

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FLOVENT DISKUS safely and effectively. See full prescribing information for FLOVENT DISKUS.

**FLOVENT DISKUS 50 mcg (fluticasone propionate inhalation powder, 50 mcg)**  
**FLOVENT DISKUS 100 mcg (fluticasone propionate inhalation powder, 100 mcg)**  
**FLOVENT DISKUS 250 mcg (fluticasone propionate inhalation powder, 250 mcg)**  
**FOR ORAL INHALATION**

Initial U.S. Approval: 1994

### RECENT MAJOR CHANGES

Warnings and Precautions, Hypersensitivity Reactions, ~~February 2010~~ **March 2010**

Including Anaphylaxis (5.6), Reduction in Bone Mineral Density (5.7), Drug Interaction With Strong Cytochrome P450 3A4 Inhibitors (5.11)

### INDICATIONS AND USAGE

FLOVENT DISKUS is an inhaled corticosteroid indicated for:

- Maintenance treatment of asthma as prophylactic therapy in patients 4 years and older. (1)
  - Treatment of asthma for patients requiring oral corticosteroid therapy. (1)
- FLOVENT DISKUS is NOT indicated for the relief of acute bronchospasm. (1)

### DOSAGE AND ADMINISTRATION

For oral inhalation only. Dosing is based on prior asthma therapy. (2)

Previous Therapy	Recommended Starting Dosage	Highest Recommended Dosage
<b>Patients aged ≥12 years</b>		
Bronchodilators alone	100 mcg twice daily	500 mcg twice daily
Inhaled corticosteroids	100-250 mcg twice daily	500 mcg twice daily
Oral corticosteroids	500-1,000 mcg twice daily	1,000 mcg twice daily
<b>Patients aged 4-11 years</b>	50 mcg twice daily	100 mcg twice daily

### DOSAGE FORMS AND STRENGTHS

Inhalation powder with 50, 100, or 250 mcg per actuation. (3)

### CONTRAINDICATIONS

- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures. (4)
- Severe hypersensitivity to milk proteins. (4)

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### WARNINGS AND PRECAUTIONS

- Localized infections: *Candida albicans* infection of the mouth and pharynx. Monitor patients periodically for signs of adverse effects on the oral cavity. Advise patients to rinse mouth following inhalation. (5.1)
- Immunosuppression: Potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infection; or ocular herpes simplex. More serious or even fatal course of chickenpox or measles in susceptible patients. Use caution in patients with above because of the potential for worsening of these infections. (5.3)
- Transferring patients from systemic corticosteroids: Risk of impaired adrenal function when transferring from oral steroids. Taper patients slowly from systemic corticosteroids if transferring to FLOVENT DISKUS. (5.4)
- Hypercorticism and adrenal suppression: May occur with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue FLOVENT DISKUS slowly. (5.5)
- Hypersensitivity reactions, including anaphylaxis, may occur after administration of FLOVENT DISKUS. Discontinue FLOVENT DISKUS if such reactions occur. (4, 5.6)
- Effect on growth: Monitor growth of pediatric patients. (5.8)
- Glaucoma and cataracts: Close monitoring is warranted. (5.9)

### ADVERSE REACTIONS

Most common adverse reactions (incidence >3%) include upper respiratory tract infection or inflammation, throat irritation, sinusitis, rhinitis, oral candidiasis, nausea and vomiting, gastrointestinal discomfort, fever, cough, bronchitis, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

Use with strong cytochrome P450 3A4 inhibitors such as ritonavir and ketoconazole is not recommended. Systemic corticosteroid effects may occur. (7.1, 7.2)

### USE IN SPECIFIC POPULATIONS

Hepatic impairment: Monitor patients for signs of increased drug exposure. (8.6)

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Revised: ~~February 2010~~  
**March 2010**

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\*Sections or subsections omitted from the full prescribing information are not listed.

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 FLOVENT<sup>®</sup> DISKUS<sup>®</sup> is indicated for the maintenance treatment of asthma as  
4 prophylactic therapy in patients 4 years and older. It is also indicated for patients requiring oral  
5 corticosteroid therapy for asthma. Many of these patients may be able to reduce or eliminate their  
6 requirement for oral corticosteroids over time.

7 FLOVENT DISKUS is NOT indicated for the relief of acute bronchospasm.

8 **2 DOSAGE AND ADMINISTRATION**

9 FLOVENT DISKUS should be administered by the orally inhaled route only in patients 4  
10 years and older. Individual patients will experience a variable time to onset and degree of  
11 symptom relief. Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting  
12 treatment.

13 After asthma stability has been achieved, it is always desirable to titrate to the lowest  
14 effective dosage to reduce the possibility of side effects. For patients who do not respond  
15 adequately to the starting dosage after 2 weeks of therapy, higher dosages may provide  
16 additional asthma control. The safety and efficacy of FLOVENT DISKUS when administered in  
17 excess of recommended dosages have not been established.

18 The recommended starting dosage and the highest recommended dosage of FLOVENT  
19 DISKUS, based on prior asthma therapy, are listed in Table 1.

20  
21 **Table 1. Recommended Dosages of FLOVENT DISKUS**

**NOTE: In all patients, it is desirable to titrate to the lowest effective dosage once asthma stability is achieved.**

Previous Therapy	Recommended Starting Dosage	Highest Recommended Dosage
<b>Adult and adolescent patients (aged ≥12 years)</b>		
Bronchodilators alone	100 mcg twice daily	500 mcg twice daily
Inhaled corticosteroids	100-250 mcg twice daily <sup>a</sup>	500 mcg twice daily
Oral corticosteroids <sup>b</sup>	500-1,000 mcg twice daily <sup>c</sup>	1,000 mcg twice daily
<b>Pediatric patients (aged 4-11 years)<sup>d</sup></b>	50 mcg twice daily <sup>a</sup>	100 mcg twice daily

22 <sup>a</sup> Starting dosages above 100 mcg twice daily for adult and adolescent patients and 50 mcg  
23 twice daily for pediatric patients aged 4 to 11 years may be considered for patients with  
24 poorer asthma control or those who have previously required doses of inhaled corticosteroids  
25 that are in the higher range for the specific agent.

26 <sup>b</sup> For patients currently receiving chronic oral corticosteroid therapy, prednisone should be  
27 reduced no faster than 2.5 to 5 mg/day on a weekly basis beginning after at least 1 week of  
28 therapy with FLOVENT DISKUS. Patients should be carefully monitored for signs of asthma

29 instability, including serial objective measures of airflow, and for signs of adrenal  
30 insufficiency [see *Warnings and Precautions (5.4)*]. Once prednisone reduction is complete,  
31 the dosage of FLOVENT DISKUS should be reduced to the lowest effective dosage.  
32 <sup>c</sup> The choice of starting dosage should be made on the basis of individual patient assessment. A  
33 controlled clinical study of 111 oral corticosteroid-dependent patients with asthma showed  
34 few significant differences between the 2 doses of FLOVENT DISKUS on safety and efficacy  
35 endpoints. However, inability to decrease the dose of oral corticosteroids further during  
36 corticosteroid reduction may be indicative of the need to increase the dose of fluticasone  
37 propionate up to the maximum of 1,000 mcg twice daily.  
38 <sup>d</sup> Because individual responses may vary, pediatric patients previously maintained on other  
39 inhaled corticosteroids may require dosage adjustments upon transfer to FLOVENT DISKUS.

### 40 **3 DOSAGE FORMS AND STRENGTHS**

41 FLOVENT DISKUS is an inhalation powder. Each actuation delivers 46, 94, or 229 mcg  
42 of fluticasone propionate from the DISKUS<sup>®</sup> inhalation unit. FLOVENT DISKUS is supplied as  
43 a disposable orange inhalation unit containing 60 blisters of powder formulation packaged in a  
44 plastic-coated, moisture-protective foil pouch.

### 45 **4 CONTRAINDICATIONS**

46 The use of FLOVENT DISKUS is contraindicated in the following conditions:

- 47 • Primary treatment of status asthmaticus or other acute episodes of asthma where intensive  
48 measures are required [see *Warnings and Precautions (5.2)*].
- 49 • Severe hypersensitivity to milk proteins [see *Warnings and Precautions (5.6), Adverse*  
50 *Reactions (6.2), Description (11)*].

### 51 **5 WARNINGS AND PRECAUTIONS**

#### 52 **5.1 Local Effects**

53 In clinical studies, the development of localized infections of the mouth and pharynx with  
54 *Candida albicans* has occurred in patients treated with FLOVENT DISKUS. When such an  
55 infection develops, it should be treated with appropriate local or systemic (i.e., oral antifungal)  
56 therapy while treatment with FLOVENT DISKUS continues, but at times therapy with  
57 FLOVENT DISKUS may need to be interrupted. Patients should rinse the mouth after inhalation  
58 of FLOVENT DISKUS [see *Adverse Reactions (6.1)*].

#### 59 **5.2 Acute Asthma Episodes**

60 FLOVENT DISKUS is not to be regarded as a bronchodilator and is not indicated for  
61 rapid relief of bronchospasm. Patients should be instructed to contact their physicians  
62 immediately when episodes of asthma that are not responsive to bronchodilators occur during the  
63 course of treatment with FLOVENT DISKUS. During such episodes, patients may require  
64 therapy with oral corticosteroids.

#### 65 **5.3 Immunosuppression**

66 Persons who are using drugs that suppress the immune system are more susceptible to  
67 infections than healthy individuals. Chickenpox and measles, for example, can have a more  
68 serious or even fatal course in susceptible children or adults using corticosteroids. In such  
69 children or adults who have not had these diseases or been properly immunized, particular care  
70 should be taken to avoid exposure. How the dose, route, and duration of corticosteroid  
71 administration affect the risk of developing a disseminated infection is not known. The  
72 contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not  
73 known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG)  
74 may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin  
75 (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing  
76 information.) If chickenpox develops, treatment with antiviral agents may be considered.

77 Because of the potential for worsening infections, inhaled corticosteroids should be used  
78 with caution, if at all, in patients with active or quiescent tuberculosis infection of the respiratory  
79 tract; untreated systemic fungal, bacterial, viral or parasitic infections; or ocular herpes simplex.

#### 80 **5.4 Transferring Patients From Systemic Corticosteroid Therapy**

81 Particular care is needed for patients who have been transferred from systemically active  
82 corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have  
83 occurred in patients with asthma during and after transfer from systemic corticosteroids to less  
84 systemically available inhaled corticosteroids. After withdrawal from systemic corticosteroids, a  
85 number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function.

86 Patients requiring oral corticosteroids should be weaned slowly from systemic  
87 corticosteroid use after transferring to FLOVENT DISKUS. In a clinical trial of 111 patients,  
88 prednisone reduction was accomplished by reducing the daily prednisone dose by 2.5 mg on a  
89 weekly basis during transfer to FLOVENT DISKUS. Successive reduction of prednisone dose  
90 was allowed only when lung function; symptoms; and as-needed, short-acting beta-agonist use  
91 were better than or comparable to that seen before initiation of prednisone dose reduction. Lung  
92 function (forced expiratory volume in 1 second [FEV<sub>1</sub>] or morning peak expiratory flow [AM  
93 PEF]), beta-agonist use, and asthma symptoms should be carefully monitored during withdrawal  
94 of oral corticosteroids. In addition to monitoring asthma signs and symptoms, patients should be  
95 observed for signs and symptoms of adrenal insufficiency such as fatigue, lassitude, weakness,  
96 nausea and vomiting, and hypotension.

97 Patients who have been previously maintained on 20 mg or more per day of prednisone  
98 (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have  
99 been almost completely withdrawn. During this period of HPA suppression, patients may exhibit  
100 signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection  
101 (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Although  
102 inhaled corticosteroids may provide control of asthma symptoms during these episodes, in  
103 recommended doses they supply less than normal physiological amounts of glucocorticoid  
104 (cortisol) systemically and do NOT provide the mineralocorticoid activity that is necessary for  
105 coping with these emergencies.

106 During periods of stress or a severe asthma attack, patients who have been withdrawn  
107 from systemic corticosteroids should be instructed to resume oral corticosteroids immediately  
108 and to contact their physicians for further instruction. These patients should also be instructed to  
109 carry a warning card indicating that they may need supplementary systemic corticosteroids  
110 during periods of stress or a severe asthma attack.

111 Transfer of patients from systemic corticosteroid therapy to FLOVENT DISKUS may  
112 unmask conditions previously suppressed by the systemic corticosteroid therapy, e.g., rhinitis,  
113 conjunctivitis, eczema, arthritis, and eosinophilic conditions. Some patients may experience  
114 symptoms of systemically active corticosteroid withdrawal, e.g., joint and/or muscular pain,  
115 lassitude, and depression, despite maintenance or even improvement of respiratory function.

### 116 **5.5 Hypercorticism and Adrenal Suppression**

117 Fluticasone propionate will often help control asthma symptoms with less suppression of  
118 HPA function than therapeutically equivalent oral doses of prednisone. Since fluticasone  
119 propionate is absorbed into the circulation and can be systemically active at higher doses, the  
120 beneficial effects of FLOVENT DISKUS in minimizing HPA dysfunction may be expected only  
121 when recommended dosages are not exceeded and individual patients are titrated to the lowest  
122 effective dose. A relationship between plasma levels of fluticasone propionate and inhibitory  
123 effects on stimulated cortisol production has been shown after 4 weeks of treatment with  
124 fluticasone propionate. Since individual sensitivity to effects on cortisol production exists,  
125 physicians should consider this information when prescribing FLOVENT DISKUS.

126 Because of the possibility of systemic absorption of inhaled corticosteroids, patients  
127 treated with FLOVENT DISKUS should be observed carefully for any evidence of systemic  
128 corticosteroid effects. Particular care should be taken in observing patients postoperatively or  
129 during periods of stress for evidence of inadequate adrenal response.

130 It is possible that systemic corticosteroid effects such as hypercorticism and adrenal  
131 suppression (including adrenal crisis) may appear in a small number of patients, particularly  
132 when FLOVENT DISKUS is administered at higher than recommended doses over prolonged  
133 periods of time. If such effects occur, the dosage of FLOVENT DISKUS should be reduced  
134 slowly, consistent with accepted procedures for reducing systemic corticosteroids and for  
135 management of asthma.

### 136 **5.6 Hypersensitivity Reactions, Including Anaphylaxis**

137 Hypersensitivity reactions, including anaphylaxis, angioedema, urticaria, and  
138 bronchospasm, may occur after administration of FLOVENT DISKUS. There have been reports  
139 of anaphylactic reactions in patients with severe milk protein allergy; therefore, patients with  
140 severe milk protein allergy should not take FLOVENT DISKUS [*see Contraindications (4)*].

### 141 **5.7 Reduction in Bone Mineral Density**

142 Decreases in bone mineral density (BMD) have been observed with long-term  
143 administration of products containing inhaled corticosteroids. The clinical significance of small  
144 changes in BMD with regard to long-term outcomes is unknown. Patients with major risk factors  
145 for decreased bone mineral content, such as prolonged immobilization, family history of

146 osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of  
147 drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored  
148 and treated with established standards of care.

### 149 **5.8 Effect on Growth**

150 Orally inhaled corticosteroids may cause a reduction in growth velocity when  
151 administered to pediatric patients [*see Use in Specific Populations (8.4)*]. Monitor the growth of  
152 pediatric patients receiving FLOVENT DISKUS routinely (e.g., via stadiometry). To minimize  
153 the systemic effects of orally inhaled corticosteroids, including FLOVENT DISKUS, titrate each  
154 patient's dose to the lowest dosage that effectively controls his/her symptoms.

### 155 **5.9 Glaucoma and Cataracts**

156 Glaucoma, increased intraocular pressure, and cataracts have been reported in patients  
157 following the long-term administration of inhaled corticosteroids, including fluticasone  
158 propionate. Therefore, close monitoring is warranted in patients with a change in vision or with a  
159 history of increased intraocular pressure, glaucoma, and/or cataracts.

### 160 **5.10 Paradoxical Bronchospasm**

161 As with other inhaled medications, bronchospasm may occur with an immediate increase  
162 in wheezing after dosing. If bronchospasm occurs following dosing with FLOVENT DISKUS, it  
163 should be treated immediately with a fast-acting inhaled bronchodilator. Treatment with  
164 FLOVENT DISKUS should be discontinued immediately and alternative therapy instituted.

### 165 **5.11 Drug Interaction With Strong Cytochrome P450 3A4 Inhibitors**

166 The use of strong cytochrome P450 [CYP] 3A4 inhibitors (e.g., ritonavir, atazanavir,  
167 clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole,  
168 telithromycin) with FLOVENT DISKUS is not recommended because increased systemic  
169 corticosteroid adverse effects may occur [*see Drug Interactions (7.1), Clinical Pharmacology*  
170 (*12.3*)].

### 171 **5.12 Eosinophilic Conditions and Churg-Strauss Syndrome**

172 In rare cases, patients on inhaled fluticasone propionate may present with systemic  
173 eosinophilic conditions. Some of these patients have clinical features of vasculitis consistent with  
174 Churg-Strauss syndrome, a condition that is often treated with systemic corticosteroid therapy.  
175 These events usually, but not always, have been associated with the reduction and/or withdrawal  
176 of oral corticosteroid therapy following the introduction of fluticasone propionate. Cases of  
177 serious eosinophilic conditions have also been reported with other inhaled corticosteroids in this  
178 clinical setting. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary  
179 symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal  
180 relationship between fluticasone propionate and these underlying conditions has not been  
181 established.

## 182 **6 ADVERSE REACTIONS**

183 Systemic and local corticosteroid use may result in the following:

- 184 • *Candida albicans* infection [*see Warnings and Precautions (5.1)*]

- 185 • Immunosuppression [see Warnings and Precautions (5.3)]
- 186 • Hypercorticism and adrenal suppression [see Warnings and Precautions (5.5)]
- 187 • Reduction in bone mineral density [see Warnings and Precautions (5.7)]
- 188 • Growth effects [see Warnings and Precautions (5.8)]
- 189 • Glaucoma and cataracts [see Warnings and Precautions (5.9)]

190 **6.1 Clinical Trials Experience**

191 Because clinical trials are conducted under widely varying conditions, adverse reaction  
 192 rates observed in the clinical trials of a drug cannot be directly compared with rates in the  
 193 clinical trials of another drug and may not reflect the rates observed in practice.

194 The incidence of common adverse reactions in Table 2 is based upon  
 195 7 placebo-controlled US clinical trials in which 1,176 pediatric, adolescent, and adult patients  
 196 (466 females and 710 males) previously treated with as-needed bronchodilators and/or inhaled  
 197 corticosteroids were treated twice daily for up to 12 weeks with FLOVENT DISKUS (doses of  
 198 50 to 500 mcg) or placebo.

199  
 200 **Table 2. Adverse Reactions With >3% Incidence in US Controlled Clinical Trials With**  
 201 **FLOVENT DISKUS in Patients With Asthma Previously Receiving Bronchodilators**  
 202 **and/or Inhaled Corticosteroids**

Adverse Event	FLOVENT DISKUS 50 mcg Twice Daily (n = 178) %	FLOVENT DISKUS 100 mcg Twice Daily (n = 305) %	FLOVENT DISKUS 250 mcg Twice Daily (n = 86) %	FLOVENT DISKUS 500 mcg Twice Daily (n = 64) %	Placebo (n = 543) %
Ear, nose, and throat					
Upper respiratory tract infection	20	18	21	14	16
Throat irritation	13	13	3	22	8
Sinusitis/sinus infection	9	10	6	6	6
Upper respiratory inflammation	5	5	0	5	3
Rhinitis	4	3	1	2	2
Oral candidiasis	<1	9	6	5	7
Gastrointestinal					
Nausea and vomiting	8	4	1	2	4

Gastrointestinal discomfort and pain	4	3	2	2	3
Viral gastrointestinal infection	4	3	3	5	1
Non-site specific					
Fever	7	7	1	2	4
Viral infection	2	2	0	5	2
Lower respiratory					
Viral respiratory infection	4	5	1	2	4
Cough	3	5	1	5	4
Bronchitis	2	3	0	8	1
Neurological					
Headache	12	12	2	14	7
Musculoskeletal and trauma					
Muscle injury	2	0	1	5	1
Musculoskeletal pain	4	3	2	5	2
Injury	2	<1	0	5	<1

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Table 2 includes all events (whether considered drug-related or nondrug-related by the investigator) that occurred at a rate of over 3% in any of the groups treated with FLOVENT DISKUS and were more common than in the placebo group. Less than 2% of patients discontinued from the studies because of adverse reactions. The average duration of exposure was 73 to 79 days in the active treatment groups compared with 56 days in the placebo group.

**Additional Adverse Reactions:** Other adverse reactions not previously listed, whether considered drug-related or not by the investigators, that were reported more frequently by patients with asthma treated with FLOVENT DISKUS compared with patients treated with placebo include the following: palpitations; soft tissue injuries; contusions and hematomas; wounds and lacerations; burns; poisoning and toxicity; pressure-induced disorders; hoarseness/dysphonia; epistaxis; ear, nose, throat, and tonsil signs and symptoms; ear, nose, and throat polyps; allergic ear, nose, and throat disorders; throat constriction; fluid disturbances; weight gain; appetite disturbances; keratitis and conjunctivitis; blepharoconjunctivitis; gastrointestinal signs and symptoms; oral ulcerations; dental discomfort and pain; oral erythema and rashes; mouth and tongue disorders; oral discomfort and pain; tooth decay; cholecystitis; arthralgia and articular rheumatism; muscle cramps and spasms; musculoskeletal inflammation; dizziness; sleep disorders; migraines; paralysis of cranial nerves; edema and swelling; bacterial infections; fungal infections; mobility disorders; mood disorders; bacterial reproductive infections; photodermatitis; dermatitis and dermatosis; viral skin infections; eczema; pruritus; acne and folliculitis; urinary infections.

Three (3) of the 7 placebo-controlled US clinical trials were pediatric studies. A total of 592 patients 4 to 11 years were treated with FLOVENT DISKUS (dosages of 50 or 100 mcg



226 twice daily) or placebo; an additional 174 patients 4 to 11 years received FLOVENT<sup>®</sup>  
227 ROTADISK<sup>®</sup> (fluticasone propionate inhalation powder) at the same doses. There were no  
228 clinically relevant differences in the pattern or severity of adverse events in children compared  
229 with those reported in adults.

230 In the first 16 weeks of a 52-week clinical trial in adult patients with asthma who  
231 previously required oral corticosteroids (daily doses of 5 to 40 mg oral prednisone), the effects  
232 of FLOVENT DISKUS 500 mcg twice daily (n = 41) and 1,000 mcg twice daily (n = 36) were  
233 compared with placebo (n = 34) for the frequency of reported adverse events. The average  
234 duration of exposure for patients taking FLOVENT DISKUS was 105 days compared with 75  
235 days for placebo. Adverse events, whether or not considered drug related by the investigators,  
236 reported in more than 5 patients in the group taking FLOVENT DISKUS and that occurred more  
237 frequently with FLOVENT DISKUS than with placebo are shown below (percent FLOVENT  
238 DISKUS and percent placebo).

239 Ear, Nose, and Throat: Hoarseness/dysphonia (9% and 0%), nasal  
240 congestion/blockage (16% and 0%), oral candidiasis (31% and 21%), rhinitis (13% and 9%),  
241 sinusitis/sinus infection (33% and 12%), throat irritation (10% and 9%), and upper respiratory  
242 tract infection (31% and 24%).

243 Gastrointestinal: Nausea and vomiting (9% and 0%).

244 Lower Respiratory: Cough (9% and 3%) and viral respiratory infections (9% and 6%).

245 Musculoskeletal: Arthralgia and articular rheumatism (17% and 3%) and muscle pain  
246 (12% and 0%).

247 Non-Site Specific: Malaise and fatigue (16% and 9%) and pain (10% and 3%).

248 Skin: Pruritus (6% and 0%) and skin rashes (8% and 3%).

## 249 **6.2 Postmarketing Experience**

250 In addition to adverse reactions reported from clinical trials, the following adverse  
251 reactions have been identified during postmarketing use of fluticasone propionate. Because these  
252 reactions are reported voluntarily from a population of uncertain size, it is not always possible to  
253 reliably estimate their frequency or establish a causal relationship to drug exposure. These events  
254 have been chosen for inclusion due to either their seriousness, frequency of reporting, or causal  
255 connection to fluticasone propionate or a combination of these factors.

256 Ear, Nose, and Throat: Aphonia, facial and oropharyngeal edema, and throat soreness.

257 Endocrine and Metabolic: Cushingoid features, growth velocity reduction in  
258 children/adolescents, hyperglycemia, and osteoporosis.

259 Eye: Cataracts.

260 Immune System Disorders: Immediate and delayed hypersensitivity reactions,  
261 including anaphylaxis, rash, angioedema, and bronchospasm, have been reported. Anaphylactic  
262 reactions in patients with severe milk protein allergy have been reported.

263 Psychiatry: Agitation, aggression, anxiety, depression, and restlessness. Behavioral  
264 changes, including hyperactivity and irritability, have been reported very rarely and primarily in  
265 children.

266            Respiratory: Asthma exacerbation, bronchospasm, chest tightness, dyspnea, immediate  
267 bronchospasm, pneumonia, and wheeze.

268            Skin: Contusions and ecchymoses.

269            Eosinophilic Conditions: In rare cases, patients on inhaled fluticasone propionate may  
270 present with systemic eosinophilic conditions, with some patients presenting with clinical  
271 features of vasculitis consistent with Churg-Strauss syndrome, a condition that is often treated  
272 with systemic corticosteroid therapy. These events usually, but not always, have been associated  
273 with the reduction and/or withdrawal of oral corticosteroid therapy following the introduction of  
274 fluticasone propionate [*see Warnings and Precautions (5.12)*].

## 275 **7        DRUG INTERACTIONS**

### 276 **7.1      Strong Cytochrome P450 3A4 Inhibitors**

277            Fluticasone propionate is a substrate of CYP 3A4. The use of strong CYP 3A4 inhibitors  
278 (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir,  
279 saquinavir, ketoconazole, telithromycin) with FLOVENT DISKUS is not recommended because  
280 increased systemic corticosteroid adverse effects may occur.

281            A drug interaction study with fluticasone propionate aqueous nasal spray in healthy  
282 subjects has shown that ritonavir (a strong CYP 3A4 inhibitor) can significantly increase plasma  
283 fluticasone propionate concentration, resulting in significantly reduced serum cortisol  
284 concentrations [*see Clinical Pharmacology (12.3)*]. During postmarketing use, there have been  
285 reports of clinically significant drug interactions in patients receiving fluticasone propionate and  
286 ritonavir, resulting in systemic corticosteroid effects including Cushing syndrome and adrenal  
287 suppression. Therefore, coadministration of fluticasone propionate and ritonavir is not  
288 recommended unless the potential benefit to the patient outweighs the risk of systemic  
289 corticosteroid side effects.

290            Coadministration of orally inhaled fluticasone propionate (1,000 mcg) and ketoconazole  
291 (200 mg once daily) resulted in a 1.9-fold increase in plasma fluticasone propionate exposure  
292 and a 45% decrease in plasma cortisol area under the curve (AUC), but had no effect on urinary  
293 excretion of cortisol. Coadministration of fluticasone propionate and ketoconazole is not  
294 recommended unless the potential benefit to the patient outweighs the risk of systemic  
295 corticosteroid side effects.

## 296 **8        USE IN SPECIFIC POPULATIONS**

### 297 **8.1      Pregnancy**

298            Pregnancy Category C: There are no adequate and well-controlled studies with  
299 FLOVENT DISKUS in pregnant women. FLOVENT DISKUS should be used during pregnancy  
300 only if the potential benefit justifies the potential risk to the fetus.

301            Teratogenic Effects: Subcutaneous studies in the mouse and rat at doses approximately  
302 0.1 and 0.4, respectively, times the maximum recommended human daily inhalation dose  
303 (MRHD) in adults on a mg/m<sup>2</sup> basis revealed fetal toxicity characteristic of potent corticosteroid

304 compounds, including embryonic growth retardation, omphalocele, cleft palate, and retarded  
305 cranial ossification.

306 In the rabbit, fetal weight reduction and cleft palate were observed at a subcutaneous dose  
307 approximately 0.03 times the MRHD in adults on a mg/m<sup>2</sup> basis. However, no teratogenic effects  
308 were reported at oral doses up to approximately 2 times the MRHD in adults on a mg/m<sup>2</sup> basis.  
309 No fluticasone propionate was detected in the plasma in this study, consistent with the  
310 established low bioavailability following oral administration [*see Clinical Pharmacology*  
311 (12.3)].

312 Experience with oral corticosteroids since their introduction in pharmacologic, as  
313 opposed to physiologic, doses suggests that rodents are more prone to teratogenic effects from  
314 corticosteroids than humans. In addition, because there is a natural increase in corticosteroid  
315 production during pregnancy, most women will require a lower exogenous corticosteroid dose  
316 and many will not need corticosteroid treatment during pregnancy.

### 317 **8.3 Nursing Mothers**

318 It is not known whether fluticasone propionate is excreted in human breast milk.  
319 However, other corticosteroids have been detected in human milk. Subcutaneous administration  
320 to lactating rats of tritiated fluticasone propionate at a dose approximately 0.04 times the MRHD  
321 in adults on a mg/m<sup>2</sup> basis resulted in measurable radioactivity in milk.

322 Since there are no data from controlled trials on the use of FLOVENT DISKUS by  
323 nursing mothers, caution should be exercised when FLOVENT DISKUS is administered to a  
324 nursing woman.

### 325 **8.4 Pediatric Use**

326 The safety and effectiveness of FLOVENT DISKUS in children 4 years and older have  
327 been established [*see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical*  
328 *Studies (14.2)*]. The safety and effectiveness of FLOVENT DISKUS in children younger than  
329 4 years have not been established.

330 Effects on Growth: Orally inhaled corticosteroids may cause a reduction in growth  
331 velocity when administered to pediatric patients. A reduction of growth velocity in children or  
332 teenagers may occur as a result of poorly controlled asthma or from use of corticosteroids  
333 including inhaled corticosteroids. The effects of long-term treatment of children and adolescents  
334 with inhaled corticosteroids, including fluticasone propionate, on final adult height are not  
335 known.

336 Controlled clinical studies have shown that inhaled corticosteroids may cause a reduction  
337 in growth in pediatric patients. In these studies, the mean reduction in growth velocity was  
338 approximately 1 cm/year (range, 0.3 to 1.8 cm/year) and appears to depend upon dose and  
339 duration of exposure. This effect was observed in the absence of laboratory evidence of HPA  
340 axis suppression, suggesting that growth velocity is a more sensitive indicator of systemic  
341 corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis  
342 function. The long-term effects of this reduction in growth velocity associated with orally  
343 inhaled corticosteroids, including the impact on final adult height, are unknown. The potential

344 for “catch-up” growth following discontinuation of treatment with orally inhaled corticosteroids  
345 has not been adequately studied. The effects on growth velocity of treatment with orally inhaled  
346 corticosteroids for over 1 year, including the impact on final adult height, are unknown. The  
347 growth of children and adolescents receiving orally inhaled corticosteroids, including  
348 FLOVENT DISKUS, should be monitored routinely (e.g., via stadiometry). The potential  
349 growth effects of prolonged treatment should be weighed against the clinical benefits obtained  
350 and the risks associated with alternative therapies. To minimize the systemic effects of orally  
351 inhaled corticosteroids, including FLOVENT DISKUS, each patient should be titrated to the  
352 lowest dose that effectively controls his/her symptoms.

353 A 52-week placebo-controlled study to assess the potential growth effects of fluticasone  
354 propionate inhalation powder (FLOVENT ROTADISK) at 50 and 100 mcg twice daily was  
355 conducted in the US in 325 prepubescent children (244 males and 81 females) aged 4 to  
356 11 years. The mean growth velocities at 52 weeks observed in the intent-to-treat population were  
357 6.32 cm/year in the placebo group (n = 76), 6.07 cm/year in the 50-mcg group (n = 98), and  
358 5.66 cm/year in the 100-mcg group (n = 89). An imbalance in the proportion of children entering  
359 puberty between groups and a higher dropout rate in the placebo group due to poorly controlled  
360 asthma may be confounding factors in interpreting these data. A separate subset analysis of  
361 children who remained prepubertal during the study revealed growth rates at 52 weeks of  
362 6.10 cm/year in the placebo group (n = 57), 5.91 cm/year in the 50-mcg group (n = 74), and  
363 5.67 cm/year in the 100-mcg group (n = 79). In children aged 8.5 years, the mean age of children  
364 in this study, the range for expected growth velocity is: boys – 3<sup>rd</sup> percentile = 3.8 cm/year, 50<sup>th</sup>  
365 percentile = 5.4 cm/year, and 97<sup>th</sup> percentile = 7.0 cm/year; girls – 3<sup>rd</sup> percentile = 4.2 cm/year,  
366 50<sup>th</sup> percentile = 5.7 cm/year, and 97<sup>th</sup> percentile = 7.3 cm/year. The clinical significance of these  
367 growth data is not certain.

## 368 **8.5 Geriatric Use**

369 Safety data have been collected on 280 patients (FLOVENT DISKUS n = 83, FLOVENT  
370 ROTADISK n = 197) 65 years or older and 33 patients (FLOVENT DISKUS n = 14, FLOVENT  
371 ROTADISK n = 19) 75 years or older who have been treated with fluticasone propionate  
372 inhalation powder in US and non-US clinical trials. No overall differences in safety or  
373 effectiveness were observed between these patients and younger patients, and other reported  
374 clinical experience has not identified differences in responses between the elderly and younger  
375 patients, but greater sensitivity of some older individuals cannot be ruled out.

## 376 **8.6 Hepatic Impairment**

377 Formal pharmacokinetic studies using FLOVENT DISKUS have not been conducted in  
378 patients with hepatic impairment. Since fluticasone propionate is predominantly cleared by  
379 hepatic metabolism, impairment of liver function may lead to accumulation of fluticasone  
380 propionate in plasma. Therefore, patients with hepatic disease should be closely monitored.

## 381 **8.7 Renal Impairment**

382 Formal pharmacokinetic studies using FLOVENT DISKUS have not been conducted in  
383 patients with renal impairment.

384 **10 OVERDOSAGE**

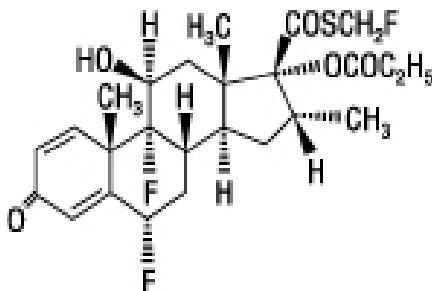
385 Chronic overdosage may result in signs/symptoms of hypercorticism [*see Warnings and*  
386 *Precautions (5.5)*]. Inhalation by healthy volunteers of a single dose of 4,000 mcg of fluticasone  
387 propionate inhalation powder or single doses of 1,760 or 3,520 mcg of fluticasone propionate  
388 CFC inhalation aerosol was well tolerated. Doses of 1,320 mcg administered to healthy human  
389 volunteers twice daily for 7 to 15 days were also well tolerated. Repeat oral doses up to 80 mg  
390 daily for 10 days in healthy volunteers and repeat oral doses up to 20 mg daily for 42 days in  
391 patients were well tolerated. Adverse reactions were of mild or moderate severity, and  
392 incidences were similar in active and placebo treatment groups.

393 No deaths were seen in mice given an oral dose of 1,000 mg/kg (approximately 2,000  
394 and 9,600 times the MRHD in adults and children aged 4 to 11 years, respectively, on a mg/m<sup>2</sup>  
395 basis). No deaths were seen in rats given an oral dose of 1,000 mg/kg (approximately 4,100 and  
396 19,000 times the MRHD in adults and children aged 4 to 11 years, respectively, on a mg/m<sup>2</sup>  
397 basis).

398 **11 DESCRIPTION**

399 The active component of FLOVENT DISKUS 50 mcg, FLOVENT DISKUS 100 mcg,  
400 and FLOVENT DISKUS 250 mcg is fluticasone propionate, a corticosteroid having the  
401 chemical name *S*-(fluoromethyl) 6 $\alpha$ ,9-difluoro-11 $\beta$ ,17-dihydroxy-16 $\alpha$ -methyl-3-oxoandrosta-  
402 1,4-diene-17 $\beta$ -carbothioate, 17-propionate and the following chemical structure:

403



404

405 Fluticasone propionate is a white powder with a molecular weight of 500.6, and the  
406 empirical formula is C<sub>25</sub>H<sub>31</sub>F<sub>3</sub>O<sub>5</sub>S. It is practically insoluble in water, freely soluble in dimethyl  
407 sulfoxide and dimethylformamide, and slightly soluble in methanol and 95% ethanol.

408 FLOVENT DISKUS 50 mcg, FLOVENT DISKUS 100 mcg, and FLOVENT DISKUS  
409 250 mcg are specially designed plastic inhalation delivery systems containing a double-foil  
410 blister strip of a powder formulation of fluticasone propionate intended for oral inhalation only.  
411 The DISKUS inhalation unit, which is the delivery component, is an integral part of the drug  
412 product. Each blister on the double-foil strip within the unit contains 50, 100, or 250 mcg of  
413 microfine fluticasone propionate in 12.5 mg of formulation containing lactose (which contains  
414 milk proteins). After a blister containing medication is opened by activating the DISKUS, the

415 medication is dispersed into the airstream created by the patient inhaling through the  
416 mouthpiece.

417 Under standardized in vitro test conditions, FLOVENT DISKUS delivers 46, 94, or  
418 229 mcg of fluticasone propionate from FLOVENT DISKUS 50 mcg, FLOVENT DISKUS  
419 100 mcg, or FLOVENT DISKUS 250 mcg, respectively, when tested at a flow rate of 60 L/min  
420 for 2 seconds. In adult patients with obstructive lung disease and severely compromised lung  
421 function (FEV<sub>1</sub> 20% to 30% of predicted), mean peak inspiratory flow (PIF) through a DISKUS  
422 was 82.4 L/min (range, 46.1 to 115.3 L/min). In children with asthma 4 and 8 years old, mean  
423 PIF through FLOVENT DISKUS was 70 and 104 L/min, respectively (range, 48 to 123 L/min).

424 The actual amount of drug delivered to the lung may depend on patient factors, such as  
425 inspiratory flow profile.

## 426 **12 CLINICAL PHARMACOLOGY**

### 427 **12.1 Mechanism of Action**

428 Fluticasone propionate is a synthetic trifluorinated corticosteroid with potent  
429 anti-inflammatory activity. In vitro assays using human lung cytosol preparations have  
430 established fluticasone propionate as a human glucocorticoid receptor agonist with an affinity 18  
431 times greater than dexamethasone, almost twice that of beclomethasone-17-monopropionate  
432 (BMP), the active metabolite of beclomethasone dipropionate, and over 3 times that of  
433 budesonide. Data from the McKenzie vasoconstrictor assay in man are consistent with these  
434 results. The clinical significance of these findings is unknown.

435 Inflammation is an important component in the pathogenesis of asthma. Corticosteroids  
436 have been shown to inhibit multiple cell types (e.g., mast cells, eosinophils, basophils,  
437 lymphocytes, macrophages, neutrophils) and mediator production or secretion (e.g., histamine,  
438 eicosanoids, leukotrienes, cytokines) involved in the asthmatic response. These  
439 anti-inflammatory actions of corticosteroids contribute to their efficacy in asthma.

440 Though effective for the treatment of asthma, corticosteroids do not affect asthma  
441 symptoms immediately. Individual patients will experience a variable time to onset and degree of  
442 symptom relief. Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting  
443 treatment. When corticosteroids are discontinued, asthma stability may persist for several days or  
444 longer.

445 Studies in patients with asthma have shown a favorable ratio between topical  
446 anti-inflammatory activity and systemic corticosteroid effects with recommended doses of orally  
447 inhaled fluticasone propionate. This is explained by a combination of a relatively high local  
448 anti-inflammatory effect, negligible oral systemic bioavailability (<1%), and the minimal  
449 pharmacological activity of the only metabolite detected in man.

### 450 **12.2 Pharmacodynamics**

451 In clinical trials with fluticasone propionate inhalation powder using dosages up to and  
452 including 250 mcg twice daily, occasional abnormal short cosyntropin tests (peak serum cortisol  
453 <18 mcg/dL assessed by radioimmunoassay) were noted both in patients receiving fluticasone

454 propionate and in patients receiving placebo. The incidence of abnormal tests at 500 mcg twice  
455 daily was greater than placebo. In a 2-year study carried out with the DISKHALER<sup>®</sup> inhalation  
456 device in 64 patients with mild, persistent asthma (mean FEV<sub>1</sub> 91% of predicted) randomized to  
457 fluticasone propionate 500 mcg twice daily or placebo, no patient receiving fluticasone  
458 propionate had an abnormal response to 6-hour cosyntropin infusion (peak serum cortisol  
459 <18 mcg/dL). With a peak cortisol threshold <35 mcg/dL, 1 patient receiving fluticasone  
460 propionate (4%) had an abnormal response at 1 year; repeat testing at 18 months and 2 years was  
461 normal. Another patient receiving fluticasone propionate (5%) had an abnormal response at  
462 2 years. No patient on placebo had an abnormal response at 1 or 2 years.

463 In a placebo-controlled clinical study conducted in patients aged 4 to 11 years, a  
464 30-minute cosyntropin stimulation test was performed in 41 patients after 12 weeks of dosing  
465 with 50 or 100 mcg twice daily of fluticasone propionate via the DISKUS device. One patient  
466 receiving fluticasone propionate via DISKUS had a prestimulation plasma cortisol concentration  
467 <5 mcg/dL, and 2 patients had a rise in cortisol of <7 mcg/dL. However, all poststimulation  
468 values were >18 mcg/dL.

469 The potential systemic effects of inhaled fluticasone propionate on the HPA axis were  
470 also studied in patients with asthma. Fluticasone propionate given by inhalation aerosol at  
471 dosages of 220, 440, 660, or 880 mcg twice daily was compared with placebo or oral prednisone  
472 10 mg given once daily for 4 weeks. For most patients, the ability to increase cortisol production  
473 in response to stress, as assessed by 6-hour cosyntropin stimulation, remained intact with inhaled  
474 fluticasone propionate treatment. No patient had an abnormal response (peak serum cortisol <18  
475 mcg/dL) after dosing with placebo or fluticasone propionate 220 mcg twice daily. For patients  
476 treated with 440, 660, and 880 mcg twice daily, 10%, 16%, and 12%, respectively, had an  
477 abnormal response as compared with 29% of patients treated with prednisone.

### 478 **12.3 Pharmacokinetics**

479 Absorption: Fluticasone propionate acts locally in the lung; therefore, plasma levels do  
480 not predict therapeutic effect. Studies using oral dosing of labeled and unlabeled drug have  
481 demonstrated that the oral systemic bioavailability of fluticasone propionate is negligible (<1%),  
482 primarily due to incomplete absorption and presystemic metabolism in the gut and liver. In  
483 contrast, the majority of the fluticasone propionate delivered to the lung is systemically  
484 absorbed. The absolute bioavailability of fluticasone propionate from the DISKUS device in  
485 healthy volunteers averages 7.8%.

486 Peak steady-state fluticasone propionate plasma concentrations in adult patients with  
487 asthma (N = 11) ranged from undetectable to 266 pg/mL after a 500-mcg twice-daily dosage of  
488 fluticasone propionate inhalation powder using the DISKUS device. The mean fluticasone  
489 propionate plasma concentration was 110 pg/mL.

490 Distribution: Following intravenous administration, the initial disposition phase for  
491 fluticasone propionate was rapid and consistent with its high lipid solubility and tissue binding.  
492 The volume of distribution averaged 4.2 L/kg.

493 The percentage of fluticasone propionate bound to human plasma proteins averages 99%.  
494 Fluticasone propionate is weakly and reversibly bound to erythrocytes and is not significantly  
495 bound to human transcortin.

496 **Metabolism:** The total clearance of fluticasone propionate is high (average, 1,093  
497 mL/min), with renal clearance accounting for less than 0.02% of the total. The only circulating  
498 metabolite detected in man is the 17 $\beta$ -carboxylic acid derivative of fluticasone propionate,  
499 which is formed through the CYP 3A4 pathway. This metabolite had less affinity  
500 (approximately 1/2,000) than the parent drug for the corticosteroid receptor of human lung  
501 cytosol in vitro and negligible pharmacological activity in animal studies. Other metabolites  
502 detected in vitro using cultured human hepatoma cells have not been detected in man.

503 **Elimination:** Following intravenous dosing, fluticasone propionate showed  
504 polyexponential kinetics and had a terminal elimination half-life of approximately 7.8 hours.  
505 Less than 5% of a radiolabeled oral dose was excreted in the urine as metabolites, with the  
506 remainder excreted in the feces as parent drug and metabolites.

507 **Specific Populations:** *Gender:* Full pharmacokinetic profiles were obtained from  
508 9 female and 16 male patients given 500 mcg twice daily. No overall differences in fluticasone  
509 propionate pharmacokinetics were observed.

510 *Pediatrics:* In a clinical study conducted in patients aged 4 to 11 years with mild to  
511 moderate asthma, fluticasone propionate concentrations were obtained in 61 patients at 20 and  
512 40 minutes after dosing with 50 and 100 mcg twice daily of fluticasone propionate inhalation  
513 powder using the DISKUS. Plasma concentrations were low and ranged from undetectable  
514 (about 80% of the plasma samples) to 88 pg/mL. Mean peak fluticasone propionate plasma  
515 concentrations at the 50- and 100-mcg dose levels were 5 and 8 pg/mL, respectively.

516 *Hepatic and Renal Impairment:* Formal pharmacokinetic studies using FLOVENT  
517 DISKUS have not been conducted in patients with hepatic or renal impairment. However, since  
518 fluticasone propionate is predominantly cleared by hepatic metabolism, impairment of liver  
519 function may lead to accumulation of fluticasone propionate in plasma. Therefore, patients with  
520 hepatic disease should be closely monitored.

521 **Drug Interactions:** *Ritonavir:* Fluticasone propionate is a substrate of CYP 3A4.  
522 Coadministration of fluticasone propionate and the strong CYP 3A4 inhibitor ritonavir is not  
523 recommended based upon a multiple-dose, crossover drug interaction study in 18 healthy  
524 subjects. Fluticasone propionate aqueous nasal spray (200 mcg once daily) was coadministered  
525 for 7 days with ritonavir (100 mg twice daily). Plasma fluticasone propionate concentrations  
526 following fluticasone propionate aqueous nasal spray alone were undetectable (<10 pg/mL) in  
527 most subjects, and when concentrations were detectable, peak levels ( $C_{max}$ ) averaged 11.9 pg/mL  
528 (range, 10.8 to 14.1 pg/mL) and  $AUC_{(0-\tau)}$  averaged 8.43 pg•hr/mL (range, 4.2 to 18.8 pg•hr/mL).  
529 Fluticasone propionate  $C_{max}$  and  $AUC_{(0-\tau)}$  increased to 318 pg/mL (range, 110 to 648 pg/mL) and  
530 3,102.6 pg•hr/mL (range, 1,207.1 to 5,662.0 pg•hr/mL), respectively, after coadministration of  
531 ritonavir with fluticasone propionate aqueous nasal spray. This significant increase in plasma



532 fluticasone propionate concentration resulted in a significant decrease (86%) in serum cortisol  
533 AUC.

534 *Ketoconazole*: In a placebo-controlled, crossover study in 8 healthy adult volunteers,  
535 coadministration of a single dose of orally inhaled fluticasone propionate (1,000 mcg) with  
536 multiple doses of ketoconazole (200 mg) to steady state resulted in increased plasma fluticasone  
537 propionate exposure, a reduction in plasma cortisol AUC, and no effect on urinary excretion of  
538 cortisol.

539 Following orally inhaled fluticasone propionate alone,  $AUC_{(2-last)}$  averaged 1.559  
540 ng•hr/mL (range, 0.555 to 2.906 ng•hr/mL) and  $AUC_{(2-\infty)}$  averaged 2.269 ng•hr/mL (range,  
541 0.836 to 3.707 ng•hr/mL). Fluticasone propionate  $AUC_{(2-last)}$  and  $AUC_{(2-\infty)}$  increased to 2.781  
542 ng•hr/mL (range, 2.489 to 8.486 ng•hr/mL) and 4.317 ng•hr/mL (range, 3.256 to 9.408  
543 ng•hr/mL), respectively, after coadministration of ketoconazole with orally inhaled fluticasone  
544 propionate. This increase in plasma fluticasone propionate concentration resulted in a decrease  
545 (45%) in serum cortisol AUC.

546 *Erythromycin*: In a multiple-dose drug interaction study, coadministration of orally  
547 inhaled fluticasone propionate (500 mcg twice daily) and erythromycin (333 mg 3 times daily)  
548 did not affect fluticasone propionate pharmacokinetics.

## 549 **13 NONCLINICAL TOXICOLOGY**

### 550 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

551 Fluticasone propionate demonstrated no tumorigenic potential in mice at oral doses up to  
552 1,000 mcg/kg (approximately 2 and 10 times the MRHD in adults and children aged 4 to 11  
553 years, respectively, on a mg/m<sup>2</sup> basis) for 78 weeks or in rats at inhalation doses up to 57 mcg/kg  
554 (approximately 0.2 times and approximately equivalent to the MRHD in adults and children aged  
555 4 to 11 years, respectively, on a mg/m<sup>2</sup> basis) for 104 weeks.

556 Fluticasone propionate did not induce gene mutation in prokaryotic or eukaryotic cells in  
557 vitro. No significant clastogenic effect was seen in cultured human peripheral lymphocytes in  
558 vitro or in the in vivo mouse micronucleus test.

559 No evidence of impairment of fertility was observed in reproductive studies conducted in  
560 male and female rats at subcutaneous doses up to 50 mcg/kg (approximately 0.2 times the  
561 MRHD in adults on a mg/m<sup>2</sup> basis). Prostate weight was significantly reduced at a subcutaneous  
562 dose of 50 mcg/kg.

### 563 **13.2 Animal Toxicology and/or Pharmacology**

564 Reproductive Toxicology: Subcutaneous studies in the mouse and rat at 45 and  
565 100 mcg/kg (approximately 0.1 and 0.4 times the MRHD in adults on a mg/m<sup>2</sup> basis,  
566 respectively) revealed fetal toxicity characteristic of potent corticosteroid compounds, including  
567 embryonic growth retardation, omphalocele, cleft palate, and retarded cranial ossification.

568 In the rabbit, fetal weight reduction and cleft palate were observed at a subcutaneous dose  
569 of 4 mcg/kg (approximately 0.03 times the MRHD in adults on a mg/m<sup>2</sup> basis). However, no  
570 teratogenic effects were reported at oral doses up to 300 mcg/kg (approximately 2 times the

571 MRHD in adults on a mg/m<sup>2</sup> basis) of fluticasone propionate. No fluticasone propionate was  
572 detected in the plasma in this study, consistent with the established low bioavailability following  
573 oral administration [see *Clinical Pharmacology (12.3)*].

574 Fluticasone propionate crossed the placenta following subcutaneous administration to  
575 mice and rats and oral administration to rabbits.

## 576 **14 CLINICAL STUDIES**

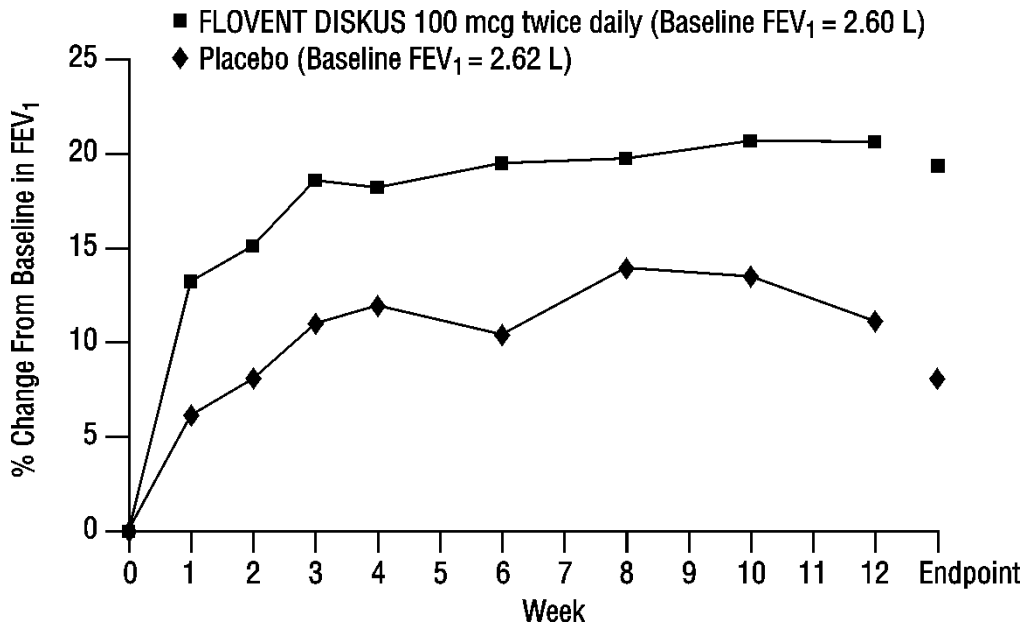
### 577 **14.1 Adult and Adolescent Patients 12 Years and Older**

578 Four randomized, double-blind, parallel-group, placebo-controlled, US clinical trials  
579 were conducted in 1,036 adult and adolescent patients (aged ≥12 years) with asthma to assess  
580 the efficacy and safety of FLOVENT DISKUS in the treatment of asthma. Fixed dosages of 100,  
581 250, and 500 mcg twice daily were compared with placebo to provide information about  
582 appropriate dosing to cover a range of asthma severity. Patients in these studies included those  
583 inadequately controlled with bronchodilators alone and those already maintained on daily  
584 inhaled corticosteroids. All doses were delivered by inhalation of the contents of 1 or 2 blisters  
585 from FLOVENT DISKUS twice daily.

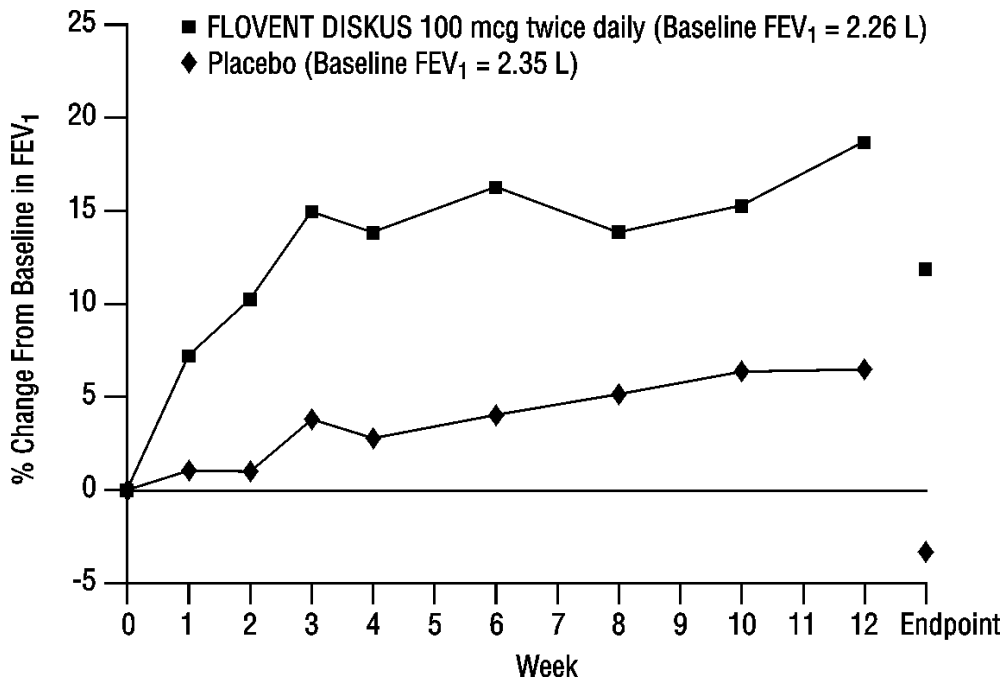
586 Figures 1 through 4 display results of pulmonary function tests (mean percent change  
587 from baseline in FEV<sub>1</sub> prior to AM dose) for 3 recommended dosages of FLOVENT DISKUS  
588 (100, 250, and 500 mcg twice daily) and placebo from the four 12-week trials in adolescents and  
589 adults. These trials used predetermined criteria for lack of efficacy (indicators of worsening  
590 asthma), resulting in withdrawal of more patients in the placebo group. Therefore, pulmonary  
591 function results at Endpoint (the last evaluable FEV<sub>1</sub> result, including most patients' lung  
592 function data) are also displayed. Pulmonary function, as determined by percent change from  
593 baseline in FEV<sub>1</sub> at recommended dosages of FLOVENT DISKUS improved significantly  
594 compared with placebo by the first week of treatment, and improvement was maintained for up  
595 to 1 year or more.

596

597 **Figure 1. A 12-Week Clinical Trial Evaluating FLOVENT DISKUS**  
 598 **100 mcg Twice Daily in Adolescents and Adults Receiving**  
 599 **Bronchodilators Alone**  
 600



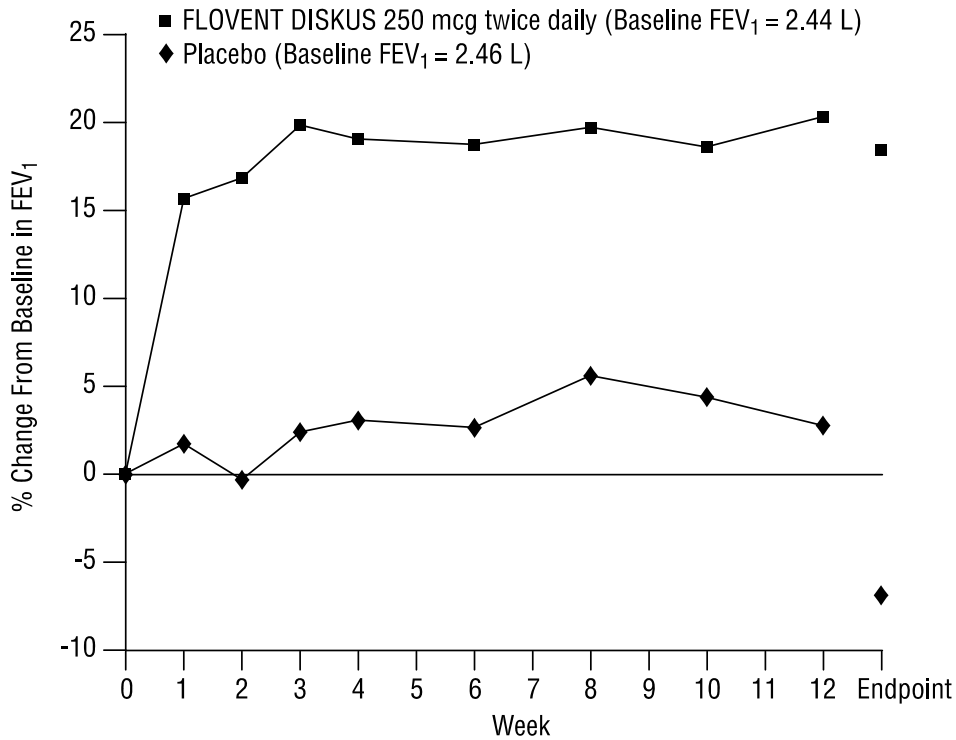
601  
 602  
 603 **Figure 2. A 12-Week Clinical Trial Evaluating FLOVENT DISKUS**  
 604 **100 mcg Twice Daily in Adolescents and Adults Receiving Inhaled**  
 605 **Corticosteroids**  
 606



607  
 608

609 **Figure 3. A 12-Week Clinical Trial Evaluating FLOVENT DISKUS**  
 610 **250 mcg Twice Daily in Adolescents and Adults Receiving Inhaled**  
 611 **Corticosteroids or Bronchodilators Alone**

612

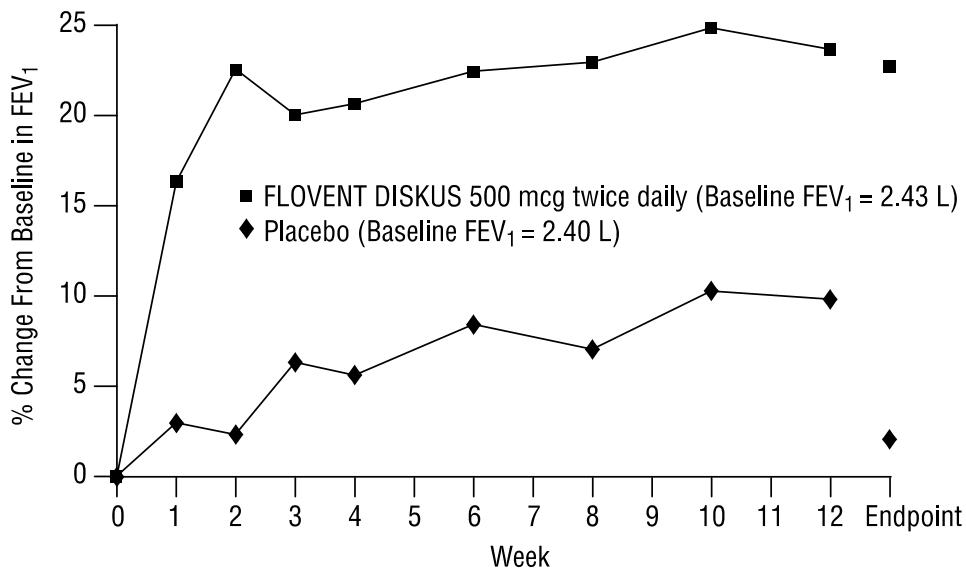


613

614

615 **Figure 4. A 12-Week Clinical Trial Evaluating FLOVENT DISKUS**  
 616 **500 mcg Twice Daily in Adolescents and Adults Receiving Inhaled**  
 617 **Corticosteroids or Bronchodilators Alone**

618



619

620

621 In all 4 efficacy trials, measures of pulmonary function (FEV<sub>1</sub>) were statistically  
622 significantly improved as compared with placebo at all twice-daily doses. Patients on all dosages  
623 of FLOVENT DISKUS were also less likely to discontinue study participation due to asthma  
624 deterioration (as defined by predetermined criteria for lack of efficacy including lung function  
625 and patient-recorded variables such as AM PEF, albuterol use, and nighttime awakenings due to  
626 asthma) compared with placebo.

627 In a clinical trial of 111 patients with severe asthma requiring chronic oral prednisone  
628 therapy (average baseline daily prednisone dose was 14 mg), fluticasone propionate given by  
629 inhalation powder at doses of 500 and 1,000 mcg twice daily was evaluated. Both doses enabled  
630 a statistically significantly larger percentage of patients to wean from oral prednisone as  
631 compared with placebo (75% of the patients on 500 mcg twice daily and 89% of the patients on  
632 1,000 mcg twice daily as compared with 9% of patients on placebo). Accompanying the  
633 reduction in oral corticosteroid use, patients treated with fluticasone propionate had significantly  
634 improved lung function and fewer asthma symptoms as compared with the placebo group.

#### 635 **14.2 Pediatric Patients Aged 4 to 11 Years**

636 A 12-week, placebo-controlled clinical trial was conducted in 437 pediatric patients (177  
637 received FLOVENT DISKUS), approximately half of whom were receiving inhaled  
638 corticosteroids at baseline. In this study, doses of fluticasone propionate inhalation powder 50  
639 and 100 mcg twice daily significantly improved FEV<sub>1</sub> (15% and 18% change from baseline at  
640 Endpoint, respectively) compared with placebo (7% change). AM PEF was also significantly  
641 improved with doses of fluticasone propionate 50 and 100 mcg twice daily (26% and 27%  
642 change from baseline at Endpoint, respectively) compared with placebo (14% change). In this  
643 study, patients on active treatment were significantly less likely to discontinue treatment due to  
644 asthma deterioration (as defined by predetermined criteria for lack of efficacy including lung  
645 function and patient recorded variables such as AM PEF, albuterol use, and nighttime  
646 awakenings due to asthma).

647 Two other 12-week placebo-controlled clinical trials were conducted in 504 pediatric  
648 patients with asthma, approximately half of whom were receiving inhaled corticosteroids at  
649 baseline. In these studies, FLOVENT DISKUS was efficacious at doses of 50 and 100 mcg twice  
650 daily when compared with placebo on major endpoints including lung function and symptom  
651 scores. Pulmonary function improved significantly compared with placebo by the first week of  
652 treatment, and patients treated with FLOVENT DISKUS were also less likely to discontinue  
653 study participation due to asthma deterioration. One hundred ninety-two (192) patients received  
654 FLOVENT DISKUS for up to 1 year during an open-label extension. Data from this open-label  
655 extension suggested that lung function improvements could be maintained up to 1 year.

## 656 **16 HOW SUPPLIED/STORAGE AND HANDLING**

657 FLOVENT DISKUS 50 mcg (NDC 0173-0600-02), FLOVENT DISKUS 100 mcg (NDC  
658 0173-0602-02), and FLOVENT DISKUS 250 mcg (NDC 0173-0601-02) are each supplied as a

659 disposable orange inhalation unit containing 60 blisters of powder formulation packaged in a  
660 plastic-coated, moisture-protective foil pouch in a carton of 1.

661 Store at controlled room temperature (see USP), 20° to 25°C (68° to 77°F) in a dry place  
662 away from direct heat or sunlight. Keep out of reach of children. The DISKUS inhalation device  
663 is not reusable. FLOVENT DISKUS should be discarded 6 weeks (50-mcg strength) or 2 months  
664 (100- and 250-mcg strengths) after removal from the moisture-protective foil pouch or after all  
665 blisters have been used (when the dose indicator reads “0”), whichever comes first. Do not  
666 attempt to take the device apart.

## 667 **17 PATIENT COUNSELING INFORMATION**

668 *See FDA-Approved Patient Labeling accompanying the product.*

### 669 **17.1 Oral Candidiasis**

670 Patients should be advised that localized infections with *Candida albicans* have occurred  
671 in the mouth and pharynx in some patients. If oropharyngeal candidiasis develops, it should be  
672 treated with appropriate local or systemic (i.e., oral antifungal) therapy while still continuing  
673 therapy with FLOVENT DISKUS, but at times therapy with FLOVENT DISKUS may need to  
674 be temporarily interrupted under close medical supervision. Rinsing the mouth after inhalation is  
675 advised.

### 676 **17.2 Status Asthmaticus and Acute Asthma Symptoms**

677 Patients should be advised that FLOVENT DISKUS is not a bronchodilator and is not  
678 intended for use as rescue medication for acute asthma exacerbations. Acute asthma symptoms  
679 should be treated with an inhaled, short-acting beta-<sub>2</sub> agonist such as albuterol. Patients should be  
680 instructed to contact their physicians immediately if there is deterioration of their asthma.

### 681 **17.3 Immunosuppression**

682 Patients who are on immunosuppressant doses of corticosteroids should be warned to  
683 avoid exposure to chickenpox or measles and if they are exposed to consult their physicians  
684 without delay. Patients should be informed of potential worsening of existing tuberculosis,  
685 fungal, bacterial, viral, or parasitic infections, or ocular herpes simplex.

### 686 **17.4 Hypercorticism and Adrenal Suppression**

687 Patients should be advised that FLOVENT DISKUS may cause systemic corticosteroid  
688 effects of hypercorticism and adrenal suppression. Additionally, patients should be instructed  
689 that deaths due to adrenal insufficiency have occurred during and after transfer from systemic  
690 corticosteroids. Patients should taper slowly from systemic corticosteroids if transferring to  
691 FLOVENT DISKUS.

### 692 **17.5 Hypersensitivity Reactions, Including Anaphylaxis**

693 Patients should be advised that hypersensitivity reactions, including anaphylaxis,  
694 angioedema, urticaria, and bronchospasm, may occur after administration of FLOVENT  
695 DISKUS. Patients should discontinue FLOVENT DISKUS if such reactions occur. There have  
696 been reports of anaphylactic reactions in patients with severe milk protein allergy; therefore,  
697 patients with severe milk protein allergy should not take FLOVENT DISKUS.

698 **17.6 Reduction in Bone Mineral Density**

699 Patients who are at an increased risk for decreased BMD should be advised that the use of  
700 corticosteroids may pose an additional risk.

701 **17.7 Reduced Growth Velocity**

702 Patients should be informed that orally inhaled corticosteroids, including FLOVENT  
703 DISKUS, may cause a reduction in growth velocity when administered to pediatric patients.  
704 Physicians should closely follow the growth of children and adolescents taking corticosteroids by  
705 any route.

706 **17.8 Ocular Effects**

707 Long-term use of inhaled corticosteroids may increase the risk of some eye problems  
708 (cataracts or glaucoma); regular eye examinations should be considered.

709 **17.9 Use Daily for Best Effect**

710 Patients should use FLOVENT DISKUS at regular intervals as directed. Individual  
711 patients will experience a variable time to onset and degree of symptom relief and the full benefit  
712 may not be achieved until treatment has been administered for 1 to 2 weeks or longer. Patients  
713 should not increase the prescribed dosage but should contact their physicians if symptoms do not  
714 improve or if the condition worsens. Patients should be instructed not to stop use of FLOVENT  
715 DISKUS abruptly. Patients should contact their physicians immediately if they discontinue use  
716 of FLOVENT DISKUS.

717  
718



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721 Research Triangle Park, NC 27709

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725 | ~~February-March~~ 2010

726 FLD:4PI

1  
2 **Patient Information**  
3

4 **FLOVENT<sup>®</sup> [flō'vent] DISKUS<sup>®</sup> 50 mcg**  
5 **(fluticasone propionate inhalation powder, 50 mcg)**  
6

7 **FLOVENT<sup>®</sup> DISKUS<sup>®</sup> 100 mcg**  
8 **(fluticasone propionate inhalation powder, 100 mcg)**  
9

10 **FLOVENT<sup>®</sup> DISKUS<sup>®</sup> 250 mcg**  
11 **(fluticasone propionate inhalation powder, 250 mcg)**  
12

13 **FOR ORAL INHALATION**  
14

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15 Read this Patient Information before you start to use FLOVENT DISKUS and each time you get  
16 a refill. There may be new information. This information does not take the place of talking with  
17 your doctor about your medical condition or your treatment.  
18

19 **What is FLOVENT DISKUS?**

20 FLOVENT DISKUS is an inhaled prescription corticosteroid medicine for the long-term  
21 treatment of asthma in people aged 4 and older.

- 22 • FLOVENT DISKUS helps to prevent symptoms of asthma  
23 • FLOVENT DISKUS does not treat the sudden symptoms of an asthma attack, such as  
24 wheezing, cough, shortness of breath, and chest pain or tightness. **Always have a fast-acting**  
25 **bronchodilator medicine (rescue inhaler) with you to treat sudden symptoms.**

26 It is not known if FLOVENT DISKUS is safe and effective in children younger than 4 years of  
27 age.  
28

29 **Who should not use FLOVENT DISKUS?**

30 Do not use FLOVENT DISKUS

- 31 • to treat sudden symptoms of asthma. **FLOVENT DISKUS is not a rescue inhaler and**  
32 **should not be used to give you fast relief from your asthma attack.** Always use a rescue  
33 inhaler such as albuterol, during a sudden asthma attack.  
34 • if you have severe allergy to milk proteins or fluticasone propionate. Ask your doctor if you  
35 are not sure.  
36

37 **What should I tell my doctor before taking FLOVENT DISKUS?**

38 Before you use FLOVENT DISKUS, tell your doctor if you:

- 39 • have liver problems.



- 40 • have been exposed to chickenpox or measles.
- 41 • have any other medical conditions.
- 42 • are pregnant or planning to become pregnant. It is not known if FLOVENT DISKUS will
- 43 harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- 44 • are breast-feeding or plan to breast-feed. It is not known if FLOVENT DISKUS passes into
- 45 your breast milk. You and your doctor should decide if you should use FLOVENT DISKUS
- 46 while you breast-feed.

47 Tell your doctor about all the medicines you take including prescription and non-prescription  
48 medicines, vitamins, and herbal supplements. FLOVENT DISKUS may affect the way other  
49 medicines work, and other medicines may affect how FLOVENT DISKUS works. Especially,  
50 tell your doctor if you take:

- 51 • anti-viral medicines, including medicines that contain ritonavir (commonly used to treat HIV
- 52 infection or AIDS).
- 53 • any other corticosteroid medicines.
- 54 • ketoconazole (NIZORAL<sup>®</sup>), an antifungal medicine.

55 This is not a complete list of medicines that can affect FLOVENT DISKUS. Ask your doctor if  
56 you are not sure if any of your medicines are the kinds listed above.

57 Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist  
58 when you get a new medicine.

59

### 60 **How should I use FLOVENT DISKUS?**

- 61 • Read the detailed Instructions for Use at the end of this leaflet.
- 62 • An adult should always watch a child use FLOVENT DISKUS to make sure that it is used
- 63 correctly, as instructed by your doctor.
- 64 • FLOVENT DISKUS comes in 3 strengths. Your doctor has prescribed the one that is best for
- 65 your condition.
- 66 • Use FLOVENT DISKUS exactly as your doctor tells you to use it. Do not change the dose
- 67 yourself. Your doctor will tell you how many times to inhale your FLOVENT DISKUS and
- 68 when to use your FLOVENT DISKUS. **Do not** inhale more doses or use your FLOVENT
- 69 DISKUS more often than your doctor has prescribed.
- 70 • FLOVENT DISKUS delivers your dose of medicine as a very fine powder **that most people,**
- 71 **but not all, can taste or feel.** Whether or not you can taste or feel your dose of medicine,
- 72 you should not take more than the prescribed dose. If you are not sure you are getting your
- 73 dose of FLOVENT DISKUS, contact your doctor or pharmacist.
- 74 • It may take 1 to 2 weeks or longer after you start FLOVENT DISKUS for your asthma
- 75 symptoms to get better. You must use FLOVENT DISKUS regularly. **Do not stop using**
- 76 **FLOVENT DISKUS, even if you are feeling better, unless your doctor tells you to.**

- 77 • If you miss a dose, just take your next dose at your regular time. **Do not take 2 doses at the**  
78 **same time unless your doctor tells you to. If you are not sure about your dosing, call**  
79 **your doctor.**
- 80 • Your doctor may prescribe a rescue inhaler for emergency relief of sudden asthma attacks.  
81 Contact your doctor right away if:
- 82 • an asthma attack does not respond to your rescue inhaler or  
83 • you need more of your rescue inhaler than usual.
- 84 • If you also use another medicine by inhalation, you should ask your doctor for instructions  
85 on when to use it while you are also using FLOVENT DISKUS.
- 86 • Do not use FLOVENT DISKUS with a spacer device.

87

### 88 **What should I avoid while taking FLOVENT DISKUS?**

89 If you have not had or have not been vaccinated against chickenpox, measles, or active  
90 tuberculosis, you should stay away from people who are infected.

91

### 92 **What are the possible side effects of FLOVENT DISKUS?**

93 FLOVENT DISKUS can cause serious side effects, including:

- 94 • **fungal infection (thrush) in your mouth and throat.** Tell your doctor if you have any  
95 redness or white-colored coating in your mouth.
- 96 • **decreased ability to fight infections.** Symptoms of infection may include: fever, pain,  
97 aches, chills, feeling tired, nausea and vomiting. Tell your doctor about any signs of infection  
98 while you use FLOVENT DISKUS.
- 99 • **decreased adrenal function (adrenal insufficiency).** Symptoms of decreased adrenal  
100 function include tiredness, weakness, nausea and vomiting, and low blood pressure.  
101 Decreased adrenal function can lead to death.
- 102 • **allergic reaction (anaphylaxis).** Call your doctor and stop FLOVENT DISKUS right away  
103 if you have any symptoms of an allergic reaction:
- swelling of the face, throat, and tongue
  - rash
  - hives
  - breathing problems
- 104 • **lower bone mineral density.** This may be a problem for people who already have a higher  
105 chance of low bone density (osteoporosis).
- 106 • **slow growth in children.** The growth of children using FLOVENT DISKUS should be  
107 checked regularly.
- 108 • **eye problems including glaucoma and cataracts.** Tell your doctor about any vision  
109 changes while using FLOVENT DISKUS. Your doctor may tell you to have your eyes  
110 checked.

- 111 • **increased wheezing (bronchospasm).** Increased wheezing can happen right away after  
112 using FLOVENT DISKUS. Always have a rescue inhaler with you to treat sudden wheezing.

113 Call your doctor right away if you have any of the serious side effects listed above or if you have  
114 worsening lung symptoms.

115 **The most common side effects of FLOVENT DISKUS include:**

- a cold or upper respiratory tract infection
- throat irritation
- nausea and vomiting
- fever
- headache

116

117 Tell your doctor if you have any side effects that bother you or that do not go away. These are  
118 not all the possible side effects of FLOVENT DISKUS. For more information ask your doctor or  
119 pharmacist.

120 Call your doctor for medical advice about side effects. You may report side effects to FDA at  
121 1-800-FDA-1088 or 1-800-332-1088.

122

123 **How should I store FLOVENT DISKUS?**

124 Store FLOVENT DISKUS at room temperature between 68°F to 77°F (20°C to 25°C). Store  
125 FLOVENT DISKUS in a dry place away from heat and sunlight.

126 FLOVENT DISKUS is not reusable. Safely throw away medicine that is out of date or no longer  
127 needed.

128 Do not try to take FLOVENT DISKUS apart.

129 **Keep FLOVENT DISKUS and all medicines out of the reach of children.**

130

131 **General information about the safe and effective use of FLOVENT DISKUS.**

132 Medicines are sometimes prescribed for purposes other than those listed in a Patient Information  
133 leaflet. Do not use FLOVENT DISKUS for a condition for which it was not prescribed. Do not  
134 give FLOVENT DISKUS to other people, even if they have the same symptoms that you have. It  
135 may harm them.

136 This Patient Information leaflet summarizes the most important information about FLOVENT  
137 DISKUS. If you would like more information, talk with your healthcare provider. You can ask  
138 your pharmacist or doctor for information about FLOVENT DISKUS that is written for health  
139 professionals.

140 For more information go to [www.floventdiskus.com](http://www.floventdiskus.com) or call 1-888-825-5249.

141

142 **What are the ingredients in FLOVENT DISKUS?**

143 Active ingredient: fluticasone propionate (microfine)

144 Inactive ingredient: lactose (which contains milk proteins)

145

146

**Instructions for Using FLOVENT DISKUS**

147

**The parts of your FLOVENT DISKUS**



148

149

**Figure 1**

The counter shows you how many doses are left. The counter number will count down each time you use FLOVENT DISKUS. After you have used 55 doses (23 doses from the sample pack), the numbers 5 to 0 will show in **red** to warn you that there are only a few doses left (see Figure 1).

**Using your FLOVENT DISKUS**

- Take FLOVENT DISKUS out of the moisture-protective foil pouch just before you use it for the first time. Safely throw away the foil pouch.
- FLOVENT DISKUS will be in the closed position. Write the “Pouch opened” and “Use by” dates in the blank lines on the label (see Figure 1). The “Use by” date for FLOVENT DISKUS 50 mcg is 6 weeks from the date you opened the pouch. The “Use by” date for FLOVENT DISKUS 100 mcg and FLOVENT DISKUS 250 mcg is 2 months from the date you opened the pouch.

Read the following steps before using FLOVENT DISKUS and follow them at each use. If you have any questions, ask your doctor or pharmacist.

**Figure 2**



**Figure 3**



**1. Open**

Hold FLOVENT DISKUS in one hand and put the thumb of your other hand on the thumbgrip. Push your thumb away from you as far as it will go until the mouthpiece shows and snaps into place (see Figure 2).

**2. Click**

Hold FLOVENT DISKUS in a level, flat position with the mouthpiece towards you. Slide the lever away from you as far as it will go until it clicks (see Figure 3). The number on the dose counter will count down by 1. FLOVENT DISKUS is now ready to use.

**To avoid releasing a dose by mistake before you are ready to inhale:**

- **Do not close FLOVENT DISKUS.**
- **Do not tilt FLOVENT DISKUS.**
- **Do not play with the lever.**
- **Do not slide the lever more than once.**



**Figure 4**



**Figure 5**

**3. Inhale**

Before you inhale your dose of FLOVENT DISKUS, breathe out as far as you can while you hold FLOVENT DISKUS level and away from your mouth (see Figure 4). **Never breathe out into the FLOVENT DISKUS mouthpiece.**

Put the mouthpiece to your lips (see Figure 5). Breathe in quickly and deeply through FLOVENT DISKUS. Do not breathe in through your nose.

Remove FLOVENT DISKUS from your mouth. Hold your breath for about 10 seconds, or for as long as is comfortable. Breathe out slowly.

Rinse your mouth with water after inhaling the medicine. Spit out the water. Do not swallow it.



**Figure 6**

- 4. Close FLOVENT DISKUS when you are finished taking a dose.** Put your thumb on the thumbgrip and slide it back towards you as far as it will go (see Figure 6). FLOVENT DISKUS will click shut. The lever will automatically return to its original position.

FLOVENT DISKUS is now ready for you to take your next scheduled dose in about 12 hours. When you are ready for your next dose, you will repeat steps 1 through 4.

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NIZORAL is a registered trademark of Janssen Pharmaceutica.



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Research Triangle Park, NC 27709

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~~February~~ March 2010

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1  
2 **Patient Information**  
3

4 **FLOVENT<sup>®</sup> [flō'vent] DISKUS<sup>®</sup> 50 mcg**  
5 **(fluticasone propionate inhalation powder, 50 mcg)**  
6

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9

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13 **FOR ORAL INHALATION**  
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25 **bronchodilator medicine (rescue inhaler) with you to treat sudden symptoms.**

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27 age.  
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- 63 correctly, as instructed by your doctor.
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- 65 your condition.
- 66 • Use FLOVENT DISKUS exactly as your doctor tells you to use it. Do not change the dose
- 67 yourself. Your doctor will tell you how many times to inhale your FLOVENT DISKUS and
- 68 when to use your FLOVENT DISKUS. **Do not** inhale more doses or use your FLOVENT
- 69 DISKUS more often than your doctor has prescribed.
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- 71 **but not all, can taste or feel.** Whether or not you can taste or feel your dose of medicine,
- 72 you should not take more than the prescribed dose. If you are not sure you are getting your
- 73 dose of FLOVENT DISKUS, contact your doctor or pharmacist.
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- 75 symptoms to get better. You must use FLOVENT DISKUS regularly. **Do not stop using**
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- 77 • If you miss a dose, just take your next dose at your regular time. **Do not take 2 doses at the**  
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- 80 • Your doctor may prescribe a rescue inhaler for emergency relief of sudden asthma attacks.  
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- 96 • **decreased ability to fight infections.** Symptoms of infection may include: fever, pain,  
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98 while you use FLOVENT DISKUS.
- 99 • **decreased adrenal function (adrenal insufficiency).** Symptoms of decreased adrenal  
100 function include tiredness, weakness, nausea and vomiting, and low blood pressure.  
101 Decreased adrenal function can lead to death.
- 102 • **allergic reaction (anaphylaxis).** Call your doctor and stop FLOVENT DISKUS right away  
103 if you have any symptoms of an allergic reaction:
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  - rash
  - hives
  - breathing problems
- 104 • **lower bone mineral density.** This may be a problem for people who already have a higher  
105 chance of low bone density (osteoporosis).
- 106 • **slow growth in children.** The growth of children using FLOVENT DISKUS should be  
107 checked regularly.
- 108 • **eye problems including glaucoma and cataracts.** Tell your doctor about any vision  
109 changes while using FLOVENT DISKUS. Your doctor may tell you to have your eyes  
110 checked.

111 • **increased wheezing (bronchospasm).** Increased wheezing can happen right away after  
112 using FLOVENT DISKUS. Always have a rescue inhaler with you to treat sudden wheezing.

113 Call your doctor right away if you have any of the serious side effects listed above or if you have  
114 worsening lung symptoms.

115 **The most common side effects of FLOVENT DISKUS include:**

- a cold or upper respiratory tract infection
- throat irritation
- nausea and vomiting
- fever
- headache

116 Tell your doctor if you have any side effects that bother you or that do not go away. These are  
117 not all the possible side effects of FLOVENT DISKUS. For more information ask your doctor or  
118 pharmacist.

119 Call your doctor for medical advice about side effects. You may report side effects to FDA at  
120 1-800-FDA-1088 or 1-800-332-1088.

121  
122 **How should I store FLOVENT DISKUS?**

123 Store FLOVENT DISKUS at room temperature between 68°F to 77°F (20°C to 25°C). Store  
124 FLOVENT DISKUS in a dry place away from heat and sunlight.

125 FLOVENT DISKUS is not reusable. Safely throw away medicine that is out of date or no longer  
126 needed.

127 Do not try to take FLOVENT DISKUS apart.

128 **Keep FLOVENT DISKUS and all medicines out of the reach of children.**

129  
130 **General information about the safe and effective use of FLOVENT DISKUS.**

131 Medicines are sometimes prescribed for purposes other than those listed in a Patient Information  
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137 your pharmacist or doctor for information about FLOVENT DISKUS that is written for health  
138 professionals.

139 For more information go to [www.floventdiskus.com](http://www.floventdiskus.com) or call 1-888-825-5249.

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143 Inactive ingredient: lactose (which contains milk proteins)

144

145 **Instructions for Using FLOVENT DISKUS**

146 **The parts of your FLOVENT DISKUS**



147

148

**Figure 1**

The counter shows you how many doses are left. The counter number will count down each time you use FLOVENT DISKUS. After you have used 55 doses (23 doses from the sample pack), the numbers 5 to 0 will show in **red** to warn you that there are only a few doses left (see Figure 1).

**Using your FLOVENT DISKUS**

- Take FLOVENT DISKUS out of the moisture-protective foil pouch just before you use it for the first time. Safely throw away the foil pouch.
- FLOVENT DISKUS will be in the closed position. Write the “Pouch opened” and “Use by” dates in the blank lines on the label (see Figure 1). The “Use by” date for FLOVENT DISKUS 50 mcg is 6 weeks from the date you opened the pouch. The “Use by” date for FLOVENT DISKUS 100 mcg and FLOVENT DISKUS 250 mcg is 2 months from the date you opened the pouch.

Read the following steps before using FLOVENT DISKUS and follow them at each use. If you have any questions, ask your doctor or pharmacist.



**Figure 2**



**Figure 3**

**1. Open**

Hold FLOVENT DISKUS in one hand and put the thumb of your other hand on the thumbgrip. Push your thumb away from you as far as it will go until the mouthpiece shows and snaps into place (see Figure 2).

## 2. Click

Hold FLOVENT DISKUS in a level, flat position with the mouthpiece towards you. Slide the lever away from you as far as it will go until it clicks (see Figure 3). The number on the dose counter will count down by 1. FLOVENT DISKUS is now ready to use.

**To avoid releasing a dose by mistake before you are ready to inhale:**

- **Do not close FLOVENT DISKUS.**
- **Do not tilt FLOVENT DISKUS.**
- **Do not play with the lever.**
- **Do not slide the lever more than once.**



**Figure 4**



**Figure 5**

## 3. Inhale

Before you inhale your dose of FLOVENT DISKUS, breathe out as far as you can while you hold FLOVENT DISKUS level and away from your mouth (see Figure 4). **Never breathe out into the FLOVENT DISKUS mouthpiece.**

Put the mouthpiece to your lips (see Figure 5). Breathe in quickly and deeply through FLOVENT DISKUS. Do not breathe in through your nose.

Remove FLOVENT DISKUS from your mouth. Hold your breath for about 10 seconds, or for as long as is comfortable. Breathe out slowly.

Rinse your mouth with water after inhaling the medicine. Spit out the water. Do not swallow it.



**Figure 6**

- 4. Close FLOVENT DISKUS when you are finished taking a dose.** Put your thumb on the thumbgrip and slide it back towards you as far as it will go (see Figure 6). FLOVENT DISKUS will click shut. The lever will automatically return to its original position.

FLOVENT DISKUS is now ready for you to take your next scheduled dose in about 12 hours. When you are ready for your next dose, you will repeat steps 1 through 4.

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