FDA Drug Safety Communication: FDA review finds no significant increase in risk of serious asthma outcomes with long-acting beta agonists (LABAs) used in combination with inhaled corticosteroids (ICS)

This is an update to the FDA Drug Safety Communication: **FDA requires post-market safety trials for Long-Acting Beta-Agonists (LABAs) (/Drugs/DrugSafety/ucm251512.htm)** issued on April 15, 2011.

Safety Announcement

[12-20-2017] A U.S. Food and Drug Administration (FDA) review of four large clinical safety trials shows that treating asthma with long-acting beta agonists (LABAs) in combination with inhaled corticosteroids (ICS) does not result in significantly more serious asthma-related side effects than treatment with ICS alone. In 2011, we required the drug companies that market LABAs to conduct these trials to evaluate the safety of LABAs when used in combination with ICS, and we reviewed the results of these recently completed trials.

Based on our review, the *Boxed Warning*, our most prominent warning, about asthma-related death has been removed from the drug labels of medicines that contain both an ICS and LABA. A description of the four trials is now also included in the *Warnings and Precautions* section of the drug labels. These trials showed that LABAs, when used with ICS, did not significantly increase the risk of asthma-related hospitalizations, the need to insert a breathing tube known as intubation, or asthma-related deaths, compared to ICS alone.

Using LABAs alone to treat asthma without an ICS to treat lung inflammation is associated with an increased risk of asthma-related death. Therefore, the *Boxed Warning* stating this will remain in the labels of all single-ingredient LABA medicines, which are approved to treat asthma, chronic obstructive pulmonary disease (COPD), and wheezing caused by exercise. The labels of medicines that contain both an ICS and LABA also retain a *Warning and Precaution* related to the increased risk of asthma-related death when LABAs are used without an ICS to treat asthma.

Medicines that contain both an ICS and LABA are FDA-approved to treat both asthma and COPD. ICS medicines help decrease inflammation in the lungs. This inflammation can lead to breathing problems. LABAs help the muscles around the airways in the lungs stay relaxed to prevent symptoms such as wheezing, coughing, chest tightness, and shortness of breath. ICS/LABA medicines are marketed under several brand names, including Advair, Airduo, Breo, Dulera, and Symbicort (see Table 1).

Health care professionals should refer to the most recently approved **drug labels (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm)** for recommendations on using ICS/LABA medicines (see links in Table 1). **Patients and parents/caregivers** should talk to your health care professional if you have any questions or concerns. Do not stop taking your asthma medicines without first talking to your health care professional. Also read the patient information leaflet that comes with every prescription.

We evaluated four recently completed clinical trials involving 41,297 patients, three conducted in patients 12 years and older, and one in children 4 to 11 years. Patients in all the trials were treated for 6 months to evaluate serious asthma outcomes including asthma-related death, intubation, or hospitalization. The results of all trials showed that the use of LABA with ICS does not significantly increase the risk of serious asthma outcomes compared to ICS alone. The trials also showed that ICS/LABA combination medicines were more effective in decreasing asthma attacks (e.g., the need to use oral corticosteroids) compared to ICS alone. This additional information has been added to the ICS/LABA labels.

To assure the ongoing evaluation of the safety of all medicines, including LABAs and ICS, we urge patients and health care professionals to report side effects involving LABAs, ICS, or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

Table 1. List of Approved ICS/LABA Combination Medicines

Brand Name	Generic Names
Advair Diskus (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021077)	fluticasone (ICS), salmeterol (LABA)
Advair HFA (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021254)	fluticasone (ICS), salmeterol (LABA)
Airduo Respiclick (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208799)	fluticasone (ICS), salmeterol (LABA)
Breo Ellipta (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=204275)	fluticasone (ICS), vilanterol (LABA)
Dulera (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=022518)	mometasone (ICS), formoterol (LABA)

Symbicort (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=021929)	budesonide (ICS), formoterol (LABA)

Data Summary

Drug Safety Communication (/downloads/Drugs/DrugSafety/UCM589997.pdf) (PDF - 66 KB)

Related Information

- **Long-Acting Beta Agonist (LABA) Information (/Drugs/DrugSafety/InformationbyDrugClass/ucm199565.htm)** Long-Acting Beta Agonists (LABAs) are inhaled medications that are used in the treatment of asthma and chronic obstuctive pulmonary disease (COPD).
- **Drugs@FDA: FDA Approved Drug Products (https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm)**
  Access drug labels by searching the drug name
- **The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective (/Drugs/ResourcesForYou/Consumers/ucm143534.htm)**
- **Think It Through: Managing the Benefits and Risks of Medicines (/Drugs/ResourcesForYou/Consumers/ucm143558.htm)**

Contact FDA

For More Info
855-543-DRUG (3784)
and press 4
druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)

Report a Serious Problem to MedWatch
Complete and submit the report **Online (https://www.accessdata.fda.gov/scripts/medwatch/)**.
Download form (http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

More in Drug Safety and Availability (/Drugs/DrugSafety/default.htm)

Drug Alerts and Statements (/Drugs/DrugSafety/ucm215175.htm)

Medication Guides (/Drugs/DrugSafety/ucm085729.htm)

Drug Safety Communications (/Drugs/DrugSafety/ucm199082.htm)

Drug Shortages (/Drugs/DrugSafety/DrugShortages/default.htm)

Postmarket Drug Safety Information for Patients and Providers (/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm)

Information by Drug Class (/Drugs/DrugSafety/InformationbyDrugClass/default.htm)

Medication Errors (/Drugs/DrugSafety/MedicationErrors/default.htm)

Drug Safety Podcasts (/Drugs/DrugSafety/DrugSafetyPodcasts/default.htm)

Safe Use Initiative (/Drugs/DrugSafety/SafeUseInitiative/default.htm)

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Drug Supply Chain Integrity (/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/default.htm)