FDA Safety Update: Asthma Medications

Asthma is a chronic, life-threatening disease that causes the airways to become inflamed or swollen. When people with asthma react to various triggers, such as upper respiratory infections, dust, pollen, or smoke, their airways become narrow. This can cause difficulty breathing, wheezing, chest tightness, or coughing. The two main types of asthma drugs are quick-relief medications that immediately treat sudden symptoms and long-term control medications that are taken regularly to prevent symptoms.

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Here is a Food and Drug Administration (FDA) update on recent safety issues with asthma medications.

INCORRECT USE OF FORADIL AEROLIZER

In February 2008, FDA issued a Public Health Advisory to highlight the correct use of Foradil capsules. Foradil Aerolizer (formoterol fumarate inhalation powder) is approved to prevent wheezing and breathing problems caused by asthma and chronic obstructive pulmonary disease (COPD).

The medication in Foradil capsules is specifically designed to be inhaled through the Foradil Aerolizer inhalation device to deliver the medicine to the lungs. FDA and the American Association of Poison Control Center's National Poison Data System have received reports of people swallowing the capsules rather than placing them in the inhalation device.

Few patients have experienced side effects from swallowing the capsules. But the medication won't work if the capsules are swallowed rather than inhaled. FDA's Public Health Advisory on Foradil also addresses similar incorrect use of Spiriva HandiHaler (tiotropium) capsules, which is approved by FDA to treat COPD.

Advice for patients ...

Patients should not swallow the Foradil or Spiriva capsules as the capsules are only to be used with the inhalation device provided with the product. Patients should follow the instructions in the patient information leaflet provided with the product.

The Public Health Advisory: Important Information on the Correct Use of Spiriva and Foradil Capsules, may be found at: *www.fda.gov/cder/drug/advisory/tiopropium_formoterol.htm*

SUICIDALITY AND BEHAVIOR/MOOD CHANGES WITH SINGULAIR

Singulair (montelukast sodium) is approved to treat asthma and symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of nose), and to prevent exercise-induced asthma. Singulair is part of a class of "anti-leukotriene" drugs. These drugs act by blocking the activity of leukotrienes, chemicals that are involved in airway inflammation.

In the past year, Merck & Company, Inc. has updated the patient information for Singulair to include these postmarketing adverse events: tremor, depression, suicidal thinking and behavior (including suicide), and anxiousness.

In March 2008, FDA issued an early communication about an ongoing safety review of Singulair. The agency is investigating a possible association between the use of Singulair and behavior/mood changes, suicidal thinking and behavior, and suicide.

Early communications are in keeping with FDA's commitment to inform the public about its ongoing safety reviews of drugs. An early communication does not mean that FDA has concluded that there is a causal relationship between the drug and the emerging safety issue. It means that FDA is considering the information but has not yet reached a conclusion.

FDA is working with Merck to perform a complex analysis of Singulair data and will communicate the conclusions and recommendations to the public. The agency is also reviewing postmarketing reports it has received of behavior/mood changes, suicidal thinking, and suicide in patients who have taken Singulair as well as other leukotriene modifying medications, such as Accolate (zafirlukast) and Zyflo (zileuton) and Zyflo CR.

Advice for patients ...

Patients should not stop taking these medications before talking to their health care professional about this information. FDA urges patients to report side effects from use of these medications to FDA's MedWatch Adverse Event Reporting Program at: *www.fda.gov/medwatch/report/consumer/consumer.htm*

The Early Communication About an Ongoing Safety Review of Montelukast (Singulair) may be found at: *www.fda.gov/cder/drug/early_comm/montelukast.htm*

SAFETY OF LONG-ACTING BETA AGONISTS (LABAs)

Bronchodilators are medications that help open up the breathing tubes, but they do not treat the underlying inflammation of asthma. Short-acting bronchodilators are quick-relief medications used for treatment of asthma symptoms. One example is Albuterol. Long-acting beta2 adrenergic agonists (LABAs) are bronchodilators used to provide long-term control of asthma. Examples of medications that contain LABAs and that are approved for use in asthma patients include Advair Diskus (fluticasone propionate; salmeterol xinafoate), Symbicort (budesonide; formoterol fumarate dihydrate), Serevent Diskus (salmeterol xinafoate), and Foradil.

In 2005, FDA issued a Public Health Advisory that alerted health care professionals and patients that LABA medicines may increase the chance of severe asthma episodes and death when the episodes occur. In this advisory, FDA highlighted several recommendations about LABA drugs. For example, LABAs should not be the first medicine used to treat asthma.

In 2006, the manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus updated product labels with these warnings. Since that time, several additional products containing LABAs have been approved, including Symbicort, Perforomist (formoterol fumarate), and Brovana (arformoterol tartrate). The labels for these products contain similar warnings regarding severe asthma episodes and death.

At a November 2007 Pediatric Advisory Committee meeting, FDA raised concerns about the safety of LABAs in children with asthma. In January 2008, FDA requested manufacturers of Advair Diskus, Advair HFA, Brovana Inhalation Solution, Foradil Aerolizer, Perforomist Inhalation Solution, Serevent Diskus, and Symbicort Inhalation Aerosol to provide information regarding controlled clinical studies conducted with these products to further evaluate their safety. Following the analysis of this data, FDA plans to discuss the benefit and risk of LABAs at a public advisory committee meeting later this year.

Advice for patients ...

Patients should understand the risks of LABAs and talk with their health care professional about their concerns.

The FDA Public Health Advisory: Advair Diskus, Advair HFA, Brovana, Foradil, Perforomist, Serevent Diskus, and Symbicort Information, may be found at: *www.fda.gov/cder/drug/infopage/LABA/default.htm*

ANAPHYLAXIS AND XOLAIR

Xolair (omalizumab) is approved for treating moderate to severe persistent asthma related to allergies in patients whose symptoms are not controlled with inhaled corticosteroids. In February 2007, FDA requested that Genentech add a boxed warning to the Xolair product label. The boxed warning emphasizes that Xolair may cause anaphylaxis, an allergic reaction that may include trouble breathing, chest tightness, dizziness, fainting, itching and hives, and swelling of the mouth and throat.

Advice for patients ...

It's important to know that patients may develop this reaction after any dose of Xolair, even if there was no reaction to the first dose. Also, anaphylaxis after administration of Xolair may be delayed up to 24 hours or more after the dose is given.

Patients who take Xolair should know the symptoms of anaphylaxis, and should also know how to initiate emergency self-treatment.

The FDA Health Care Professional Alert: Stronger Warning Proposed for Xolair, may be found at: *www.fda.gov/cder/drug/infopage/omalizumab/default.htm*

For More Information

Albuterol Inhalers: Time to Transition
www.fda.gov/consumer/updates/albuterol053008.html

How is Asthma Treated?
National Heart Lung and Blood Institute
www.nhlbi.nih.gov/health/dci/Diseases/Asthma/Asthma_Treatments.html

A Guide to Drug Safety Terms at FDA
www.fda.gov/consumer/updates/drugterms041108.html