum recommended daily
628 inhalation dose in humans.

629 **DOSAGE AND ADMINISTRATION**

630 Foradil capsules should be administered only by the oral inhalation route (see the
631 accompanying Patient Instructions for Use) and only using the Aerolizer Inhaler. Foradil
632 capsules should not be ingested (i.e., swallowed) orally. Foradil capsules should always be
633 stored in the blister, and only removed IMMEDIATELY BEFORE USE.

634 **For Maintenance Treatment of Asthma**

635 For adults and children 5 years of age and older, the usual dosage is the inhalation of the
636 contents of one 12-mcg Foradil capsule every 12 hours using the Aerolizer™ Inhaler. The
637 patient must not exhale into the device. The total daily dose of Foradil should not exceed one
638 capsule twice daily (24 mcg total daily dose). More frequent administration or administration
639 of a larger number of inhalations is not recommended. If symptoms arise between doses, an
640 inhaled short-acting beta₂-agonist should be taken for immediate relief.

641 If a previously effective dosage regimen fails to provide the usual response, medical
642 advice should be sought immediately as this is often a sign of destabilization of asthma. Under
643 these circumstances, the therapeutic regimen should be reevaluated and additional therapeutic
644 options, such as inhaled or systemic corticosteroids, should be considered.

645 **For Prevention of Exercise-Induced Bronchospasm (EIB)**

646 For adults and adolescents 12 years of age or older, the usual dosage is the inhalation of the
647 contents of one 12-mcg Foradil capsule at least 15 minutes before exercise administered on an
648 occasional as-needed basis.

649 Additional doses of FORADIL AEROLIZER should not be used for 12 hours after the
650 administration of this drug. Regular, twice-daily dosing has not been studied in preventing
651 EIB. Patients who are receiving FORADIL AEROLIZER twice daily for maintenance
652 treatment of their asthma should not use additional doses for prevention of EIB and may
653 require a short-acting bronchodilator.

654 **For Maintenance Treatment of Chronic Obstructive Pulmonary Disease
655 (COPD)**

656 The usual dosage is the inhalation of the contents of one 12 mcg Foradil capsule every 12
657 hours using the Aerolizer™ inhaler.

658 A total daily dose of greater than 24 mcg is not recommended.

659 If a previously effective dosage regimen fails to provide the usual response, medical
660 advice should be sought immediately as this is often a sign of destabilization of COPD. Under
661 these circumstances, the therapeutic regimen should be re-evaluated and additional therapeutic
662 options should be considered.

663 **HOW SUPPLIED**

664 FORADIL® AEROLIZER™ contains: aluminum blister-packaged 12-mcg Foradil (formoterol
665 fumarate) clear gelatin capsules with “CG” printed on one end and “FXF” printed on the
666 opposite end; one Aerolizer™ Inhaler; and Patient Instructions for Use

667 Unit Dose (blister pack)

668 Box of 18 (strips of 6).....**NDC 0083-0167-11**

669 Unit Dose (blister pack)

670 Box of 60 (strips of 6).....**NDC 0083-0167-74.**

671 Foradil® capsules should be used with the Aerolizer™ Inhaler only. The Aerolizer™
672 Inhaler should not be used with any other capsules.

673 **Prior to dispensing:** Store in a refrigerator, 2°C-8°C (36°F-46°F)

674 **After dispensing to patient:** Store at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room
675 Temperature]. Protect from heat and moisture. CAPSULES SHOULD ALWAYS BE
676 STORED IN THE BLISTER AND ONLY REMOVED FROM THE BLISTER
677 IMMEDIATELY BEFORE USE.

678 Always discard the Foradil® capsules and Aerolizer™ Inhaler by the “Use by” date and
679 always use the new Aerolizer Inhaler provided with each new prescription.

680 Keep out of the reach of children.

681

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FORADIL® AEROLIZER™ (formoterol fumarate inhalation powder)

T2001-69
89012502

FOR ORAL INHALATION ONLY

Patient Instructions for Use

NEVER PLACE A CAPSULE IN THE INHALER'S MOUTHPIECE

READ ALL INSTRUCTIONS BEFORE USE

FORADIL AEROLIZER consists of Foradil® capsules and Aerolizer™ Inhaler. Both the capsules and the inhaler should be used by the "Use by" date written by your pharmacist on the sticker on the outside of the FORADIL AEROLIZER box. Upon receipt of FORADIL AEROLIZER from the pharmacy, remove the sticker with the "Use by" date from the outside of the box and place it on the Aerolizer Inhaler cover. If the "Use by" date on the sticker is blank, you will need to count 4 months from the date of purchase and write this date on the sticker. Please check the product expiration date stamped on the box. If the product expiration date is less than 4 months from the purchase date, then you should write the expiration date on the sticker instead. Foradil capsules are provided in aluminum blisters wrapped in a foil pouch. You should open the pouch when you are ready to use Foradil Aerolizer.

This leaflet provides summary information about FORADIL AEROLIZER. Before you start to take FORADIL AEROLIZER, read this leaflet carefully and keep it for future use. You should read the leaflet that comes with your prescription every time you refill it because there may be new information. This leaflet does not contain the complete information about your medication.

For more information ask your health-care provider or pharmacist.

What you should know about FORADIL AEROLIZER

FORADIL AEROLIZER contains Foradil (formoterol fumarate), a medication that is provided as a powder inside a gelatin capsule, and an Aerolizer Inhaler. Each gelatin capsule contains 12 mcg of active drug (formoterol fumarate) mixed with lactose, which is a sugar. The contents of the capsule (the powder) are inhaled, using the Aerolizer Inhaler that is provided. **THE CAPSULES SHOULD NOT BE SWALLOWED.**

FORADIL AEROLIZER is used for the treatment of breathing problems experienced by people who have asthma, or chronic obstructive pulmonary disease (chronic bronchitis or emphysema). Foradil is a long-acting bronchodilator. It acts to help keep the airways open, making it easier to breathe, and reduces the symptoms of asthma, chronic bronchitis and emphysema. Symptoms of asthma and chronic obstructive pulmonary disease that are caused by airflow obstruction include shortness of breath, wheezing, chest tightness, and cough. A single dose of FORADIL AEROLIZER acts up to 12 hours, and therefore, should only be used twice daily.

Important Points to Remember About Using FORADIL AEROLIZER

1. TELL YOUR HEALTH-CARE PROVIDER BEFORE STARTING TO TAKE THIS MEDICINE:

- If you are pregnant or want to become pregnant,
- If you are breastfeeding a baby,
- If you are allergic to formoterol, or any other inhaled bronchodilator. In some circumstances, this medicine may not

- be right for you and your health-care provider may wish to give you a different medicine.
- Make sure that your health-care provider knows what other medicines you are taking.

3. It is important that you inhale each dose as your health-care provider has advised. **Do not use FORADIL AEROLIZER more frequently than 2 times daily, morning and evening, approximately 12 hours apart, at the recommended dose.**

4. It is **IMPORTANT THAT YOU USE FORADIL AEROLIZER REGULARLY. DO NOT STOP TREATMENT EVEN IF YOU ARE FEELING BETTER** unless told to do so by your health-care provider.

5. If you miss a dose, just take your next scheduled dose when it is due. **DO NOT DOUBLE** the dose.

6. If you use FORADIL AEROLIZER more frequently than your health-care provider has prescribed, tell your health-care provider immediately. If you develop nausea and/or vomiting, shakiness, headache, fast or irregular heartbeat, or sleeplessness, tell your health-care provider immediately.

7. **DO NOT USE FORADIL AEROLIZER TO RELIEVE SUDDEN ASTHMA SYMPTOMS** (For example, sudden severe onset or worsening of wheezing, cough, chest tightness, and/or shortness of breath that has been diagnosed by your health-care provider as due to asthma). Sudden asthma symptoms should be treated with an inhaled, short-acting bronchodilator. If you do not have an inhaled, short-acting bronchodilator, contact your health-care provider to have one prescribed for you.

8. **Tell your health-care provider immediately if your asthma is getting worse, as indicated by any of the following situations** since you may need a re-evaluation of your treatment.

- The relief of your wheezing or chest tightness is not as good as usual or does not last for as long as usual.
- Your inhaled, short-acting bronchodilator becomes less effective.
- You need more inhalations than usual of your inhaled, short-acting bronchodilator.
- You have a significant decrease in your peak flow measurement as previously defined by your health-care provider.

9. Likewise, **tell your health-care provider immediately if your chronic obstructive pulmonary disease symptoms worsen, as indicated by any of the following situations** since you may need a re-evaluation of your treatment.

- The relief of your wheezing or chest tightness is not as good as usual or does not last for as long as usual, or your shortness of breath increases.
- Your inhaled, short-acting bronchodilator becomes less effective.
- You need more inhalations than usual of your inhaled, short-acting bronchodilator.
- You have a significant decrease in your peak flow measurement as previously defined by your health-care provider.
- Your sputum expectoration increases and becomes purulent.

10. Use other inhaled medicines only as directed by your health-care provider.

11. Do not use the Aerolizer Inhaler with a spacer device.

How to use FORADIL AEROLIZER

Follow the instructions below. If you have any questions, ask your health-care provider or pharmacist.

Foradil capsules and the Aerolizer Inhaler should be used by the "Use by" date written by your pharmacist on the sticker on the outside of the FORADIL AEROLIZER box. Upon receipt of FORADIL AEROLIZER from the pharmacy, remove the sticker with the "Use by" date from the outside of the box and place it on the Aerolizer Inhaler cover. If the "Use by" date on the sticker is blank, you will need to count 4 months from the date of purchase and write this date on the sticker. Please check the product expiration date stamped on the box. If the product expiration date is less than 4 months from the purchase date, then you should write the expiration date on the sticker instead.

Your health-care provider will advise you how to use FORADIL AEROLIZER. Do not inhale more doses or use FORADIL AEROLIZER more often than your health-care provider advises.

USE ONLY AS DIRECTED BY YOUR HEALTH-CARE PROVIDER

For the long-term treatment of asthma, the recommended dose for adults and children 5 years of age and older is one Foradil capsule inhaled with the use of the Aerolizer Inhaler (as described below) twice a day, approximately every 12 hours.

In patients 12 years of age and older, FORADIL AEROLIZER may be used to help prevent asthma attacks, brought on by physical activity or exercise. Inhale the contents of one capsule, as directed by your health-care provider, about 15 minutes before you start the activity or exercise.

Do not inhale more than the contents of one capsule at any one time. Additional doses of FORADIL AEROLIZER should not be used for 12 hours. If you are receiving FORADIL AEROLIZER twice daily for long-term treatment of asthma, you should not use additional doses of FORADIL AEROLIZER for prevention of asthma attacks brought on by physical activity or exercise, instead you should use a short-acting bronchodilator that is prescribed for you by your health-care provider.

For the long-term treatment of chronic obstructive pulmonary disease (chronic bronchitis or emphysema), the recommended dose is one Foradil capsule inhaled with the use of the Aerolizer Inhaler (as described below) twice a day, approximately every 12 hours.

How to use the Foradil capsules with your Aerolizer Inhaler

Keep your Foradil and Aerolizer Inhaler dry. Handle with DRY hands.

Foradil capsules are to be administered only with the Aerolizer Inhaler provided. Do not use Foradil capsules with any other capsule inhaler, and do not use the Aerolizer Inhaler to administer any other capsule medication. Do not use a spacer with the Aerolizer Inhaler.

Check the "Use by" date on the Aerolizer Inhaler cover. If the "Use by" date has passed, replace the product and Aerolizer Inhaler. Remove the aluminum pouch covering the foil blister cards which contain the Foradil capsules.

1. Pull off the Aerolizer Inhaler cover. (Figure 1)

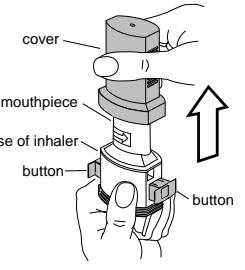


Figure 1

- Hold the base of the Aerolizer Inhaler firmly and twist the mouthpiece in the direction of the arrow to open. (Figure 2) Push the buttons in to make sure that the 4 pins are visible in the capsule well on each side.

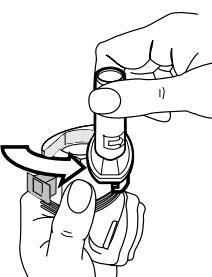


Figure 2

- Twist the mouthpiece back to the closed position. (Figure 6)

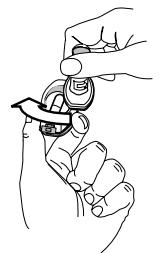


Figure 6

- Remove capsule from foil blister IMMEDIATELY BEFORE USE.

- Separate one blistered capsule by tearing at intersecting perforations. (Figure 3)

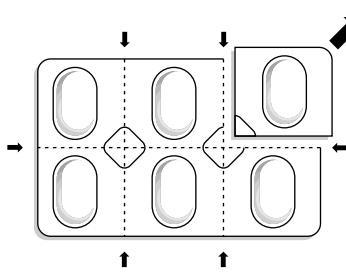


Figure 3

- Peel paper backing from blister and push capsule through the remaining foil. (Figure 4)

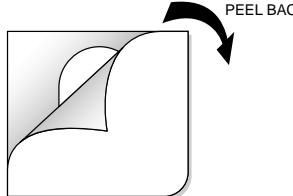


Figure 4

- Place the capsule in the capsule-chamber in the base of the Aerolizer Inhaler cover. NEVER PLACE A CAPSULE DIRECTLY INTO THE MOUTHPIECE. (Figure 5)

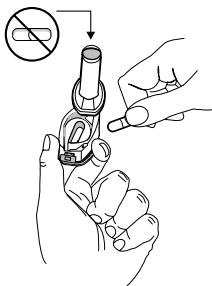


Figure 5

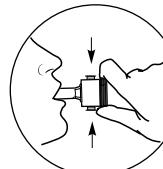
- Release the buttons. If the buttons stick in the depressed position, grasp the wings on the buttons to retract them before the inhalation step. Do not depress the buttons a second time, since in rare cases, this may cause the capsule to shatter into small pieces. These pieces should be retained by the screen built into the Aerolizer Inhaler. It remains possible that rarely, tiny pieces of gelatin capsule might reach your mouth or throat upon inhalation. Gelatin is not harmful if accidentally swallowed or inhaled. The capsule is less likely to shatter when pierced if capsules are removed from the foil blister IMMEDIATELY before use; storage conditions are strictly followed; and the capsule is only pierced ONCE.

- Exhale fully. DO NOT EXHALE INTO THE MOUTHPIECE. (Figure 8)



Figure 8

- Tilt your head back slightly. Keeping the Aerolizer Inhaler horizontal, with the blue buttons to the left and right (NOT up and down), place the mouthpiece in your mouth, closing your lips around the mouthpiece. (Figure 9 and 10)

CORRECT
Figure 9INCORRECT
Figure 10

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Foradil® Aerolizer™
(formoterol fumarate inhalation powder)

12. Breathe in rapidly but steadily, as deeply as you can (Figure 11). As the capsule spins around in the chamber dispensing the medication, you will experience a sweet taste and hear a whirring noise. If you have not heard the whirring noise, the capsule may be stuck. If this occurs, open the Aerolizer Inhaler and loosen the capsule allowing it to spin freely. DO NOT try to loosen the capsule by repeatedly pressing the buttons.

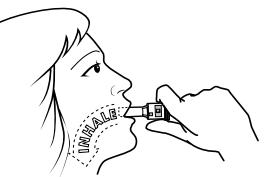


Figure 11

13. While removing the Aerolizer Inhaler from your mouth, continue to hold your breath as long as comfortably possible, then exhale.

14. Open the Aerolizer Inhaler to see if any powder is still in the capsule. If any powder remains in the capsule repeat steps 10 to 13. Most people are able to empty the capsule in one or two inhalations.

15. After use, open the Aerolizer Inhaler, remove and discard the empty capsule. Do not leave a used capsule in the chamber.

16. Close the mouthpiece and replace the cover.

REMEMBER:

- Never exhale into the Aerolizer Inhaler device.
- Never attempt to take the Aerolizer Inhaler apart.
- Never place a capsule directly into the mouthpiece of the Aerolizer Inhaler.
- Never leave a used capsule in the Aerolizer Inhaler chamber.
- Always use the Aerolizer Inhaler in a level, horizontal position.
- Never wash the Aerolizer Inhaler. KEEP IT DRY.
- Always keep the Aerolizer Inhaler and Foradil capsules in a dry place.
- Always use the new Aerolizer Inhaler that comes with your refill.

Side effects you may experience with FORADIL AEROLIZER

Along with its beneficial effects, a medicine may cause certain unwanted effects. FORADIL AEROLIZER may occasionally cause tremor, fast and irregular heart beat, or headache. Muscle cramps and pain, agitation, dizziness, nervousness or fatigue, difficulties with sleeping and irritation of the mouth or throat occur rarely. Some of these effects may go away as your body gets used to the medicine. Check with your doctor if any of these unwanted effects continues to bother you. Paradoxical bronchospasm, a narrowing of the airways, occurs very rarely, but may be serious. Report any increased difficulty in breathing after use of FORADIL AEROLIZER to your health-care provider immediately. You should also tell the health-care provider if you notice any other undesirable effects.

Expiration date

Use Foradil capsules before the "Use by" date on the Aerolizer Inhaler cover. The "Use by" date is either 4 months from the

purchase date, or the product expiration date, whichever comes first.

Always discard the old Aerolizer Inhaler by the "Use by" date and use the new one provided with each new prescription.

Storing your FORADIL AEROLIZER
Once dispensed, store at controlled room temperature,
20°C to 25°C (68°F to 77°F). Protect from heat and
moisture. CAPSULES SHOULD ALWAYS BE STORED IN
THE BLISTER AND ONLY REMOVED FROM THE BLISTER
IMMEDIATELY BEFORE USE.

Keep this and all drugs out of the reach of children.

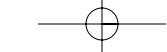
REMEMBER: This medicine has been prescribed for you
by your health-care provider. DO NOT give this medicine
to anyone else.

Your health-care provider has determined that this product is likely to help your personal health. **USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR HEALTH-CARE PROVIDER.** If you have any further questions about the use of FORADIL AEROLIZER, consult with your health-care provider or call 1-877-FORADIL (1-877-367-2345).

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SEPTEMBER 2001 Printed in U.S.A. 89012502

 NOVARTIS

Distributed by
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936



89012302

FORADIL® AEROLIZER™ (formoterol fumarate inhalation powder)

FOR ORAL INHALATION ONLY

Patient Instructions for Use

NEVER PLACE A CAPSULE IN THE INHALER'S MOUTHPIECE

READ ALL INSTRUCTIONS BEFORE USE

FORADIL AEROLIZER consists of Foradil® capsules and Aerolizer™ Inhaler. Both the capsules and the inhaler should be used by the "Use by" date written by your pharmacist on the sticker on the outside of the FORADIL AEROLIZER box. Upon receipt of FORADIL AEROLIZER from the pharmacy, remove the sticker with the "Use by" date from the outside of the box and place it on the Aerolizer Inhaler cover. If the "Use by" date on the sticker is blank, you will need to count 4 months from the date of purchase and write this date on the sticker. Please check the product expiration date stamped on the box. If the product expiration date is less than 4 months from the purchase date, then you should write the expiration date on the sticker instead. Foradil capsules are provided in aluminum blisters wrapped in a foil pouch. You should open the pouch when you are ready to use Foradil Aerolizer.

This leaflet provides summary information about FORADIL AEROLIZER. Before you start to take FORADIL AEROLIZER, read this leaflet carefully and keep it for future use. You should read the leaflet that comes with your prescription every time you refill it, because there may be new information. This leaflet does not contain the complete information about your medication.

For more information ask your health-care provider or pharmacist.

What you should know about FORADIL AEROLIZER

FORADIL AEROLIZER contains Foradil (formoterol fumarate), a medication that is provided as a powder inside a gelatin capsule, and an Aerolizer Inhaler. Each gelatin capsule contains 12 mcg of active drug (formoterol fumarate) mixed with lactose, which is a sugar. The contents of the capsule (the powder) are inhaled, using the Aerolizer Inhaler that is provided. **THE CAPSULES SHOULD NOT BE SWALLOWED.**

FORADIL AEROLIZER is used for the treatment of breathing problems experienced by people who have asthma, or chronic obstructive pulmonary disease (chronic bronchitis or emphysema). Foradil is a long-acting bronchodilator. It acts to help keep the airways open, making it easier to breathe, and reduces the symptoms of asthma, chronic bronchitis and emphysema. Symptoms of asthma and chronic obstructive pulmonary disease that are caused by airflow obstruction include shortness of breath, wheezing, chest tightness, and cough. A single dose of FORADIL AEROLIZER acts up to 12 hours, and therefore, should only be used twice daily.

Important Points to Remember About Using FORADIL AEROLIZER

1. TELL YOUR HEALTH-CARE PROVIDER BEFORE STARTING TO TAKE THIS MEDICINE:

- If you are pregnant or want to become pregnant,
- If you are breastfeeding a baby,
- If you are allergic to formoterol, or any other inhaled

bronchodilator. In some circumstances, this medicine may not be right for you and your health-care provider may wish to give you a different medicine.

2. Make sure that your health-care provider knows what other medicines you are taking.

3. It is important that you inhale each dose as your health-care provider has advised. **DO NOT USE FORADIL AEROLIZER more frequently than 2 times daily, morning and evening, approximately 12 hours apart, at the recommended dose.**

4. It is **IMPORTANT THAT YOU USE FORADIL AEROLIZER REGULARLY. DO NOT STOP TREATMENT EVEN IF YOU ARE FEELING BETTER** unless told to do so by your health-care provider.

5. If you miss a dose, just take your next scheduled dose when it is due. **DO NOT DOUBLE** the dose.

6. If you use FORADIL AEROLIZER more frequently than your health-care provider has prescribed, tell your health-care provider immediately. If you develop nausea and/or vomiting, shakiness, headache, fast or irregular heartbeat, or sleeplessness, tell your health-care provider immediately.

7. **DO NOT USE FORADIL AEROLIZER TO RELIEVE SUDDEN ASTHMA SYMPTOMS** (For example, sudden severe onset or worsening of wheezing, cough, chest tightness, and/or shortness of breath that has been diagnosed by your health-care provider as due to asthma). Sudden asthma symptoms should be treated with an inhaled, short-acting bronchodilator. If you do not have an inhaled, short-acting bronchodilator, contact your health-care provider to have one prescribed for you.

8. **Tell your health-care provider immediately if your asthma is getting worse, as indicated by any of the following situations** since you may need a re-evaluation of your treatment.

- The relief of your wheezing or chest tightness is not as good as usual or does not last for as long as usual.
- Your inhaled, short-acting bronchodilator becomes less effective.
- You need more inhalations than usual of your inhaled, short-acting bronchodilator.
- You have a significant decrease in your peak flow measurement as previously defined by your health-care provider.

9. Likewise, **tell your health-care provider immediately if your chronic obstructive pulmonary disease symptoms worsen, as indicated by any of the following situations** since you may need a re-evaluation of your treatment.

- The relief of your wheezing or chest tightness is not as good as usual or does not last for as long as usual, or your shortness of breath increases.
- Your inhaled, short-acting bronchodilator becomes less effective.
- You need more inhalations than usual of your inhaled, short-acting bronchodilator.
- You have a significant decrease in your peak flow measurement as previously defined by your health-care provider.
- Your sputum expectoration increases and becomes purulent.

10. Use other inhaled medicines only as directed by your health-care provider.

11. Do not use the Aerolizer Inhaler with a spacer device.

How to use FORADIL AEROLIZER

Follow the instructions below. If you have any questions, ask your health-care provider or pharmacist.

Foradil capsules and the Aerolizer Inhaler should be used by the "Use by" date written by your pharmacist on the sticker on the outside of the FORADIL AEROLIZER box. Upon receipt of FORADIL AEROLIZER from the pharmacy, remove the sticker with the "Use by" date from the outside of the box and place it on the Aerolizer Inhaler cover. If the "Use by" date on the sticker is blank, you will need to count 4 months from the date of purchase and write this date on the sticker. Please check the product expiration date stamped on the box. If the product expiration date is less than 4 months from the purchase date, then you should write the expiration date on the sticker instead.

Your health-care provider will advise you how to use FORADIL AEROLIZER. Do not inhale more doses or use FORADIL AEROLIZER more often than your health-care provider advises.

USE ONLY AS DIRECTED BY YOUR HEALTH-CARE PROVIDER

For the long-term treatment of asthma, the recommended dose for adults and children 5 years of age and older is one Foradil capsule inhaled with the use of the Aerolizer Inhaler (as described below) twice a day, approximately every 12 hours.

In patients 12 years of age and older, FORADIL AEROLIZER may be used to help prevent asthma attacks, brought on by physical activity or exercise. Inhale the contents of one capsule, as directed by your health-care provider, about 15 minutes before you start the activity or exercise.

Do not inhale more than the contents of one capsule at any one time. Additional doses of FORADIL AEROLIZER should not be used for 12 hours. If you are receiving FORADIL AEROLIZER twice daily for long-term treatment of asthma, you should not use additional doses of FORADIL AEROLIZER for prevention of asthma attacks brought on by physical activity or exercise, instead you should use a short-acting bronchodilator that is prescribed for you by your health-care provider.

For the long-term treatment of chronic obstructive pulmonary disease (chronic bronchitis or emphysema), the recommended dose is one Foradil capsule inhaled with the use of the Aerolizer Inhaler (as described below) twice a day, approximately every 12 hours.

How to use the Foradil capsules with your Aerolizer Inhaler

Keep your Foradil and Aerolizer Inhaler dry. Handle with DRY hands.

Foradil capsules are to be administered only with the Aerolizer Inhaler provided. Do not use Foradil capsules with any other capsule inhaler, and do not use the Aerolizer Inhaler to administer any other capsule medication. **Do not use a spacer with the Aerolizer Inhaler.**

Check the "Use by" date on the Aerolizer Inhaler cover. If the "Use by" date has passed, replace the product and Aerolizer Inhaler. Remove the aluminum pouch covering the foil blister cards which contain the Foradil capsules.

1. Pull off the Aerolizer Inhaler cover. (Figure 1)

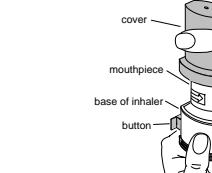


Figure 1

2. Hold the base of the Aerolizer Inhaler firmly and twist the mouth piece in the direction of the arrow to open. (Figure 2) Push the buttons in to make sure that the 4 pins are visible in the capsule well on each side.



Figure 2

3. Remove capsule from foil blister IMMEDIATELY BEFORE USE.

4. Separate one blistered capsule by tearing at intersecting perforations.

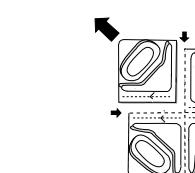


Figure 3

5. With foil-side up, fold back along perforation and flatten. (Figure 4)

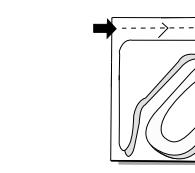


Figure 4

6. Starting at slit, tear off corner. (Figure 5)

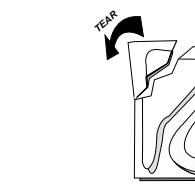


Figure 5

7. Separate/peel foil from paper backing and remove capsule. (Figure 6)

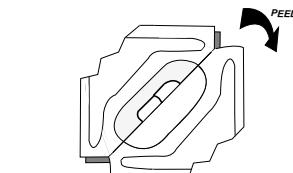


Figure 6

8. Place the capsule in the capsule-chamber in the base of the Aerolizer Inhaler. NEVER PLACE A CAPSULE DIRECTLY INTO THE MOUTHPIECE. (Figure 7)

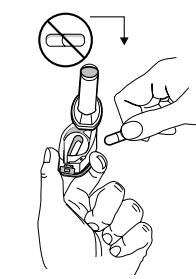


Figure 7

9. Twist the mouthpiece back to the closed position. (Figure 8)



Figure 8

10. With the mouthpiece of the Aerolizer Inhaler upright, simultaneously press both buttons ONCE! You should hear a click as the capsule is being pierced. (Figure 9)

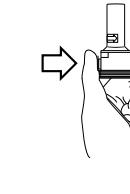


Figure 9

11. Release the buttons. If the buttons stick in the depressed position, grasp the wings on the buttons to retract them before the inhalation step. Do not depress the buttons a second time, since in rare cases, this may cause the capsule to shatter into small pieces. These pieces should be retained by the screen built into the Aerolizer Inhaler. It remains possible that rarely, tiny pieces of gelatin capsule might reach your mouth or throat upon inhalation. Gelatin is not harmful if accidentally swallowed or inhaled. The capsule is less likely to shatter when pierced if capsules are removed from the foil blister IMMEDIATELY before use; storage conditions are strictly followed; and the capsule is only pierced ONCE.



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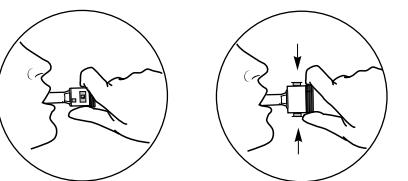
Foradil® Aerolizer™
(formoterol fumarate inhalation powder)

12. Exhale fully. DO NOT EXHALE INTO THE MOUTHPIECE.
 (Figure 10)



Figure 10

13. Tilt your head back slightly. Keeping the Aerolizer Inhaler horizontal, with the blue buttons to the left and right (NOT up and down), place the mouthpiece in your mouth, closing your lips around the mouthpiece. (Figure 11 and 12)



CORRECT
 Figure 11

INCORRECT
 Figure 12

14. Breathe in rapidly but steadily, as deeply as you can (Figure 13). As the capsule spins around in the chamber dispensing the medication, you will experience a sweet taste and hear a whirring noise. If you have not heard the whirring noise, the capsule may be stuck. If this occurs, open the Aerolizer Inhaler and loosen the capsule allowing it to spin freely. DO NOT try to loosen the capsule by repeatedly pressing the buttons.



Figure 13

15. While removing the Aerolizer Inhaler from your mouth, continue to hold your breath as long as comfortably possible, then exhale.

16. Open the Aerolizer Inhaler to see if any powder is still in the capsule. If any powder remains in the capsule repeat steps 12 to 15. Most people are able to empty the capsule in one or two inhalations.

17. After use, open the Aerolizer Inhaler, remove and discard the empty capsule. Do not leave a used capsule in the chamber.

18. Close the mouthpiece and replace the cover.

REMEMBER:

- Never exhale into the Aerolizer Inhaler device.
- Never attempt to take the Aerolizer Inhaler apart.
- Never place a capsule directly into the mouthpiece of the Aerolizer Inhaler.
- Never leave a used capsule in the Aerolizer Inhaler chamber.
- Always use the Aerolizer Inhaler in a level, horizontal position.
- Never wash the Aerolizer Inhaler. KEEP IT DRY.
- Always keep the Aerolizer Inhaler and Foradil capsules in a dry place.
- Always use the new Aerolizer Inhaler that comes with your refill.

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Side effects you may experience with FORADIL AEROLIZER

Along with its beneficial effects, a medicine may cause certain unwanted effects. FORADIL AEROLIZER may occasionally cause tremor, fast and irregular heart beat, or headache. Muscle cramps and pain, agitation, dizziness, nervousness or fatigue, difficulties with sleeping and irritation of the mouth or throat occur rarely. Some of these effects may go away as your body gets used to the medicine. Check with your doctor if any of these unwanted effects continues to bother you. Paradoxical bronchospasm, a narrowing of the airways, occurs very rarely, but may be serious. Report any increased difficulty in breathing after use of FORADIL AEROLIZER to your health-care provider immediately. You should also tell the health-care provider if you notice any other undesirable effects.

Expiration date

Use Foradil capsules before the "Use by" date on the Aerolizer Inhaler cover. The "Use by" date is either 4 months from the purchase date, or the product expiration date, whichever comes first.

Always discard the old Aerolizer Inhaler by the "Use by" date and use the new one provided with each new prescription.

Storing your FORADIL AEROLIZER

Once dispensed, store at controlled room temperature, 20°C to 25°C (68°F to 77°F). Protect from heat and moisture. CAPSULES SHOULD ALWAYS BE STORED IN THE BLISTER AND REMOVED FROM THE BLISTER IMMEDIATELY BEFORE USE.

Keep this and all drugs out of the reach of children.

REMEMBER: This medicine has been prescribed for you by your health-care provider. DO NOT give this medicine to anyone else.

Your health-care provider has determined that this product is likely to help your personal health. **USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR HEALTH-CARE PROVIDER.** If you have any further questions about the use of FORADIL AEROLIZER, consult with your health-care provider or call 1-877-FORADIL (1-877-367-2345).

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/s/

Robert Meyer
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