

Please read the FORADIL AEROLIZER Prescribing Information, including the Boxed Warning about asthma-related death.

Recent Safety-Related Labeling Updates to Prescribing Information and Medication Guide for FORADIL[®] AEROLIZER[®] (formoterol fumarate inhalation powder) in the treatment of asthma and prevention of bronchospasm in patients 5 years of age and older.

Dear Pharmacy Colleagues,

The purpose of this letter is to inform you of recent safety-related labeling updates to the Prescribing Information and Medication Guide for FORADIL AEROLIZER in the treatment of asthma and prevention of bronchospasm in patients 5 years of age and older. As described by U.S. Food and Drug Administration (FDA) in a drug-safety communication posted on the FDA website on June 2, 2010, safety labeling changes will be made to the Prescribing Information and Medication Guides of all Long-Acting Beta Agonists (LABAs) used in the treatment of asthma, like FORADIL, as well as to the Prescribing Information and Medication Guides of all LABA-containing products. These safety labeling changes pertain to the use of FORADIL in the treatment of asthma and prevention of bronchospasm only. No changes were made to the labeling of FORADIL for use in patients with chronic obstructive pulmonary disease (COPD).

The Prescribing Information and Medication Guide for FORADIL have been updated to reflect the following recommendations from the FDA:

- Use of a LABA alone without use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated (absolutely advised against) in the treatment of asthma.
- LABAs should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.
- LABAs should only be used as additional therapy for patients with asthma who are currently taking but are not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid.
- Once asthma control is achieved and maintained, patients should be assessed at regular intervals and step down therapy should begin (e.g., discontinue LABA), if possible without loss of asthma control, and the patient should continue to be treated with a long-term asthma control medication, such as an inhaled corticosteroid.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure adherence with both medications.

FDA has stated its belief that when LABAs are used according to the recommendations outlined above and in the approved drug labels, the benefits of LABAs in improving asthma symptoms outweigh their risks of increasing severe asthma exacerbations and deaths from asthma.

The safety of patients is a primary concern at Merck. Together with Novartis Pharmaceuticals Corporation, who has granted exclusive marketing and distribution rights to FORADIL in the US to Merck, we have worked with the FDA to update the Prescribing Information and Medication Guide for FORADIL to ensure appropriate use of the medicine, including updating language in the "Boxed Warnings" section of the Prescribing Information. In addition, revisions to the Indications and Usage, Contraindications, Warnings, Precautions/Information for Patients, Pediatric Use for Asthma, Adverse Reactions, and Dosage and Administration have also been made as part of the updates to the Prescribing Information along with changes to the Medication Guide that is issued to patients who have been prescribed FORADIL.

Please see the accompanying updated Prescribing Information and Medication Guide.

Additional directional information provided by FDA for Healthcare Professionals includes the following:

- Long-Acting Beta Agonists (LABAs) should not be started in patients with acutely deteriorating asthma.
- Discuss with patients and families the warning signs of worsening asthma and advise them to seek immediate medical attention should their condition deteriorate.
- LABAs do not relieve sudden-onset asthma symptoms. A rescue inhaler, such as an albuterol inhaler, should be prescribed to treat sudden asthma symptoms.
- Encourage patients, families, and caregivers to read the Medication Guide that accompanies LABA prescriptions.
- In pediatric and adolescent patients who need the addition of a LABA to an inhaled corticosteroid, prescribe a combination inhaled corticosteroid – LABA product. Using a combination product will help ensure adherence with both of these medications.

Merck remains confident in the efficacy and safety of FORADIL in the treatment of asthma when used in accordance with the prescribing information. We are committed to helping ensure that healthcare providers and patients have the most accurate and complete information regarding the safe and appropriate use of FORADIL. We will continue communicating with patients, caregivers and healthcare providers about FORADIL in ways that will help inform their decisions about appropriate treatment choices.

Patients or caregivers should talk with their healthcare providers if they have any questions about the appropriate use of FORADIL. Patients currently being treated with FORADIL should not make any changes to their current treatment regimen, except as directed by their healthcare provider.

INFORMATION ABOUT FORADIL[®] AEROLIZER[®] (formoterol fumarate inhalation powder)

Asthma Indication

FORADIL AEROLIZER is indicated for the treatment of asthma and in the prevention of bronchospasm only as concomitant therapy with a long-term asthma control medication, such as

an inhaled corticosteroid, in adults and children 5 years of age and older with reversible obstructive airways disease, including patients with symptoms of nocturnal asthma.

Long-acting β_2 -agonists (LABAs), such as formoterol, the active ingredient in FORADIL AEROLIZER, increase the risk of asthma-related death (see WARNINGS). Use of FORADIL AEROLIZER for the treatment of asthma without concomitant use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated. Use FORADIL AEROLIZER only as additional therapy for patients with asthma who are currently taking but are inadequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid.

Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (eg, discontinue FORADIL AEROLIZER) if possible without loss of asthma control, and maintain the patient on a long-term asthma control medication, such as an inhaled corticosteroid. Do not use FORADIL AEROLIZER for patients whose asthma is adequately controlled on low- or medium-dose inhaled corticosteroids.

Pediatric and Adolescent Patients

Available data from controlled clinical trials suggest that LABAs increase the risk of asthma-related hospitalization in pediatric and adolescent patients (see WARNINGS). For pediatric and adolescent patients with asthma who require addition of a LABA to an inhaled corticosteroid, a fixed-dose combination product containing both an inhaled corticosteroid and a LABA should ordinarily be used to ensure adherence with both drugs. In cases where use of a separate long-term asthma control medication (eg, inhaled corticosteroid) and a LABA is clinically indicated, appropriate steps must be taken to ensure adherence with both treatment components. If adherence cannot be assured, a fixed-dose combination product containing both an inhaled corticosteroid and a LABA is recommended.

Exercise-Induced Bronchospasm

FORADIL AEROLIZER is also indicated for the acute prevention of exercise-induced bronchospasm (EIB) in adults and children 5 years of age and older, when administered on an occasional, as-needed basis. Use of FORADIL AEROLIZER as a single agent for the prevention of exercise-induced bronchospasm may be clinically indicated in patients who do not have persistent asthma. In patients with persistent asthma, use of FORADIL AEROLIZER for the prevention of exercise-induced bronchospasm may be clinically indicated, but the treatment of asthma should include a long-term asthma control medication, such as an inhaled corticosteroid.

FORADIL capsules should be administered only by the oral inhalation route using only the AEROLIZER inhaler. The recommended total daily dose of FORADIL AEROLIZER should not exceed 24 mcg (1 capsule twice daily).

COPD Indication

FORADIL AEROLIZER is indicated for long-term, twice-daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with COPD including chronic bronchitis and emphysema.

FORADIL capsules should be administered only by the oral inhalation route using only the AEROLIZER inhaler. The recommended total daily dose of FORADIL[®] AEROLIZER[®] (formoterol fumarate inhalation powder) should not exceed 24 mcg (1 capsule twice daily).

SELECTED SAFETY INFORMATION ABOUT FORADIL AEROLIZER IN THE TREATMENT OF ASTHMA

WARNING: ASTHMA RELATED DEATH

Long-acting β_2 -agonists (LABAs), such as formoterol, the active ingredient in FORADIL[®] AEROLIZER[®] (formoterol fumarate inhalation powder) increase the risk of asthma-related death. Data from a large placebo-controlled US study that compared the safety of another LABA (salmeterol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of LABAs, including formoterol (see WARNINGS). Currently available data are inadequate to determine whether concurrent use of inhaled corticosteroids or other long-term asthma control drugs mitigates the increased risk of asthma-related death from LABA.

Because of this risk, use of FORADIL AEROLIZER for the treatment of asthma without a concomitant long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated. Use FORADIL AEROLIZER only as additional therapy for patients with asthma who are currently taking but are inadequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (eg, discontinue FORADIL AEROLIZER) if possible without loss of asthma control, and maintain the patient on a long-term asthma control medication, such as an inhaled corticosteroid. Do not use FORADIL AEROLIZER for patients whose asthma is adequately controlled on low- or medium-dose inhaled corticosteroids.

Pediatric and Adolescent Patients

Available data from controlled clinical trials suggest that LABA increase the risk of asthma-related hospitalization in pediatric and adolescent patients. For pediatric and adolescent patients with asthma who require addition of a LABA to an inhaled corticosteroid, a fixed-dose combination product containing both an inhaled corticosteroid and a LABA should ordinarily be considered to ensure adherence with both drugs. In cases where use of a separate long-term asthma control medication (eg, inhaled corticosteroid) and a LABA is clinically indicated, appropriate steps must be taken to ensure adherence with both treatment components. If adherence cannot be assured, a fixed-dose combination product containing both an inhaled corticosteroid and a LABA is recommended.

Because of the risk of asthma-related death and hospitalization, use of FORADIL AEROLIZER for the treatment of asthma without concomitant use of a long-term asthma control medication, such as an inhaled corticosteroid, is contraindicated (see Warnings-Asthma Related Death).

FORADIL AEROLIZER should not be used to treat acute asthma symptoms or used more than twice daily.

FORADIL AEROLIZER should be used with caution in patients with cardiovascular disorders.

Adverse reactions with FORADIL AEROLIZER are similar to other selective long-acting β_2 -agonists; eg, angina, hypertension or hypotension, tachycardia, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, metabolic acidosis, and insomnia.

In asthma clinical trials, the most common adverse events for FORADIL AEROLIZER and placebo groups were viral infection, bronchitis, and chest infection. Other adverse events greater than or equal to 1% for FORADIL AEROLIZER and placebo, respectively, included dyspnea (2.1% vs 1.7%), chest pain (1.9% vs 1.3%), tremor (1.9% vs 0.4%), dizziness (1.6% vs 1.5%), insomnia (1.5% vs 0.8%), tonsillitis (1.2% vs 0.7%), rash (1.1% vs 0.7%), and dysphonia (1.0% vs 0.9%).

FORADIL capsules should only be inhaled orally using the AEROLIZER inhaler. The capsules should not be swallowed.

SELECTED SAFETY INFORMATION ABOUT FORADIL AEROLIZER IN THE TREATMENT OF COPD

The safety labeling for the use of FORADIL in COPD patients has not changed.

FORADIL AEROLIZER should be used with caution in patients with cardiovascular disorders.

Adverse reactions with FORADIL AEROLIZER are similar to other selective long-acting β_2 -agonists; eg, angina, hypertension or hypotension, tachycardia, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, muscle cramps, nausea, dizziness, fatigue, malaise, hypokalemia, hyperglycemia, metabolic acidosis, and insomnia.

In COPD trials, the most common adverse events reported with FORADIL AEROLIZER and placebo groups, respectively, were upper respiratory infection (7.4% vs 5.7%), back pain (4.2% vs 4.0%), and pharyngitis (3.5% vs 2.4%).

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please read the FORADIL[®] AEROLIZER[®] (formoterol fumarate inhalation powder) Prescribing Information, including the Boxed Warning about asthma-related death.

Sincerely,



Julie Gerhart
Merck & Co., Inc.