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Advair HFA

(Salmeterol, Fluticasone Propionate) - GlaxoSmithKline

BOXED WARNING

Long-acting β_2-adrenergic agonists (LABA), such as salmeterol, increase the risk of asthma-related death. LABA may increase the risk of asthma-related hospitalization in pediatrics and adolescents. Use only for patients not adequately controlled on a long-term asthma control medication (eg, inhaled corticosteroid) or whose disease severity clearly warrants initiation of treatment with both an inhaled corticosteroid and LABA. Do not use if asthma is adequately controlled on low- or medium-dose inhaled corticosteroids.

THERAPEUTIC CLASS

Beta$_2$-agonist/corticosteroid

DEA CLASS

RX

INDICATIONS

Treatment of asthma in patients ≥12 yrs of age.

ADULT DOSAGE

Adults: Initial: Based upon asthma severity. Usual: 2 inh bid (am and pm, q12h). May replace current strength with a higher strength if response to initial dose after 2 weeks is inadequate. Max: 2 inh of 230/21 bid. Elderly: Start at lower end of dosing range.

PEDIATRIC DOSAGE

Pediatrics: ≥12 Yrs: Initial: Based upon asthma severity. Usual: 2 inh bid (am and pm, q12h). May replace current strength with a higher strength if response to initial dose after 2 weeks is inadequate. Max: 2 inh of 230/21 bid.

HOW SUPPLIED

MDI: (Fluticasone Propionate-Salmeterol) (45/21) 45mcg-21mcg/inh, (115/21) 115mcg-21mcg/inh, (230/21) 230mcg-21mcg/inh [60, 120 inhalations]

CONTRAINDICATIONS

Primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required.

WARNINGS/PRECAUTIONS

Do not initiate during rapidly deteriorating or potentially life-threatening episodes of asthma; serious acute respiratory events, including fatalities, reported. Do not use for the relief of acute symptoms; use inhaled short-acting β_2-agonists (SABA). D/C regular use of oral/inhaled SABA when beginning treatment. Do not use more often or at higher doses than recommended; clinically significant cardiovascular (CV) effects and fatalities reported with excessive use. *Candida albicans* infections of mouth and pharynx reported; treat and if needed, interrupt therapy. Lower respiratory tract infections (eg, pneumonia) reported in patients with chronic obstructive pulmonary disease (COPD). Increased susceptibility to infections. May lead to serious/fatal course of chickenpox or measles; avoid exposure and if exposed, consider prophylaxis/treatment. Caution in patients with active/quiescent tuberculosis (TB), untreated systemic fungal, bacterial, viral, or parasitic infections, or ocular herpes simplex. Deaths due to adrenal insufficiency reported during and after transfer from systemic to inhaled corticosteroids. Resume oral corticosteroids during periods of stress or a severe asthma attack in patients previously withdrawn from systemic corticosteroids. Wean slowly from systemic corticosteroid use after transferring to therapy. Transferring from systemic to inhaled corticosteroid may unmask conditions previously suppressed by systemic therapy (eg, rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions). Monitor for systemic corticosteroid effects. Reduce dose slowly if hypercorticism and adrenal suppression appear. May produce paradoxical bronchospasm; treat immediately, d/c therapy, and institute alternative therapy. Upper airway symptoms reported. Immediate hypersensitivity reactions may occur. CV and CNS effects may occur. Caution with CV disorders. Decreases in bone mineral density (BMD) reported with long-term use; caution with major risk factors for decreased bone mineral content, including chronic use of drugs that can reduce bone mass (eg, anticonvulsants, corticosteroids). May reduce growth velocity in pediatrics; monitor growth routinely. Glaucoma, increased intraocular pressure (IOP), and cataracts reported with long-term use. Systemic eosinophilic conditions (eg, Churg-Strauss syndrome) may occur. Caution with convulsive disorders or thyrotoxicosis, diabetes mellitus (DM), ketoacidosis, hepatic disease, in patients unusually responsive to sympathomimetic amines, and elderly. Clinically significant changes in blood glucose and/or serum K^+ reported.

ADVERSE REACTIONS

Upper respiratory tract infection, headache, throat irritation, musculoskeletal pain, N/V, dizziness, viral GI/respiratory infection, hoarseness/dysphonia, GI signs and symptoms, upper respiratory inflammation.

DRUG INTERACTIONS

Do not use with other medications containing LABA. Not recommended with strong CYP3A4 inhibitors (eg, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin); increased systemic corticosteroid and increased CV

adverse effects may occur. Extreme caution with TCAs or MAOIs, or within 2 weeks of discontinuing of such agents; action on the vascular system may be potentiated by these agents. β-blockers may block pulmonary effects and produce severe bronchospasm in patients with reversible obstructive airways disease; if such therapy is needed, consider cardioselective β-blockers and use them with caution. ECG changes and/or hypokalemia that may result from non-K^+-sparing diuretics (eg, loop or thiazide diuretics) may be acutely worsened; use with caution.

PREGNANCY
Category C, caution in nursing.

MECHANISM OF ACTION
Fluticasone: Corticosteroid; shown to inhibit multiple cell types (eg, mast cells, eosinophils, basophils, lymphocytes, macrophages, neutrophils) and mediator production or secretion (eg, histamine, eicosanoids, leukotrienes, cytokines) involved in the asthmatic response. Salmeterol: LABA; attributable to stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of ATP to cAMP. Increased cAMP levels cause relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

PHARMACOKINETICS
Absorption: Fluticasone: Absolute bioavailability (5.3%); AUC=274pg•hr/mL; C_{max}=41pg/mL (45/21), 108pg/mL (115/21), 173pg/mL (230/21); T_{max}=0.33-1.5 hrs. Salmeterol: AUC=53pg•hr/mL; C_{max}=220-470pg/mL; T_{max}=5-10 min. **Distribution:** Fluticasone: (IV) V_d=4.2L/kg; plasma protein binding (99%). Salmeterol: Plasma protein binding (96%). **Metabolism:** Fluticasone: 17β-carboxylic acid via CYP3A4. Salmeterol: Extensive by hydroxylation; α-hydroxysalmeterol via CYP3A4. **Elimination:** Fluticasone: Urine (<5%, metabolites), feces; $T_{1/2}$=5.6 hrs. Salmeterol: Feces (60%), urine (25%); $T_{1/2}$=5.5 hrs.

ASSESSMENT
Assess for status asthmaticus, acute asthma episodes, rapidly deteriorating asthma, COPD, active/quiescent TB, untreated systemic infections, ocular herpes simplex, CV disorders, risk factors for decreased bone mineral content, history of increased IOP, glaucoma, and/or cataracts, convulsive disorders, thyrotoxicosis, DM, ketoacidosis, hepatic disease, drug hypersensitivity, pregnancy/nursing status, and possible drug interactions. Assess use in patients unusually responsive to sympathomimetic amines.

MONITORING
Monitor for localized oral *C. albicans* infections, lower respiratory tract infections, deteriorating asthma, hypercorticism, adrenal suppression, paradoxical bronchospasm, upper airway symptoms, hypersensitivity reactions, CV/CNS effects, glaucoma, cataracts, IOP, eosinophilic conditions, and other adverse reactions. Monitor growth in pediatrics, BMD, blood glucose, and serum K^+ levels.

PATIENT COUNSELING
Inform about increased risk of asthma-related hospitalization in pediatric/adolescent patients and asthma-related death. Advise not to use to relieve acute asthma symptoms, and, if symptoms arise in the period between doses, to use an inhaled SABA for immediate relief. Instruct to seek medical attention immediately if experiencing a decrease in effectiveness of inhaled SABA, a need for more inhalations than usual of inhaled SABA, or a significant decrease in lung function. Advise not to d/c therapy without physician's guidance and not to use additional LABA. Instruct to contact physician if oropharyngeal candidiasis or symptoms of pneumonia develop. Advise to avoid exposure to chickenpox or measles, and, if exposed, to consult physician without delay. Inform about risk of immunosuppression, hypercorticism and adrenal suppression, reduction in BMD, reduced growth velocity in pediatrics, ocular effects, and of adverse effects such as palpitations, chest pain, rapid HR, tremor, or nervousness.

ADMINISTRATION/STORAGE
Administration: Oral inhalation route. After inhalation, rinse mouth with water without swallowing. Shake well for 5 sec before using. Refer to PI for priming and administration instructions. **Storage:** 25°C (77°F); excursions permitted to 15-30°C (59-86°F). Store with the mouthpiece down. Do not puncture, use/store near heat or open flame, or throw container into fire/incinerator. Discard when the counter reads "000."