HIGHLIGHTS OF PRESCRIBING INFORMATION

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

FLOVENT HFA 44 mcg (fluticasone propionate 44 mcg) Inhalation Aerosol
FLOVENT HFA 110 mcg (fluticasone propionate 110 mcg) Inhalation Aerosol
FLOVENT HFA 220 mcg (fluticasone propionate 220 mcg) Inhalation Aerosol
FOR ORAL INHALATION
Initial U.S. Approval: 1994

----------INDICATIONS AND USAGE----------

FLOVENT HFA is an inhaled corticosteroid indicated for:

- Maintenance treatment of asthma as prophylactic therapy in patients aged 4 years and older. (1)
- Treatment of asthma in patients requiring oral corticosteroid therapy. (1)

Important limitation:

- 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
Patients aged 12 years and older		
Bronchodilators alone	88 mcg twice daily	440 mcg twice daily
Inhaled corticosteroids	88-220 mcg twice daily	440 mcg twice daily
Oral corticosteroids	440 mcg twice daily	880 mcg twice daily
Patients aged 4-11 years	88 mcg twice daily	88 mcg twice daily

---------- DOSAGE FORMS AND STRENGTHS ----------

Inhalation Aerosol. Inhaler containing fluticasone propionate (44, 110, or 220 mcg) as an aerosol formulation for oral inhalation. (3)

----------CONTRAINDICATIONS----------

- Primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures. (4)
- Hypersensitivity to any ingredient. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- *Candida albicans* infection of the mouth and pharynx may occur. Monitor patients periodically. Advise the patient to rinse his/her mouth with water without swallowing after inhalation to help reduce the risk. (5.1)
- Potential worsening of infections (e.g., existing tuberculosis; fungal, bacterial, viral, or parasitic infection; ocular herpes simplex). Use with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients. (5.3)
- Risk of impaired adrenal function when transferring from systemic corticosteroids. Taper patients slowly from systemic corticosteroids if transferring to FLOVENT HFA. (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 HFA slowly. (5.5)
- Assess for decrease in bone mineral density initially and periodically thereafter. (5.7)
- Monitor growth of pediatric patients. (5.8)
- Close monitoring for glaucoma and cataracts is warranted. (5.9)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (incidence greater than 3%) are upper respiratory tract infection or inflammation, throat irritation, sinusitis, dysphonia, candidiasis, 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.

----------DRUG INTERACTIONS----------

Strong cytochrome P450 3A4 inhibitors (e.g., ritonavir, ketoconazole): Use not recommended. May increase risk of systemic corticosteroid effects. (7.1)

---------- USE IN SPECIFIC POPULATIONS ----------

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

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FLOVENT® HFA Inhalation Aerosol is indicated for the maintenance treatment of asthma as prophylactic therapy in patients aged 4 years and older. It is also indicated for patients requiring oral corticosteroid therapy for asthma. Many of these patients may be able to reduce or eliminate their requirement for oral corticosteroids over time.

Important Limitation of Use: FLOVENT HFA is NOT indicated for the relief of acute bronchospasm.

2 DOSAGE AND ADMINISTRATION

FLOVENT HFA should be administered by the orally inhaled route only in patients aged 4 years and older. After inhalation, the patient should rinse his/her mouth with water without swallowing to help reduce the risk of oropharyngeal candidiasis.

Individual patients will experience a variable time to onset and degree of symptom relief. Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting treatment.

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

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

Table 1. Recommended Dosages of FLOVENT HFA Inhalation Aerosol
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
Adult and adolescent patients (aged 12 years and older)		
Bronchodilators alone	88 mcg twice daily	440 mcg twice daily
Inhaled corticosteroids	88-220 mcg twice daily[a]	440 mcg twice daily
Oral corticosteroids[b]	440 mcg twice daily	880 mcg twice daily
Pediatric patients (aged 4-11 years)[c]	88 mcg twice daily	88 mcg twice daily

[a] Starting dosages above 88 mcg twice daily may be considered for patients with poorer asthma control or those who have previously required doses of inhaled corticosteroids that are in the higher range for the specific agent.

[b] For patients currently receiving chronic oral corticosteroid therapy, prednisone should be

reduced no faster than 2.5 to 5 mg/day on a weekly basis beginning after at least 1 week of therapy with FLOVENT HFA. Patients should be carefully monitored for signs of asthma instability, including serial objective measures of airflow, and for signs of adrenal insufficiency *[see Warnings and Precautions (5.4)]*. Once prednisone reduction is complete, the dosage of FLOVENT HFA should be reduced to the lowest effective dosage.

[c] Recommended pediatric dosage is 88 mcg twice daily regardless of prior therapy. A valved holding chamber and mask may be used to deliver FLOVENT HFA to young patients.

Prime FLOVENT HFA before using for the first time by releasing 4 sprays into the air away from the face, shaking well for 5 seconds before each spray. In cases where the inhaler has not been used for more than 7 days or when it has been dropped, prime the inhaler again by shaking well for 5 seconds and releasing 1 spray into the air away from the face.

3 DOSAGE FORMS AND STRENGTHS

Inhalation Aerosol. Dark orange plastic inhaler with a peach strapcap containing a pressurized metered-dose aerosol canister containing 120 metered inhalations and fitted with a counter. Each actuation delivers 44, 110, or 220 mcg of fluticasone propionate from the mouthpiece.

4 CONTRAINDICATIONS

The use of FLOVENT HFA is contraindicated in the following conditions:

- Primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required *[see Warnings and Precautions (5.2)]*.
- Hypersensitivity to any of the ingredients *[see Warnings and Precautions (5.6), Adverse Reactions (6.2), Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Local Effects of Inhaled Corticosteroids

In clinical trials, the development of localized infections of the mouth and pharynx with *Candida albicans* has occurred in subjects treated with FLOVENT HFA. When such an infection develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy while treatment with FLOVENT HFA continues, but at times therapy with FLOVENT HFA may need to be interrupted. Advise the patient to rinse his/her mouth with water without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.

5.2 Acute Asthma Episodes

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

5.3 Immunosuppression

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

Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.

5.4 Transferring Patients from Systemic Corticosteroid Therapy

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

Patients who have been previously maintained on 20 mg or more of prednisone (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have been almost completely withdrawn. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Although FLOVENT HFA may control asthma symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of glucocorticoid systemically and does NOT provide the mineralocorticoid activity that is necessary for coping with these emergencies.

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

Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to FLOVENT HFA. Prednisone reduction can be accomplished by reducing the daily prednisone dose by 2.5 mg on a weekly basis during therapy with FLOVENT HFA. Lung function (mean forced expiratory volume in 1 second [FEV_1] or morning peak expiratory flow [AM PEF]), beta-agonist use, and asthma symptoms should be carefully monitored during withdrawal of oral corticosteroids. In addition, patients should be

observed for signs and symptoms of adrenal insufficiency such as fatigue, lassitude, weakness, nausea and vomiting, and hypotension.

Transfer of patients from systemic corticosteroid therapy to FLOVENT HFA may unmask allergic conditions previously suppressed by the systemic corticosteroid therapy (e.g., rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions).

During withdrawal from oral corticosteroids, some patients may experience symptoms of systemically active corticosteroid withdrawal (e.g., joint and/or muscular pain, lassitude, depression) despite maintenance or even improvement of respiratory function.

5.5 Hypercorticism and Adrenal Suppression

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

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

It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, FLOVENT HFA should be reduced slowly, consistent with accepted procedures for reducing systemic corticosteroids, and other treatments for management of asthma symptoms should be considered.

5.6 Immediate Hypersensitivity Reactions

Immediate hypersensitivity reactions (e.g., urticaria, angioedema, rash, bronchospasm, hypotension), including anaphylaxis, may occur after administration of FLOVENT HFA *[see Contraindications (4)]*.

5.7 Reduction in Bone Mineral Density

Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing inhaled corticosteroids. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids), should be monitored and treated with established standards of care.

A 2-year trial in 160 subjects (females aged 18 to 40 years, males 18 to 50) with asthma receiving chlorofluorocarbon (CFC)-propelled fluticasone propionate inhalation aerosol 88 or 440 mcg twice daily demonstrated no statistically significant changes in BMD at any time point (24, 52, 76, and 104 weeks of double-blind treatment) as assessed by dual-energy x-ray absorptiometry at lumbar regions L1 through L4.

5.8 Effect on Growth

Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Monitor the growth of pediatric patients receiving FLOVENT HFA routinely (e.g., via stadiometry). To minimize the systemic effects of orally inhaled corticosteroids, including FLOVENT HFA, titrate each patient's dosage to the lowest dosage that effectively controls his/her symptoms *[see Dosage and Administration (2), Use in Specific Populations (8.4)]*.

5.9 Glaucoma and Cataracts

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

5.10 Paradoxical Bronchospasm

As with other inhaled medicines, bronchospasm may occur with an immediate increase in wheezing after dosing. If bronchospasm occurs following dosing with FLOVENT HFA, it should be treated immediately with an inhaled, short-acting bronchodilator; FLOVENT HFA should be discontinued immediately; and alternative therapy should be instituted.

5.11 Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors

The use of strong cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with FLOVENT HFA is not recommended because increased systemic corticosteroid adverse effects may occur *[see Drug Interactions (7.1), Clinical Pharmacology (12.3)]*.

5.12 Eosinophilic Conditions and Churg-Strauss Syndrome

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

6 ADVERSE REACTIONS

Systemic and local corticosteroid use may result in the following:

- *Candida albicans* infection *[see Warnings and Precautions (5.1)]*
- Immunosuppression *[see Warnings and Precautions (5.3)]*
- Hypercorticism and adrenal suppression *[see Warnings and Precautions (5.5)]*
- Reduction in bone mineral density *[see Warnings and Precautions (5.7)]*
- Growth effects *[see Warnings and Precautions (5.8)]*
- Glaucoma and cataracts *[see Warnings and Precautions (5.9)]*

6.1 Clinical Trials Experience

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

The incidence of common adverse reactions in Table 2 is based upon 2 placebo-controlled US clinical trials in which 812 adult and adolescent subjects (457 females and 355 males) previously treated with as-needed bronchodilators and/or inhaled corticosteroids were treated twice daily for up to 12 weeks with 2 inhalations of FLOVENT HFA 44 mcg Inhalation Aerosol, FLOVENT HFA 110 mcg Inhalation Aerosol, FLOVENT HFA 220 mcg Inhalation Aerosol (dosages of 88, 220, or 440 mcg twice daily), or placebo.

Table 2. Adverse Reactions with FLOVENT HFA with >3% Incidence and More Common than Placebo in Subjects Aged 12 Years and Older with Asthma

Adverse Event	FLOVENT HFA 88 mcg Twice Daily (n = 203) %	FLOVENT HFA 220 mcg Twice Daily (n = 204) %	FLOVENT HFA 440 mcg Twice Daily (n = 202) %	Placebo (n = 203) %
Ear, nose, and throat				
Upper respiratory tract infection	18	16	16	14
Throat irritation	8	8	10	5
Upper respiratory inflammation	2	5	5	1
Sinusitis/sinus infection	6	7	4	3
Hoarseness/dysphonia	2	3	6	<1
Gastrointestinal				
Candidiasis mouth/throat and non-site specific	4	2	5	<1
Lower respiratory				
Cough	4	6	4	5
Bronchitis	2	2	6	5

Neurological				
Headache	11	7	5	6

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 HFA and were more common than in the placebo group. Less than 2% of subjects discontinued from the trials because of adverse reactions. The average duration of exposure was 73 to 76 days in the active treatment groups compared with 60 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 subjects with asthma treated with FLOVENT HFA compared with subjects treated with placebo include the following: rhinitis, rhinorrhea/post-nasal drip, nasal sinus disorders, laryngitis, diarrhea, viral gastrointestinal infections, dyspeptic symptoms, gastrointestinal discomfort and pain, hyposalivation, musculoskeletal pain, muscle pain, muscle stiffness/tightness/rigidity, dizziness, migraines, fever, viral infections, pain, chest symptoms, viral skin infections, muscle injuries, soft tissue injuries, urinary infections.

Fluticasone propionate inhalation aerosol (440 or 880 mcg twice daily) was administered for 16 weeks to 168 subjects with asthma requiring oral corticosteroids (Trial 3). Adverse reactions not included above, but reported by more than 3 subjects in either group treated with FLOVENT HFA and more commonly than in the placebo group included nausea and vomiting, arthralgia and articular rheumatism, and malaise and fatigue.

In 2 long-term trials (26 and 52 weeks), the pattern of adverse reactions in subjects treated with FLOVENT HFA at dosages up to 440 mcg twice daily was similar to that observed in the 12-week trials. There were no new and/or unexpected adverse reactions with long-term treatment.

Pediatric Subjects Aged 4 to 11 Years: FLOVENT HFA has been evaluated for safety in 56 pediatric subjects who received 88 mcg twice daily for 4 weeks. Types of adverse reactions in these pediatric subjects were generally similar to those observed in adults and adolescents.

6.2 Postmarketing Experience

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

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

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

Eye: Cataracts.

Gastrointestinal Disorders: Dental caries and tooth discoloration.

Immune System Disorders: Immediate and delayed hypersensitivity reactions, including urticaria, anaphylaxis, rash, and angioedema and bronchospasm, have been reported.

Infections and Infestations: Esophageal candidiasis.

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

Respiratory: Asthma exacerbation, chest tightness, cough, dyspnea, immediate and delayed bronchospasm, paradoxical bronchospasm, pneumonia, and wheeze.

Skin: Contusions, cutaneous hypersensitivity reactions, ecchymoses, and pruritus.

7 DRUG INTERACTIONS

7.1 Inhibitors of Cytochrome P450 3A4

Fluticasone propionate is a substrate of CYP3A4. The use of strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with FLOVENT HFA is not recommended because increased systemic corticosteroid adverse effects may occur.

Ritonavir: A drug interaction trial with fluticasone propionate aqueous nasal spray in healthy subjects has shown that ritonavir (a strong CYP3A4 inhibitor) can significantly increase plasma fluticasone propionate exposure, resulting in significantly reduced serum cortisol concentrations *[see Clinical Pharmacology (12.3)]*. During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression.

Ketoconazole: Coadministration of orally inhaled fluticasone propionate (1,000 mcg) and ketoconazole (200 mg once daily) resulted in a 1.9-fold increase in plasma fluticasone propionate exposure and a 45% decrease in plasma cortisol area under the curve (AUC), but had no effect on urinary excretion of cortisol.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C. There are no adequate and well-controlled trials with FLOVENT HFA in pregnant women. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Because animal reproduction studies are not always predictive of human response, FLOVENT HFA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women should be advised to contact their physicians if they become pregnant while taking FLOVENT HFA.

Mice and rats at fluticasone propionate doses approximately 0.1 and 0.5 times, respectively, the maximum recommended human daily inhalation dose (MRHDID) for adults (on

a mg/m^2 basis at maternal subcutaneous doses of 45 and 100 mcg/kg/day, respectively) showed fetal toxicity characteristic of potent corticosteroid compounds, including embryonic growth retardation, omphalocele, cleft palate, and retarded cranial ossification. No teratogenicity was seen in rats at doses up to 0.3 times the MRHDID (on a mcg/m^2 basis at maternal inhaled doses up to 68.7 mcg/kg/day).

In rabbits, fetal weight reduction and cleft palate were observed at a fluticasone propionate dose approximately 0.04 times the MRHDID for adults (on a mg/m^2 basis at a maternal subcutaneous dose of 4 mcg/kg/day). However, no teratogenic effects were reported at fluticasone propionate doses up to approximately 3 times the MRHDID for adults (on a mg/m^2 basis at a maternal oral dose up to 300 mcg/kg/day). No fluticasone propionate was detected in the plasma in this study, consistent with the established low bioavailability following oral administration *[see Clinical Pharmacology (12.3)]*.

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

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

Nonteratogenic Effects: Hypoadrenalism may occur in infants born of mothers receiving corticosteroids during pregnancy. Such infants should be carefully monitored.

8.3 Nursing Mothers

It is not known whether fluticasone propionate is excreted in human breast milk. However, other corticosteroids have been detected in human milk. Subcutaneous administration to lactating rats of tritiated fluticasone propionate at a dose approximately 0.05 times the MRHDID in adults on a mg/m^2 basis) resulted in measurable radioactivity in milk.

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

8.4 Pediatric Use

The safety and effectiveness of FLOVENT HFA in children aged 4 years and older have been established *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), Clinical Studies (14.2)]*. The safety and effectiveness of FLOVENT HFA in children younger than 4 years have not been established. Use of FLOVENT HFA in patients aged 4 to 11 years is supported by evidence from adequate and well-controlled trials in adults and adolescents aged 12 years and older, pharmacokinetic trials in patients aged 4 to 11 years, established efficacy of fluticasone propionate formulated as FLOVENT® DISKUS® (fluticasone propionate inhalation powder) and FLOVENT® ROTADISK® (fluticasone propionate inhalation powder) in patients aged 4 to 11 years, and supportive findings with FLOVENT HFA in a trial conducted in subjects aged 4 to 11 years.

the plasma samples from subjects randomized to placebo. Efficacy in subjects aged 4 to 11 years is extrapolated from adult data with FLOVENT HFA and other supporting data *[see Use in Specific Populations (8.4)]*.

16 HOW SUPPLIED/STORAGE AND HANDLING

FLOVENT HFA 44 mcg Inhalation Aerosol is supplied in 10.6-g pressurized aluminum canisters containing 120 metered actuations in boxes of 1 (NDC 0173-0718-20).

FLOVENT HFA 110 mcg Inhalation Aerosol is supplied in 12-g pressurized aluminum canisters containing 120 metered actuations in boxes of 1 (NDC 0173-0719-20).

FLOVENT HFA 220 mcg Inhalation Aerosol is supplied in 12-g pressurized aluminum canisters containing 120 metered actuations in boxes of 1 (NDC 0173-0720-20).

Each canister is fitted with a counter and supplied with a dark orange actuator with a peach strapcap. Each inhaler is packaged with a Patient Information leaflet.

The dark orange actuator supplied with FLOVENT HFA should not be used with any other product canisters, and actuators from other products should not be used with a FLOVENT HFA canister.

The correct amount of medication in each actuation cannot be assured after the counter reads 000, even though the canister is not completely empty and will continue to operate. The inhaler should be discarded when the counter reads 000.

Keep out of reach of children. Avoid spraying in eyes.

Contents Under Pressure: Do not puncture. Do not use or store near heat or open flame. Exposure to temperatures above 120°F may cause bursting. Never throw canister into fire or incinerator.

Store at room temperature between 68°F and 77°F (20°C and 25°C; excursions permitted from 59°F to 86°F (15°C to 30°C) [See USP Controlled Room Temperature]. Store the inhaler with the mouthpiece down. For best results, the inhaler should be at room temperature before use. SHAKE WELL BEFORE EACH SPRAY.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Local Effects: Inform patients that localized infections with *Candida albicans* occurred in the mouth and pharynx in some patients. If oropharyngeal candidiasis develops, treat it with appropriate local or systemic (i.e., oral) antifungal therapy while still continuing therapy with FLOVENT HFA, but at times therapy with FLOVENT HFA may need to be temporarily interrupted under close medical supervision. Advise patients to rinse the mouth with water without swallowing after inhalation to help reduce the risk of thrush.

Status Asthmaticus and Acute Asthma Symptoms: Inform patients that FLOVENT HFA is not a bronchodilator and is not intended for use as rescue medicine for acute asthma exacerbations. Advise patients to treat acute asthma symptoms with an inhaled, short-acting beta$_2$-agonist such as albuterol. Instruct patients to contact their physicians immediately if there

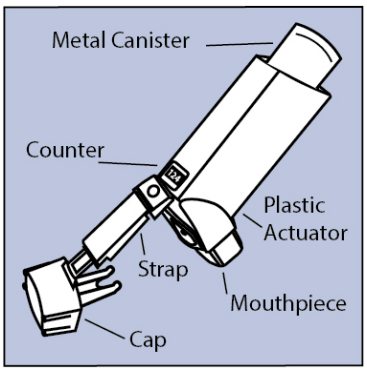

Figure A

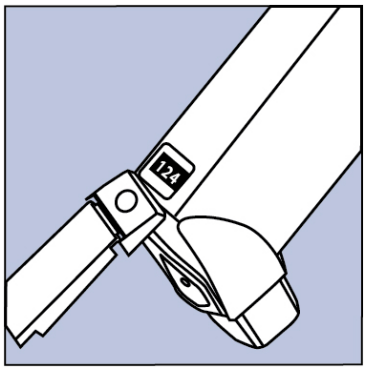

Figure B

- The metal canister holds the medicine. **See Figure A.**
- The canister has a counter to show how many sprays of medicine you have left. The number shows through a window in the back of the actuator. **See Figure B.**
- The counter starts at **124**. The number will count down by 1 each time you spray the inhaler. The counter will stop counting at **000**.
- **Do not try to change the numbers or take the counter off the metal canister.** The counter cannot be reset, and it is permanently attached to the canister.
- The dark orange plastic actuator sprays the medicine from the canister. The actuator has a protective cap that covers the mouthpiece. **See Figure A.** Keep the protective cap on the mouthpiece when the canister is not in use. The strap keeps the cap attached to the actuator.
- **Do not** use the actuator with a canister of medicine from any other inhaler.
- **Do not** use a FLOVENT HFA canister with an actuator from any other inhaler.

Before using your FLOVENT HFA inhaler

- The inhaler should be at room temperature before you use it.
- If a child needs help using the inhaler, an adult should help the child use the inhaler with or without a valved holding chamber, which may also be attached to a mask. The adult should follow the instructions that came with the valved holding chamber. An adult should watch a child use the inhaler to be sure it is used correctly.

Priming your FLOVENT HFA inhaler

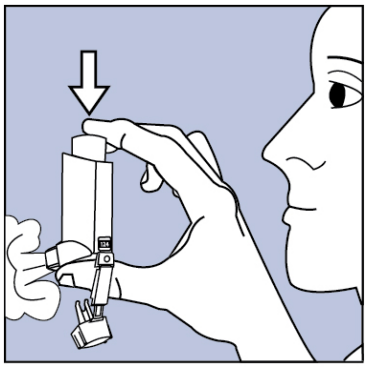

Figure C

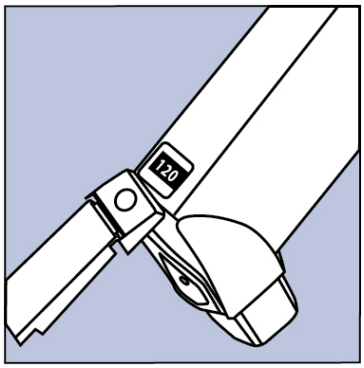

Figure D

- **Before you use FLOVENT HFA for the first time, you must prime the inhaler so that you will get the right amount of medicine when you use it.**
- To prime the inhaler, take the cap off the mouthpiece and shake the inhaler well for 5 seconds. Then spray the inhaler 1 time into the air away from your face. **See Figure C. Avoid spraying in eyes.**
- Shake and spray the inhaler like this 3 more times to finish priming it. The counter should now read **120**. **See Figure D.**
- You must prime your inhaler again if you have not used it in more than 7 days or if you drop it. Take the cap off the mouthpiece and shake the inhaler well for 5 seconds. Then spray it 1 time into the air away from your face.

How to use your FLOVENT HFA inhaler

Follow these steps every time you use FLOVENT HFA.

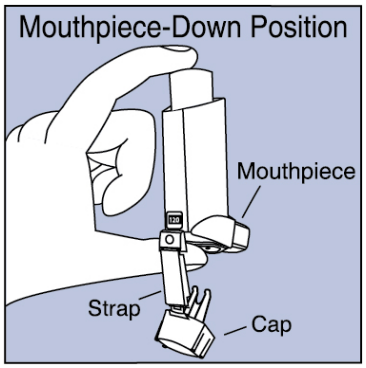

Figure E

Step 1. Make sure the canister fits firmly in the actuator. The counter should show through the window in the actuator.

Shake the inhaler well for 5 seconds before each spray.

Take the cap off the mouthpiece of the actuator. Look inside the mouthpiece for foreign objects, and take out any you see.

Step 2. Hold the inhaler with the mouthpiece down. **See Figure E.**

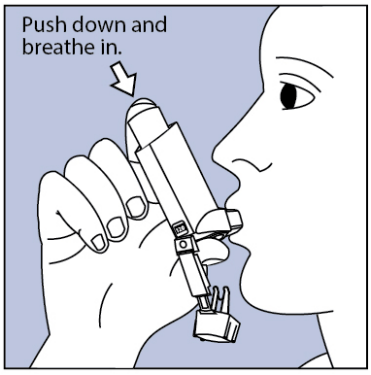

Figure F

Figure G

Step 3. Breathe out through your mouth and push as much air from your lungs as you can. Put the mouthpiece in your mouth and close your lips around it. **See Figure F.**

Step 4. Push the top of the canister **all the way down** while you breathe in deeply and slowly through your mouth. **See Figure F.**

Step 5. After the spray comes out, take your finger off the canister. After you have breathed in all the way, take the inhaler out of your mouth and close your mouth.

Step 6. **Hold your breath for about 10 seconds,** or for as long as is comfortable. **Breathe out slowly as long as you can.**

Wait about 30 seconds and shake the inhaler well for 5 seconds. Repeat steps 2 through 6.

Step 7. **Rinse your mouth with water after breathing in the medicine.** Spit out the water. Do not swallow it. **See Figure G.**

Step 8. Put the cap back on the mouthpiece after every time you use the inhaler. Make sure it snaps firmly into place.

Cleaning your FLOVENT HFA inhaler

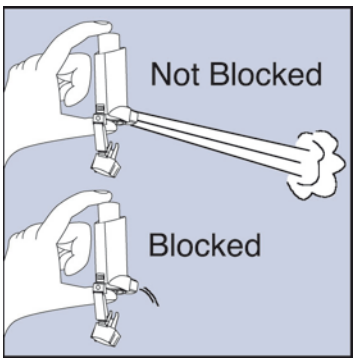

Figure H

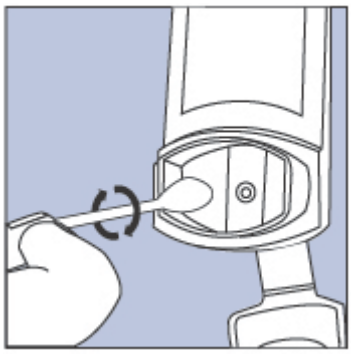

Figure I

Clean your inhaler at least 1 time each week after your evening dose. You may not see any medicine build-up on the inhaler, but it is important to keep it clean so medicine build-up will not block the spray. **See Figure H.**

Step 9. Take the cap off the mouthpiece. The strap on the cap will stay attached to the actuator. Do not take the canister out of the plastic actuator.

Step 10. Use a clean cotton swab dampened with water to clean the small circular opening where the medicine sprays out of the canister. Gently twist the swab in a circular motion to take off any medicine. **See Figure I.** Repeat with a new swab dampened with water to take off any medicine still at the opening.

Step 11. Wipe the inside of the mouthpiece with a clean tissue dampened with water. Let the actuator air-dry overnight.

Step 12. Put the cap back on the mouthpiece after the actuator has dried.

Replacing your FLOVENT HFA inhaler

- **When the counter reads 020**, you should refill your prescription or ask your healthcare provider if you need another prescription for FLOVENT HFA.
- **When the counter reads 000, throw the inhaler away.** You should not keep using the inhaler when the counter reads **000** because you may not receive the right amount of medicine.
- **Do not use the inhaler** after the expiration date, which is on the packaging it comes in.

For correct use of your FLOVENT HFA inhaler, remember:

- The canister should always fit firmly in the actuator.
- Breathe in deeply and slowly to make sure you get all the medicine.
- Hold your breath for about 10 seconds after breathing in the medicine. Then breathe out fully.
- After each dose, rinse your mouth with water and spit it out. **Do not** swallow the water.
- **Do not** take the inhaler apart.
- Always keep the protective cap on the mouthpiece when your inhaler is not in use.
- Always store your inhaler with the mouthpiece pointing down.
- Clean your inhaler at least 1 time each week.

If you have questions about FLOVENT HFA or how to use your inhaler, call GlaxoSmithKline (GSK) at 1-888-825-5249 or visit www.flovent.com.

This Patient Information and Instructions for Use have been approved by the U.S. Food and Drug Administration.

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GlaxoSmithKline
Research Triangle Park, NC 27709

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