FDA Alert for Healthcare Professionals

Formoterol fumarate inhalation powder (marketed as Foradil Aerolizer)

7/2006: The issues described in this alert have been addressed in product labeling.

FDA ALERT [11/2005]: Long-acting beta$_2$-adrenergic agonists, such as formoterol, the active ingredient in Foradil Aerolizer, have been associated with an increased risk of serious asthma exacerbations and asthma-related death. FDA has requested that the package insert (labeling) for Foradil Aerolizer be revised to provide more information about this possible increased risk. FDA has also requested that a Medication Guide (FDA-approved patient information) containing information about these risks for patients and caregivers be dispensed with each prescription. FDA advises that, in the treatment of asthma, Foradil Aerolizer should only be used as additional therapy in patients who have not adequately responded to other asthma-controller medications, such as low-to-medium dose inhaled corticosteroids.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

Recommendations

Physicians with asthma patients using Foradil Aerolizer, or who are considering prescribing the drug for asthma, should consider the following:

- Foradil Aerolizer should not be the first medicine prescribed to treat a patient's asthma.
- Use Foradil Aerolizer only for patients who have not adequately responded to other asthma-controller medications, such as inhaled corticosteroids. The National Heart, Lung, and Blood Institute (NHLBI) and World Health Organization (WHO) guidelines recommend inhaled corticosteroids as the first step in controller therapy, with long-acting beta$_2$-agonists as an option if low-to-medium dose inhaled corticosteroids do not adequately control the patient's asthma.
- Advise patients to seek medical treatment immediately if their asthma worsens.

Data Summary

No study adequate to determine whether the rate or relative risk of asthma-related death is increased with Foradil Aerolizer has been conducted, but smaller clinical studies with Foradil Aerolizer have suggested a higher incidence of serious worsening of asthma in patients who received Foradil Aerolizer compared to placebo.

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In two, 12-week controlled trials with combined enrollment of 1095 patients with asthma 12 years of age and older, low and high dose Foradil Aerolizer were compared with albuterol and placebo. Serious asthma exacerbations (acute worsening of asthma resulting in hospitalization) occurred more commonly in the higher dose Foradil Aerolizer group.

NUMBER AND FREQUENCY OF SERIOUS ASTHMA EXACERBATIONS IN PATIENTS 12 YEARS OF AGE AND OLDER FROM TWO 12-WEEK CONTROLLED CLINICAL TRIALS

	Foradil 12 mcg twice daily	Foradil 24 mcg twice daily	Albuterol 180 mcg four times daily	Placebo
		Trial #1		
Serious asthma exacerbations	0/136 (0)	4/135 (3.0%)[1]	2/134 (1.5%)	0/136 (0)
		Trial #2		
Serious asthma exacerbations	1/139 (0.7%)	5/136 (3.7%)[2]	0/138 (0)	2/141 (1.4%)

[1]1 patient required intubation
[2]2 patients had respiratory arrest; 1 of the patients died

In a 16-week, randomized, multi-center, double-blind, parallel-group trial of 1568 patients, Foradil Aerolizer at the low and high doses was compared with placebo. Again, serious asthma exacerbations occurred more commonly in the higher dose Foradil Aerolizer group.

NUMBER AND FREQUENCY OF SERIOUS ASTHMA EXACERBATIONS IN PATIENTS 12 YEARS OF AGE AND OLDER FROM A 16-WEEK TRIAL

	Foradil 12 mcg twice daily	Foradil 24 mcg twice daily	Placebo
Serious asthma exacerbations	3/527 (0.6%)	2/527 (0.4%)	1/514 (0.2%)

The Salmeterol Multi-center Asthma Research Trial (SMART) was a large, placebo-controlled US study that compared the safety of another long-acting beta$_2$-adrenergic agonist, salmeterol (Serevent Inhalation Aerosol, 42 mcg twice daily over 28 weeks), or placebo added to usual asthma therapy. A planned interim analysis showed an increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks) versus those on placebo (3deaths out of 13,179 patients).