

Sample Worstpills.org Subscriber Search ADVAIR

Jump to: [Search Results](#) [Drug Profile](#) [Disease Info](#) [Articles](#) [SUBSCRIBE NOW](#)

This PDF will guide you through a search on worstpills.org. It provides several in-depth pages including a drug profile, disease information, and articles written about ADVAIR.

We have chosen ADVAIR because it is a top-selling drug and chances are high that you have heard of it. The results for each drug vary; most drugs will return information in some, but not all, of the categories listed above. We review over 500 prescription drugs and 13 popular dietary supplements, but we do not claim to review all drugs. You can generate a sample search on any drug before you have purchased a subscription, and we recommend that you search for the drugs you are most interested in before subscribing.




Margin notes explain the layout of search results and offer additional information.

The Search Results Page (complimentary for subscribers and non-subscribers)


After selecting your drug from the search page, you will be presented with a page like the one below (a search for ADVAIR DISKUS), which displays links to any information that pertains to your drug. These links might include:

- A comprehensive drug profile
- Drug e-alerts
- Information about the disease being treated
- Information about similar drugs
- Relevant articles written for worstpills.org

For each result, it will be noted whether your drug is a **primary** or **secondary** subject of discussion.

 **worstpills.org**
your expert, independent source for prescription drug information

Home Search Last Search Recent Postings Glossary Free Drug Information

[ print friendly]

Search Type: drug name
Search Term: fluticasone and salmeterol inhalation powders (ADVAIR DISKUS)

Drug Profiles - A comprehensive review of the safety and effectiveness of this drug. If the drug is not a Do Not Use drug, information on adverse effects, drug interactions and how to use the medication are included.

Search results below include drug profiles where your selected drug is a **primary** subject of discussion

- **fluticasone and salmeterol inhalation powders (ADVAIR DISKUS)**
We list this drug as a Do Not Use drug because it has been associated with an increased death rate and safer alternatives are available.

Disease and Drug Family Information

Search results below include Disease and Drug Family Information where your selected drug is a **primary** subject of discussion

- **Allergy and Hayfever**
If you suffer from an itchy and runny nose, watery eyes, sneezing, and a tickle in the back of your throat, then you probably have an allergy. An allergy means a hypersensitivity to a particular substance called an allergen. Hypersensitivity means that the body's immune system, which defends against infection, disease, and foreign bodies, reacts inappropriately to the allergen. Examples of common allergens are pollen, mold, ragweed, dust, feathers, cat hair, makeup, walnuts, aspirin, shellfish, poison ivy, and chocolate.
- **Asthma, Chronic Bronchitis and Emphysema**

Drug Profiles describe the primary characteristics of a drug and may include similar drugs that share key components.

The disease your drug is approved to treat or the drug family to which it belongs is highlighted in this section. Online subscribers can click on the blue link to access the full article.

Sample Subscriber Search – ADVAIR

Do not try to diagnose or treat yourself. Asthma, chronic bronchitis, and emphysema must be diagnosed and treated by a doctor or other health professional. Two other common conditions that cause breathing difficulties, congestive heart failure and pneumonia, have similar symptoms, and many of the drugs used to treat asthma or COPD may worsen these conditions. Therefore, it is extremely important that you have your condition properly diagnosed before starting any medication.

Worst Pills, Best Pills Newsletter Articles

Search results below include Worst Pills, Best Pills Newsletter Articles where your selected drug is a **primary** subject of discussion

- **DO NOT USE! FDA Relegates ADVAIR and SEREVENT to Last Choice Status for Asthma Treatment**
(May 2006)
ADVAIR DISKUS is not indicated in patients whose asthma can be successfully managed by inhaled corticosteroids along with occasional use of inhaled, short-acting beta2-agonists.
- **Asthma Drugs Salmeterol (SEREVENT), Salmeterol with Fluticasone (ADVAIR), and Formoterol (FORADIL)**
(March 2006)
The Food and Drug Administration requested that additional new safety warnings be added to the professional product labels for the popular asthma drugs salmeterol (SEREVENT), salmeterol with fluticasone (ADVAIR), and formoterol (FORADIL). The new warnings concern the possibility that these drugs may increase the chance of severe asthma attacks and asthma-related death. **DO NOT STOP ANY ASTHMA MEDICATION WITHOUT FIRST CONSULTING YOUR PHYSICIAN. ABRUPTLY STOPPING A MEDICATION MAY RESULT IN ACUTELY DETERIORATING ASTHMA CONTROL.**
- **Asthma Medicines That Can Cause Asthma Attacks: Do Not Use SEREVENT, ADVAIR or FORADIL**
(September 2005)
Do not stop any asthma medication without first consulting your physician. Abruptly stopping a medication may result in acutely deteriorating asthma control. You should not use salmeterol (SEREVENT), the combination of salmeterol with the steroid fluticasone (ADVAIR), or formoterol (FORADIL) for the treatment of your asthma.

Worst Pills, Best Pills News is a newsletter published once a month designed for concerned healthcare consumers like you. As a [worstpills.org](http://www.worstpills.org) subscriber, you have instant access to the latest articles on the drugs doctors are prescribing.

Drug Profile (available by subscription only)

Each drug profile provides a comprehensive review of the safety and effectiveness of drugs. All profiles—with the exception of Do Not Use drugs—include information on adverse effects, drug interactions and how to use different medications. We provide this type of information for over 500 drugs, including the 200 top-selling drugs in the US.

Do Not Use drugs are a special case in which we provide a detailed discussion of our reasons for recommending against a drug's use.

Profiles are updated every six months.

Profiles will be added for new drugs over time, particularly newly approved drugs.



worstpills.org


your expert, independent source for prescription drug information




Home	Search	Last Search	Recent Postings	Glossary	Free Drug Information
------	--------	-------------	-----------------	----------	-----------------------

Drug Profile

Do NOT stop taking this or any drug without the advice of your physician. Some drugs can cause severe adverse effects when they are stopped suddenly.

 **Do Not Use** [[what does this mean?](#)]

Generic drug name: **fluticasone and salmeterol inhalation powders**

(FLEW ti cas sone and sall MET er all) 

Brand name(s): **ADVAIR DISKUS** (GlaxoSmithKline)

FAMILY: Beta Agonists, Inhaled Steroids

Alternative Treatment:

See [Asthma: Inhaled Steroids](#) and [Asthma: Short-acting Beta Agonists](#).

Pregnancy and Breast-feeding Warnings

Pregnancy Warning

Fluticasone and salmeterol caused fetal harm in animal studies, including delayed bone formation, malformations, and fetal death. Because of the potential for serious adverse effects to the fetus, this drug should not be used by pregnant women.

Breast-feeding Warning

Fluticasone is excreted in animal milk, and it is likely that this occurs in humans. Although fluticasone was not tested, other corticosteroids have been detected in human milk. Because of the potential for serious adverse effects in nursing infants, you should not take fluticasone and salmeterol while nursing.

Prominently featured at the top of every Drug Profile is whether a drug is on the Do Not Use list and its generic and brand names. Links to the FDA-approved drug label are often provided ("Read the Drug Label").

Pregnancy and safety warnings, if any, always follow the information described above.

Safety Warnings For This Drug:

FDA BLACK BOX WARNING

Long-acting beta2-adrenergic agonists, such as salmeterol, one of the active ingredients in ADVAIR DISKUS, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, physicians should only prescribe ADVAIR DISKUS for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies. Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT® Inhalation Aerosol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks on salmeterol versus 3 deaths out of 13,179 patients on placebo).

Do not stop any asthma medication without first consulting your physician. Abruptly stopping a medication may result in acutely deteriorating asthma control.

ADDITIONAL PRECAUTIONS FOR ASTHMA

Avoid exposure to things that trigger your allergies or asthma, such as animals, bedding, chemicals, cosmetics, drugs, dust, mold, foods, pollens, or smoke. Wearing a mask reduces inhalation of drugs, pollens, and smoke.

Aspirin can trigger asthma in people who are aspirin-allergic, as can beta-blockers. Infections aggravate lung problems. During epidemics of respiratory illnesses, avoid crowded places and wash your hands frequently to help prevent infection. If you have asthma, get a flu vaccination.

Note: The information in this profile addresses the care of asthma that is not serious enough to need emergency treatment.

Facts About This Drug:

The Advair Diskus combines powders of a steroid called **fluticasone (FLOVENT)** with a long-acting beta-blocker called **salmeterol (SEREVENT)**. The diskus is used to inhale the powders by mouth. The combination allows a lower dose of fluticasone to be used, reducing steroid exposure and its attendant dangers.¹ It is approved by the FDA for the treatment of chronic asthma but is not intended for treatment of acute episodes, or if asthma is rapidly deteriorating.

Combination salmeterol and fluticasone decreases constriction of bronchial smooth muscle and inflammation of the airway. This may reduce the need for rescue medications, such as albuterol, reduce severity of shortness of breath, reduce mortality, improve lung function, improve ability to endure strenuous activity, and increase the number of symptom-free days.^{2, 3, 4}

In August 2003, the FDA announced that a black-box warning (see above) would be required on the professional product labeling or package inserts for drug products containing salmeterol. This requirement applies to both **salmeterol (SEREVENT)** alone and fluticasone and salmeterol together. The FDA has the regulatory authority to require box warnings for drugs that have been associated with the deaths or serious injuries of patients and may also require them if there is strong evidence from animal experiments that they may be dangerous. A black-box warning is the strongest type of

FDA Black Box warnings are the strongest warnings the FDA can request for a drug, and we always note them with a heavy black line.

This section is reserved for detailed information about why a drug should not be used or, if safe for use, summarizes a drug's safety and efficacy.

Sample Subscriber Search – ADVAIR

safety warning that the FDA can mandate in a drug's professional product labeling.

The black-box warning was the result of a study known as the Salmeterol Multicenter Asthma Research Trial (SMART for short), that was terminated early. This study was initiated by GlaxoSmithKline in 1996 and was designed to assess the safety of salmeterol because of concerns regarding the safety of regular use of the combination of short- and long-acting beta agonists in the management of asthma after reports of death had been submitted to the FDA. Data revealed by the FDA in July 2005 lead us to conclude that you should not use combination salmeterol and fluticasone because of the increased risk of asthma deaths with its ingredient salmeterol.

In November 2005, the FDA notified manufacturers of Advair Diskus to update its existing product label with a new warning and a Medication Guide for patients to alert health care professionals and patients that this medicine may increase the chance of severe asthma episodes, and death when those episodes occur. Even though this drug decreases the frequency of asthma episodes, it may make asthma episodes more severe when they do occur.⁵

In March of 2006, the FDA officially designated this drug as “last choice” for the treatment and management of asthma. They released the following guidelines for the use of the combination of salmeterol and fluticasone:

Long-acting beta2-adrenergic agonists, such as salmeterol, one of the active ingredients in ADVAIR DISKUS, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, physicians should only prescribe ADVAIR DISKUS for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies. ADVAIR DISKUS is not indicated in patients whose asthma can be successfully managed by inhaled corticosteroids along with occasional use of inhaled, short-acting beta2-agonists.⁵

The FDA-approved Medication Guide for Advair can be found [here](#).

While inhaled steroids reduce the likelihood of systemic effects compared to steroids taken by mouth, the risks are not eliminated. Steroids can damage adrenal glands and potentially reduce bone mineral density.^{6, 7, 8} High-dose steroids used over six months are more associated with adrenal crisis than those taken at lower doses or for shorter periods.⁹ Suppression of adrenal glands can cause low blood sugar, unconsciousness, convulsions, coma, or death. Onset in adults may start with drowsiness and nausea.

A detachment of the retina called chorioretinopathy has been associated with steroid inhalers, especially in women.¹⁰

last reviewed March 31, 2006

1 Busse W, Koenig SM, Oppenheimer J, Sahn SA, Yancey SW, Reilly D, Edwards LD, Dorinsky PM. Steroid-sparing effects of fluticasone propionate 100 microg and salmeterol 50 microg administered twice daily in a single product in patients previously controlled with fluticasone propionate 250 microg administered twice daily. *Journal of Allergy and Clinical Immunology* Jan 2003; 111: 57 - 65.

The Drug Profile ends here if the drug is on the Do Not Use list. For other drugs, the Profile identifies important issues, special instructions, warning signs, adverse (side) effects, overdose symptoms, possible interactions with other drugs and periodic tests you and your doctor should consider.

Drug profiles are updated every 6 months. The “last reviewed” date can be found at the bottom of the profile.

Sample Subscriber Search – ADVAIR

- 2 Calverley P, Pauwels R, Vestbo J, Jones P, Pride N, Gulsvik A, Anderson J, Maden C. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: A randomised controlled trial. *Lancet* Feb 8, 2003; 361: 449 - 456.
- 3 Mahler DA, Wire P, Horstman D, Chang CN, Yates J, Fischer T, Shah T. Effectiveness of fluticasone propionate and salmeterol combination delivered via the Diskus device in the treatment of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* Oct 15, 2002; 166: 1084 - 1091.
- 4 Nelson HS, Chapman KR, Pyke SD, Johnson M, Pritchard JN. Enhanced synergy between fluticasone propionate and salmeterol inhaled from a single inhaler versus separate inhalers. *Journal of Allergy and Clinical Immunology* Jul 2003; 112: 29 - 36.
- 5 Food and Drug Administration. FDA Public Health Advisory: Increased Risk of Death with Long-Acting Beta Agonists, Nov 18, 2005.
- 6 Pescollderung L, Radetti G, Gottardi E, Peroni DG, Pietrobelli A, Boner AL. Systemic activity of inhaled corticosteroid treatment in asthmatic children: Corticotrophin releasing hormone test. *Thorax* Mar 2003; 58: 227 - 230.
- 7 Sim D, Griffiths A, Armstrong D, Clarke C, Rodda C, Freezer N. Adrenal suppression from high-dose inhaled fluticasone propionate in children with asthma. *European Respiratory Journal* Apr 2003; 21: 633 - 636.
- 8 Todd GR, Acerini CL, Ross-Russell R, Zahra S, Warner JT, McCance D. Survey of adrenal crisis associated with inhaled corticosteroids in the United Kingdom. *Archives of Diseases in Children* Dec 2002; 87: 457 - 461.
- 9 Nguyen KL, Lauver D, Kim I, Aresery M. The effect of a steroid 'burst' and long-term, inhaled fluticasone propionate on adrenal reserve. *Annals of Allergy, Asthma and Immunology* Jul 2003; 91: 38 - 43.
- 10 Haimovici R, Gragoudas ES, Duker JS, Sjaarda RN, Elliott D. Central serous chorioretinopathy associated with inhaled or intranasal corticosteroids. *Ophthalmology* Oct 1997; 104: 1653 - 1660.

Recommendations are based on our analysis of the same data the FDA uses to approve the drugs, to which we apply the best medical research practices. We cite every step in the process.

Disease and Drug Family Information (available by subscription only)

Often, a drug belongs to a class of drugs with similar characteristics. In these cases, we include information that pertains to all the drugs in a particular category. We may also include information about a particular disease or condition that is commonly treated with the drug you select. In the case of ADVAIR, we've included information about two sets of conditions frequently treated with this medication.



worstpills.org
your expert, independent source for prescription drug information



Home	Search	Last Search	Recent Postings	Glossary	Free Drug Information
------	--------	-------------	-----------------	----------	-----------------------

Allergy and Hayfever

If you suffer from an itchy and runny nose, watery eyes, sneezing, and a tickle in the back of your throat, then you probably have an allergy. An allergy means a hypersensitivity to a particular substance called an allergen. Hypersensitivity means that the body's immune system, which defends against infection, disease, and foreign bodies, reacts inappropriately to the allergen. Examples of common allergens are pollen, mold, ragweed, dust, feathers, cat hair, makeup, walnuts, aspirin, shellfish, poison ivy, and chocolate.

There are four common types of allergic responses, although many substances can cause more than one type of response in a given person:

- Itchy and runny nose, watery eyes, sneezing, and a tickle in the back of your throat. This type of allergy is sometimes called allergic rhinitis and is commonly caused by exposure to allergens in the air, such as pollen, dust, and animal feathers or hair. It is called hay fever when it occurs seasonally, in response to ragweed in the fall.
- Hives or other skin reactions. These commonly result from something you eat or from skin exposure to an allergenic substance, such as poison ivy or chemicals. Allergic skin reactions may also follow insect bites or an emotional disturbance.
- [Asthma](#).
- Sudden, generalized itching, rapidly followed by difficulty breathing, and possible shock (extremely low blood pressure) or death. This rare and serious allergic response, called anaphylaxis, usually occurs as a response to certain injections (including allergy shots), drugs (including antibiotics such as penicillin and many arthritis drugs such as celecoxib [CELEBREX]), and insect bites as from a bee or wasp. This reaction may become increasingly severe with repeated exposures. Anaphylaxis is a medical emergency requiring an immediate trip to an emergency room, clinic, or doctor's office. If you are likely to have an anaphylactic response to an allergen, such as a bee sting, in a locale where medical attention may be out of reach, you should obtain a prescription from a doctor for an emergency kit containing injectable epinephrine to keep with you, and learn how to use it.

How to Treat Allergic Symptoms

The best way to treat an allergy is to discover its cause and, if possible, to avoid the substance. Sometimes this is easy, but in many cases it is not. If, for example, your eyes swell, your nose runs, and you break out in hives each time you are around cats, avoid cats and you have solved your problem.

If, however, you sneeze during one particular season (typically, late spring, summer, or fall) each year or all year round, there is not too much you can do to avoid the pollens, dust, or grass particles in the air. Some people find relief in an indoor retreat where it is cooler, closed, and less dusty, but this is not always possible.

If you can't seem to figure out the cause of your allergy, have tried eliminating most of the common allergens from your environment, and are still suffering significant discomfort, you may have to see your doctor or another health professional. It is possible that you may be an appropriate candidate for skin testing and may be referred to a doctor specializing in allergies.

Beware of the allergist who sends you home with a long list of substances to avoid because they gave positive patch tests. Even if you avoid all of them, you may be left with your allergy if none of the substances on the list is the particular one responsible for your symptoms.

When identifying the cause of your allergy is not possible, you may choose to treat the symptoms. Allergy symptoms are caused primarily by the release of a chemical in your body called histamine, and a class of drugs known as the antihistamines is the most effective initial treatment available. We recommend that you use antihistamines in a single-ingredient preparation to treat your symptoms. Another choice are the [steroid-containing nasal sprays](#).

Allergic rhinitis should not be treated with topical nasal decongestants (drops, sprays, and inhalers) that are recommended for treating the temporary stuffy nose of a cold. Allergies are long-term conditions, lasting for weeks, months, or years, and use of these topical decongestants for more than a few days can lead to rebound congestion (an increase in nasal stuffiness after the medication wears off) and sometimes permanent damage to the membranes lining the nose. If you think your congestion is caused by allergies, don't use an OTC nasal spray, or you may eventually find that you cannot breathe through your nose without it.

Drugs for Allergy

Antihistamines: Of all the products sold for allergy, we recommend that you use a single-ingredient product containing only an antihistamine. Antihistamines are the most effective ingredients you can buy for treating an allergy, and you will minimize the adverse effects by buying the single-ingredient formulation.

A major adverse effect of antihistamines is drowsiness. If they make you drowsy, you should avoid driving a motor vehicle or operating heavy machinery while taking these drugs. Even if they don't make you drowsy, they may still slow your reaction time. Additionally, keep in mind that drowsiness is increased dramatically by adding other sedatives, including alcoholic beverages.

The amount of drowsiness produced by an antihistamine differs depending on the person who takes it and the antihistamine that is used. Of antihistamines classified by the FDA as safe and effective for OTC use, those causing the least drowsiness are chlorpheniramine maleate, brompheniramine maleate, pheniramine maleate, and clemastine. For daytime use, we urge you to use one

of these.

Other FDA-approved antihistamines causing a great deal of drowsiness include diphenhydramine hydrochloride and doxylamine succinate, which are the ingredients in some currently available OTC sleep aids.

The advent of the less sedating but dangerous prescription antihistamines, the first of which were astemizole and terfenadine, now banned, has lessened the tendency of physicians and patients to use the lowest possible dose of the older, less expensive, and safer antihistamines such as chlorpheniramine maleate, the active ingredient in Chlor-Trimeton and dozens of other prescription and over-the-counter allergy medicines. By trying a lower dose, you may find that you significantly reduce the sedating effects. There are now other, [less dangerous nonsedating antihistamines](#) on the market.

Another common adverse effect of antihistamines is dryness of the mouth, nose, and throat. Other less common adverse effects include blurred vision, dizziness, loss of appetite, nausea, upset stomach, low blood pressure, headache, and loss of coordination. Difficulty in urinating is often a problem in older men with enlarged prostate glands. Antihistamines occasionally cause nervousness, restlessness, or insomnia, especially in children.

For antihistamine treatment of allergies, your first choice should be a low dose of chlorpheniramine in an OTC single-ingredient product such as Chlor-Trimeton. Check the label and be sure that nothing else is in the product. Chlor-Trimeton Decongestant and Dimetapp both contain an additional ingredient that is not necessary for the treatment of allergy. Less expensive store brand or generic equivalents are often available and should be purchased if possible. If you can't find them, ask the pharmacist.

You should not use antihistamines for self-medication if you have asthma, glaucoma, or difficulty urinating due to enlargement of the prostate gland.

Nasal decongestants: Many over-the-counter products sold for allergies contain amphetamine-like nasal decongestants, such as pseudoephedrine hydrochloride or ingredients found in many oral cold preparations (see earlier discussion on oral decongestants for colds). Some of these adverse effects and adverse reactions (such as jitteriness, sleeplessness, and potential heart problems) occur even more frequently when they are used to treat allergies, because allergy medication is usually taken for a longer period of time than a cold remedy is.

More to the point, nasal decongestants do not treat the symptoms most frequently experienced by allergy sufferers: the runny nose, itchy and watery eyes, sneezing, cough, and the tickle in the back of the throat. They treat only a stuffy nose, which is not the major problem for most allergy sufferers.

Examples of OTC nasal decongestants that are labeled to treat symptoms "without drowsiness" (since they do not contain antihistamines) include Afrinol and Sudafed. We do not recommend the use of these products for allergies.

Combination allergy products: As usual in the OTC market (particularly in the cold and allergy area), most products available are fixed-combination products using a "shotgun" approach to your ailment. The majority of allergy combination products contain antihistamines and nasal decongestants; some also contain pain relievers. We do not recommend any of these for self-treatment.

It is our opinion that nasal decongestants should not be used for allergy

symptoms that are appropriate for self-treatment. The likelihood of adverse effects is increased by taking a combination product, and decongestants are seldom useful for allergy symptoms.

Examples of OTC combination drugs for allergy, which we cannot recommend, are Actifed Cold & Allergy Tablets, Chlor-Trimeton Allergy-D 12 Hour Tablets, and Drixoral Cold & Allergy Tablets. Many of the combination cold products that we urge you not to use are also marketed for allergic symptoms and hay fever. We do not recommend using any of these products for allergies either.

Asthma, Chronic Bronchitis and Emphysema

Asthma, chronic bronchitis, and emphysema all occur commonly, may occur together, and may have similar treatments.

Asthma is a disease in which the smaller air passages in the lungs are hyperirritable. Attacks, which may be initiated by various influences, lead to narrowing of the airways and difficulty breathing. Wheezing, chest tightness, and an unproductive cough usually accompany the sensation of shortness of breath. Most asthmatics have only occasional trouble breathing.

Asthma attacks are commonly caused by exposure to specific allergens, air pollutants, industrial chemicals, or infection. They can be caused by exercise (especially in cold air). Asthma can be worsened by emotional factors, and the disease often runs in families. Other ailments common to many asthma sufferers, or their family members, are hay fever and an allergic skin condition called eczema.

Chronic bronchitis is a disease in which the cells lining the lungs secrete excess mucus, leading to a chronic cough, usually accompanied by phlegm.

Emphysema is due to destruction of the walls of lung air sacs and is characterized by shortness of breath, with or without a cough. There is a fair degree of overlap between chronic bronchitis and emphysema, and the two are sometimes lumped together into "chronic obstructive pulmonary disease," or COPD. Wheezing may occur with chronic bronchitis or emphysema.

Chronic bronchitis or emphysema is most commonly the end result of many years of cigarette smoking. Other causes include occupational or environmental air pollution, chronic lung infections, and hereditary factors.

Asthma, chronic bronchitis, and emphysema may be occupational illnesses (a problem related to the workplace). Asthma frequently occurs among meat wrappers, bakers, woodworkers, and farmers, and among workers exposed to specific chemicals. Chronic bronchitis frequently is the result of exposure to dusts and noxious gases.

Asthma, bronchitis, and emphysema may be mild. For some people, however, these diseases can become life-threatening or can cause restriction in lifestyle. For all people afflicted with these problems, the types of drugs prescribed to treat or prevent the attacks are quite strong. If used incorrectly, they may have an immediate and dangerous effect on the health of the user.

Do not try to diagnose or treat yourself. Asthma, chronic bronchitis, and

emphysema must be diagnosed and treated by a doctor or other health professional. Two other common conditions that cause breathing difficulties, congestive heart failure and pneumonia, have similar symptoms, and many of the drugs used to treat asthma or COPD may worsen these conditions. Therefore, it is extremely important that you have your condition properly diagnosed before starting any medication.

Treatment

Like its diagnosis, the treatment of asthma or COPD should be determined by a doctor. Attacks of asthma can be very frightening, and sufferers often overtreat themselves, especially when the desired relief has not been provided by the recommended dosage. Do not use more or less than the prescribed dose of any asthma or bronchitis medication without first consulting your doctor.

All medications for the treatment of these disorders, including those available without a prescription, should be chosen by you and your doctor together. A doctor is likely to prescribe one or more prescription drugs for the asthmatic. The currently available nonprescription (over-the-counter) drugs should not be used even for the treatment of minor or infrequent asthmatic episodes. The drug of choice for treatment of occasional acute symptoms of asthma is an inhaled short-acting beta2-agonist, such as albuterol (PROVENTIL, VENTOLIN), or pirbuterol (MAXAIR).¹ These drugs are also commonly used for chronic bronchitis or emphysema.

Corticosteroids such as oral prednisone (DELTASONE, METICORTEN), or inhaled beclomethasone (BECLOVENT, VANCERIL), flunisolide (AEROBID), and triamcinolone (AZMACORT) are commonly used when severe acute symptoms of asthma do not improve after treatment with inhaled albuterol.¹ These are not used in COPD unless there is a component of asthma on top of the COPD.

Theophylline and aminophylline are commonly used for suppressing the symptoms of chronic asthma, bronchitis, or emphysema. Aminophylline is identical to theophylline except that aminophylline contains a salt called ethylenediamine, which has caused rashes and hives in some people. Oxtriphylline (CHOLEDYL) is not recommended because it is no more effective than theophylline and costs more. These drugs must be taken exactly as prescribed, and the level of drug in the bloodstream must be monitored by a doctor. These measures will prevent adverse effects and ensure the optimal dose.

Montelukast (SINGULAIR) and zafirlukast (ACCOLATE) are members of a family of asthma drugs called leukotriene antagonists. Both of these drugs are approved only to prevent asthma attacks in people with chronic asthma, not to treat acute attacks of asthma. Montelukast is also approved for seasonal allergy.² Montelukast is associated with liver toxicity. Production of the third leukotriene antagonist zileutin (ZYFLOW) was halted in December 2003. The manufacturer cited poor sales as the reasons; however, zileutin was also associated with liver toxicity.

The National Institutes of Health's 1997 Guidelines for the Diagnosis and Management of Asthma said of the leukotriene inhibitors that "further clinical experience and study are needed to establish their roles in therapy." At this time, the role of the leukotriene inhibitors in the management of asthma is still far from established.³

The leukotriene inhibitors are promoted as useful in helping patients reduce their dosages of steroid drugs, for example triamcinolone (AZMACORT). The

Cochrane Database of Systematic Reviews published in 2002 found, in comparing leukotriene inhibitors to placebo in people also using steroids, that the dosage of inhaled steroids can be safely reduced without requiring the use of leukotriene inhibitors. Furthermore, the dose of leukotriene inhibitors required to achieve a significant reduction in steroid dosage is several times the currently approved maximum dosage.

Proper Use of Inhalers

To receive the most benefit from your inhaler, follow the directions below,⁴ even though they may not agree with the directions on the drug manufacturer's packaging. Always shake well before taking each dose. Remove the plastic cap that covers the mouthpiece. Hold the inhaler upright, approximately 1 to 11DA2 inches from your lips. Open your mouth widely. Breathe out as fully as you comfortably can. Breathe in deeply as you press down on the can with your index finger. When you have finished breathing in, hold your breath as long as you comfortably can (try to hold it for 10 seconds). This allows time for the medication to treat your lungs before you breathe it out. If you have difficulty with hand-breath coordination, as many people do, ask your doctor for an "add-on" device that attaches to your inhaler. It allows you to close your lips around the inhaler, yet still receive the full therapeutic benefit from that dose.

If your doctor has told you to take more than one puff at each treatment, wait one minute, shake the can again, and repeat. If you also take a bronchodilator in addition to the corticosteroids, you should inhale the bronchodilator first. Wait 15 minutes before inhaling the corticosteroids. This allows more corticosteroid to be absorbed into the lungs.

Your inhaler should be cleaned every day. To do this properly, remove the can from the plastic case. Rinse the plastic case and cap under warm running water. Dry thoroughly. Using a gentle, twisting motion, replace the metal can into the case. Put the cap on the mouthpiece.

1 Drugs for asthma. *Medical Letter on Drugs and Therapeutics* Jan 30, 1987; 29: 11 - 16.

2 *Physicians' Desk Reference*. 58th ed. Montvale, NJ: Thomson PDR, 2004: 2076 - 2081.

3 National Heart LaBI. National Asthma Education and Prevention Program Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma, Jul 1, 1997. Accessed 2004 Apr 27.

4 Newhouse MT, Dolovich MB. Control of asthma by aerosols. *New England Journal of Medicine* Oct 2, 1986; 315: 870 - 874.

Newsletter Articles (available by subscription only)

Worst Pills, Best Pills News Articles are derived from our monthly print newsletter. *Worst Pills, Best Pills News* provides monthly updates both for the drugs on which we have detailed drug profiles and other drugs. Often this includes more specific information about safety or efficacy concerns or new data that either support or resolve concerns regarding particular drugs. *Worst Pills, Best Pills News* also contains our assessment of data available on the safety and efficacy of drugs newly approved by the FDA. These articles are available for the past five years, and new articles are added monthly. Entire issues of the print newsletter will be available in PDF format for three months after publication. You can access all the information published in the newsletters simply by searching for a relevant drug, disease, drug-induced disease or condition, drug family, or policy issue.

Health Letter Articles come from the other monthly publication of Public Citizen's Health Research Group. These articles deal primarily with policy issues related to prescription drugs such as prescription drug reimportation and issues related to the pharmaceutical industry. These articles are available for five years after publication.



Home Search Last Search Recent Postings Glossary Free Drug Information

DO NOT USE! FDA Relegates ADVAIR and SEREVENT to Last Choice Status for Asthma Treatment

Worst Pills Best Pills Newsletter article May, 2006

DO NOT STOP ANY ASTHMA MEDICATIONS WITHOUT FIRST CONSULTING THE HEALTHCARE PROVIDER WHO PRESCRIBED THE DRUG.

FDA BLACK BOX WARNING FOR SALMETEROL WITH FLUTICASONE

Long-acting beta2-adrenergic agonists, such as salmeterol, one of the active ingredients in ADVAIR DISKUS, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, physicians should only prescribe ADVAIR DISKUS for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies. Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT Inhalation Aerosol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving

Sample Subscriber Search – ADVAIR

salmeterol (13 deaths out of 13,176 patients treated for 28 weeks on salmeterol versus 3 deaths out of 13,179 patients on placebo).

The Food and Drug Administration-approved professional product labels for the asthma drugs Advair and Serevent now state that these drugs should only be used when nothing else works to control asthma symptoms. Salmeterol, a component of these two widely-prescribed asthma drugs, is associated with an increased risk of asthma-related death. The change became effective on March 2, 2006.

Salmeterol was approved by the FDA in 1994 to treat asthma, and later approval was extended for the treatment of chronic obstructive pulmonary disease (COPD). The drug belongs to a family of asthma medications known as long acting beta2-receptor agonists. Drugs such as albuterol (PROVENTIL, VENTOLIN), metaproterenol (ALUPENT) and pirbuterol (MAXAIR) are short-acting beta agonists. This new safety labeling change does not apply to these drugs.

Salmeterol is produced by GlaxoSmithKline of Research Triangle, NC. In 2005, there were almost 20 million prescriptions dispensed in U.S. pharmacies for salmeterol (SEREVENT) and salmeterol with fluticasone (ADVAIR). Combined sales approached \$3.0 billion.

We listed salmeterol as a DO NOT USE drug in the [March 2003 Worst Pills, Best Pills News](#) after a study known as the Salmeterol Multi-center Asthma Research Trial, or SMART for short, was prematurely terminated because of an excess of asthma related deaths in patients receiving salmeterol. This study was initiated by GlaxoSmithKline in 1996. It was designed to assess the safety of salmeterol because of concerns regarding the safety of regular use of short- and long-acting beta agonists in the management of asthma. We also designated ADVAIR as a DO NOT USE drug after we learned more details concerning the SMART study.

The labeling change will appear under the "Approved Uses" section of the professional product label. The new section in the label of ADVAIR will read:

Long-acting beta2-adrenergic agonists, such as salmeterol, one of the active ingredients in ADVAIR DISKUS, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, physicians should only prescribe ADVAIR DISKUS for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies. ADVAIR DISKUS is not indicated in patients whose asthma can be successfully managed by inhaled corticosteroids along with occasional use of inhaled, short-acting beta2-agonists.

The new section in the label of salmeterol contains similar warnings.

In addition to the new labeling changes, the FDA now requires that a Medication Guide be distributed with each and refill prescription for salmeterol-containing products. Since 1998, the FDA has had the regulatory authority to require Medication Guides for drugs that present significant public health concerns. The purpose of Medication Guides is to give patients enough information to decide if they wish to use, or continue use, a particular drug. At this time there are about 80 drugs that require Medication Guides.

The full text of the [Advair Medication Guide](#) can be found online at the FDA's web site. Anyone receiving a prescription for either of these drugs should receive a copy of the FDA-approved Medication Guide.

A black box warning was added to the professional product labeling for salmeterol-containing products on Aug. 14, 2003 and was subsequently strengthened (see *Worst Pills, Best Pills News* November 2003 and September 2005). A black box warning is the strongest type of warning that the FDA can request from a manufacturer and the usual standard used by the FDA for requesting such a warning is death in patients.

The most up-to-date black box warning for salmeterol with fluticasone appears at the beginning of this article.

What You Can Do

Do not stop these asthma medications without first consulting the healthcare provider who prescribed the drugs.

You should not use salmeterol (SEREVENT) or the combination of salmeterol with the steroid fluticasone (ADVAIR) as your only treatment of your asthma.

You should read the FDA-approved Medication Guide before filling a new prescription for a salmeterol containing product or a refill prescription for a salmeterol containing product. If you do not have access to the Internet, ask your pharmacist for a copy of the Medication Guide.

You should report any increased need for a short-acting beta agonist to your healthcare provider. This is a sign of deteriorating asthma control.

Asthma Drugs Salmeterol (SEREVENT), Salmeterol with Fluticasone (ADVAIR), and Formoterol (FORADIL)

Worst Pills Best Pills Newsletter article March, 2006

DO NOT STOP ANY ASTHMA MEDICATION WITHOUT FIRST CONSULTING YOUR PHYSICIAN. ABRUPTLY STOPPING A MEDICATION MAY RESULT IN ACUTELY DETERIORATING ASTHMA CONTROL.

FDA BLACK BOX WARNING FOR SEREVENT

Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT Inhalation Aerosol) or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks) versus those on placebo (3 of 13,179)

On Nov. 18, 2005, the Food and Drug Administration requested that additional new safety warnings be added to the professional product labels for the popular asthma drugs salmeterol (SEREVENT), salmeterol with fluticasone (ADVAIR), and formoterol (FORADIL). The new warnings concern the possibility that these drugs may increase the chance of severe asthma attacks and asthma-related death.

The FDA will also require that a Medication Guide be distributed with each new and refill prescription for these drugs. A Medication Guide is FDA-approved, scientifically accurate drug information that is written specifically for patients.

Articles end with news you can use. This section contains clear, concise advice on how to avoid taking unnecessary drug risks.

Sample Subscriber Search – ADVAIR

The FDA has the regulatory authority to require that pharmacists distribute Medication Guides for drugs that present a significant public health risk.

Salmeterol and formoterol belong to the family of asthma drugs known as long-acting beta-agonist bronchodilators. Note that this is a different family than asthma drugs such as albuterol (PROVENTIL, VENTOLIN) and metaproterenol (ALUPENT), which are short-acting beta-agonist bronchodilators. The new warnings do not apply to the short-acting beta-agonist bronchodilators.

Fluticasone is an anti-inflammatory corticosteroid, or steroid, and in combination with salmeterol is sold as Advair. The warning also does not apply to fluticasone when it is used by itself.

The FDA made the following recommendations about the use of salmeterol, formoterol, and Advair:

- These drugs should not be the first ones prescribed to treatment for asthma.
- These drugs should not be used by themselves to treat asthma.
- These drugs should always be used with another asthma treatment drug and only after the other asthma treatment, such as a low-to-medium dose inhaled corticosteroid, has not controlled the asthma.

GlaxoSmithKline of Research Triangle Park, N.C., sells both of the salmeterol-containing products. Salmeterol by itself was dispensed over 2.1 million times in U.S. pharmacies in 2004 with sales exceeding \$200 million. The combination product, Advair, is what Wall Street calls a “blockbuster.” More than 16.1 million Advair prescriptions were sold in the U.S. in 2004; sales topped \$2.1 billion for the year.

Formoterol is produced by the Schering Corp. of Kenilworth, N.J. It is not a top seller and sales figures for 2004 are not available.

We listed salmeterol as a DO NOT USE drug in January 2003. We did so because the FDA announced that a large safety study had been terminated early due to the fact that data from the trial suggested an increased risk of life-threatening asthma episodes or asthma-related deaths with the use of the drug (see *Worst Pills, Best Pills News* March 2003).

The terminated safety study was called the Salmeterol Multi-center Asthma Research Trial, or SMART for short. This study was initiated by GlaxoSmithKline in 1996. It was designed to assess the safety of salmeterol because concerns existed regarding the safety of the regular use of both short- and long-acting beta agonists in the management of asthma.

A black box warning was added to the professional product labeling for salmeterol-containing products on Aug. 14, 2003 and was subsequently strengthened (see *Worst Pills, Best Pills News* November 2003 and September 2005). A black box warning is the strongest type of warning that the FDA can request from a manufacturer and the usual standard used by the FDA for requesting such a warning is death in patients.

What You Can Do

Do not stop any asthma medication without first consulting your physician. Abruptly stopping a medication may result in acutely deteriorating asthma control.

You should not use salmeterol (SEREVENT), the combination of salmeterol with the steroid fluticasone (ADVAIR), or formoterol (FORADIL) as the only treatment of your asthma.

You should report to your physician any increased need for a short-acting beta agonist. This is a sign of deteriorating asthma.

Asthma Medicines That Can Cause Asthma Attacks: Do Not Use SEREVENT, ADVAIR or FORADIL

Worst Pills Best Pills Newsletter article September, 2005

DO NOT STOP ANY ASTHMA MEDICATION WITHOUT FIRST CONSULTING YOUR PHYSICIAN. ABRUPTLY STOPPING A MEDICATION MAY RESULT IN ACUTELY DETERIORATING ASTHMA CONTROL.

The Food and Drug Administration (FDA) advisory committee has voted in favor of putting stronger warnings on three widely used asthma inhalers — salmeterol (SEREVENT), salmeterol with the steroid fluticasone (ADVAIR) and formoterol (FORADIL). These medicines are long-acting asthma inhalers, used to keep asthma under control over time, rather than helping to stop an acute asthma attack.

The FDA convened a meeting of its Pulmonary-Allergy Drugs Advisory Committee on July 13, 2005 to discuss the safety of these drugs. The advisory committee voted to keep these drugs on the market but recommend stronger safety warnings on the professional product labels for all three drugs.

These inhalers are in the family of asthma drugs known as long-acting beta-agonist bronchodilators. Note that this is a different family of medicines than the asthma drugs albuterol (PROVENTIL, VENTOLIN), metaproterenol (ALUPENT) and pirbuterol (MAXAIR). Those are short-acting beta-agonist bronchodilators, and are used to improve breathing during an asthma attack.

GlaxoSmithKline of Research Triangle Park, N.C., sells both of the salmeterol-containing products. Salmeterol by itself was dispensed over 2.1 million times in U.S. pharmacies in 2004 with sales exceeding \$200 million. The combination product, Advair, is what Wall Street terms a “blockbuster.” More than 16.1 million Advair prescriptions were sold in the U.S. in 2004; sales topped \$2.1 billion for the year.

Formoterol is produced by the Schering Corp. of Kenilworth, N.J. Formoterol is not a top seller and sales figures for 2004 are not available.

We listed salmeterol as a DO NOT USE drug in the [March 2003](#) issue of *Worst Pills, Best Pills News* after the FDA announced on January 23, 2003 that a large safety study involving salmeterol had been halted prematurely. The study was halted because an interim analysis of outcomes suggested that the drug may be associated with an increased risk of life-threatening asthma episodes or asthma-related deaths.

The prematurely terminated study went by the name of the Salmeterol Multi-center Asthma Research Trial, or SMART for short. GlaxoSmithKline initiated the study in 1996. It was designed to assess the safety of salmeterol because of concerns regarding the safety of regular use of short- and long-acting beta agonists in the management of asthma. There were 25,858 patients recruited before the study was stopped.

At that time, Public Citizen’s attempts to obtain detailed information about the SMART study from the FDA were fruitless. Because the SMART study was

Sample Subscriber Search – ADVAIR

conducted after salmeterol was approved and did not fulfill any regulatory requirement on the part of GlaxoSmithKline, details of the study could not be released under the FDA's interpretation of the Freedom of Information Act. The agency considered this important safety information to be protected confidential commercial information that could not be released to the public.

On August 14, 2003, the FDA announced that a black box warning was added to the professional product labeling for drug products containing salmeterol. This warning applied to both salmeterol by itself and Advair. The FDA can ask for black box warnings for drugs that have been associated with the deaths of patients and may also require them if there is strong evidence from animal experiments. A black box warning is the strongest type of safety warning that the FDA can seek for a drug's professional product labeling (see *Worst Pills, Best Pills News* November 2003).

In the first serious congressional hearings examining drug safety held in almost 14 years, Dr. David Graham, an FDA medical epidemiologist, testified before Senator Charles Grassley's Senate Finance Committee in October 2004 that the safety of salmeterol was of concern to the FDA.

It was not until the day before the July 13, 2005 Pulmonary-Allergy Drugs Advisory Committee meeting, when the FDA posted its review on the Internet, that the public was able for the first time to view the details of the SMART study. This was an unacceptable 31 months after the SMART study was stopped prematurely. The FDA's review of the SMART study is available at http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4148B1_03_00-FDA-TOC.htm.

The main purpose of the SMART study was to measure the combined number of respiratory-related deaths or respiratory-related life-threatening experiences such as the need for intubation and mechanical ventilation in patients taking salmeterol. This is called the primary endpoint. The study consisted of a single clinic visit for each participant during which the person's eligibility status was evaluated. To be eligible to participate, patients had to have a clinical diagnosis of asthma and currently take prescription asthma medications. During the single clinic visit, patients were randomly assigned to receive either two puffs daily of salmeterol or a placebo.

At the end of the 28-week study, 50 patients out of 13,176 given salmeterol either died or suffered a life-threatening event compared to 36 receiving the placebo. The difference in life-threatening respiratory events and asthma-related deaths between the groups was significant in the FDA analysis.

The following is the proposed revised black box warning for salmeterol.

FDA RECOMMENDED BLACK BOX WARNING:

WARNING: Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT Inhalation Aerosol) or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks) versus those on placebo (3 of 13,179).

The black box warning added to salmeterol's labeling on August 14, 2003 suggested that the risk may be greater in African-American patients compared to Caucasians. The FDA has proposed deleting this information from the black box warning because the risk for asthma-related deaths in Caucasians and African Americans treated with salmeterol relative to being treated with placebo were quite similar.

Warnings for Formoterol

The advisory committee also voted that formoterol should carry stronger warnings. At this time, formoterol does not have a black box warning in its professional product labeling as do salmeterol and Advair. The evidence for problems with formoterol is not as strong as it is with salmeterol.

In the three studies submitted by formoterol's manufacturer to the FDA before the drug was approved, two dosages were evaluated: 12 micrograms and 24 micrograms, each given twice daily. The drug's approval was restricted to the lower dosage because serious worsening of asthma occurred with more frequency in both adult and pediatric patients who received the higher dose. This result was serious enough to warrant a commitment from the manufacturer to conduct a post-marketing safety study, known as a phase IV study, to further examine the relative safety of the different doses of formoterol. No deaths occurred in this study.

The FDA concluded that the formoterol phase IV study was too small to provide a strong answer similar to the SMART study for salmeterol, but the results were generally compatible with the decision not to approve the higher 24-microgram-twice-daily dose of the drug.

The long-acting beta agonist asthma drugs should not be used as a replacement for inhaled steroids. These drugs should not be started in patients whose asthma is significantly worsening or acutely deteriorating. This may be life threatening. The long-acting beta agonists should not be used to treat acute asthma symptoms.

The weight of the available scientific evidence points to the long-acting beta agonists as being less safe than their short-acting counterparts. There is no evidence that patient outcomes are better with the long-acting agents compared to the older short-acting drugs.

What You Can Do

Do not stop any asthma medication without first consulting your physician. Abruptly stopping a medication may result in acutely deteriorating asthma control.

You should not use salmeterol (SEREVENT), the combination of salmeterol with the steroid fluticasone (ADVAIR), or formoterol (FORADIL) for the treatment of your asthma.

You should report to your physician any increased need for a short-acting beta agonist. This is a sign of deteriorating asthma.

Get a second opinion on your drugs.

[Subscribe Now](#)

Do you have more questions about worstpills.org? Check out our [FAQ page](#), perform a [sample search](#) on a drug you are interested in, or [drop us a note](#).