SEREVENT™ DISKUS™

Presentation

Serevent Diskus
Serevent Diskus, a multidose powder inhaler device, comprises 60 regularly distributed blisters each containing a mixture of 50mcg salmeterol (as xinafoate) and lactose.

Indications

Adults: Salmeterol provides long-lasting (12 hour) bronchodilation in reversible airways obstruction due to asthma (including patients with nocturnal asthma and activity-induced asthma), chronic bronchitis and emphysema. It is suitable for long-term regular, twice daily treatment to control symptoms, but in view of its slower onset (10 to 20 minutes) it should not be used to relieve acute asthmatic symptoms, for which a faster acting (within 5 minutes) inhaled bronchodilator (eg. salbutamol) should be given.

Salmeterol is indicated when regular bronchodilator is required, and to prevent night-time symptoms and/or day-time fluctuations in asthma control (eg. before exercise or unavoidable allergen challenge).

Salmeterol as twice daily regular treatment, can replace a short-acting (4 hour) inhaled bronchodilator (eg. salbutamol), when it is required more than once a day, or an oral bronchodilator (eg. salbutamol, theophylline).

There is no evidence that salmeterol is a replacement for corticosteroids and these should not be stopped or reduced when salmeterol is prescribed. In patients not already receiving anti-inflammatory therapy, this should be considered when starting salmeterol.

Patients must be warned not to stop steroid therapy or reduce it without medical advice, even if they feel better on salmeterol.

Children: Regular treatment of reversible airway obstruction in asthma including long lasting prevention of activity-induced bronchospasm.

Dosage and Administration

Serevent Diskus is administered by the inhaled route only.

Adults
One inhalation of Serevent Diskus (50mcg of salmeterol) twice daily.

In patients with more severe airways obstruction in whom symptoms persist, the dose may be increased to a maximum of two inhalations of Serevent Diskus(2x50mcg of salmeterol) twice daily.

Children 4 years and older
One inhalation of Serevent Diskus (50mcg of salmeterol) twice daily.
There are insufficient clinical data at present to recommend the use of salmeterol in children under 4 years of age.

Special Patient Group: There is no need to adjust the dose in the elderly, or in those with impaired renal function.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

Contraindications

Hypersensitivity to any ingredient of the preparation.

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Precautions

Bronchodilators should not be the only or the main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment including lung function testing as patients are at risk of severe attacks and even death.
Physicians should consider using oral corticosteroid therapy and/or maximum recommended dose of inhaled corticosteroid in these patients.

Serevent should not be initiated in patients with significantly worsening or acutely deteriorating asthma.

Patients with severe asthma have constant symptoms and frequent exacerbations with limited physical capacity, and PEF values below 60% predicted at baseline with greater than 30% variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled (e.g. >1 mg/day beclomethasone dipropionate) or oral corticosteroid therapy. With optimal background steroid therapy, Serevent can offer additional symptomatic treatment. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

The management of asthma should normally follow a stepwise programme, and patient response should be monitored clinically and by lung function tests. Increasing use of short acting inhaled beta-2 agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

Serevent is not a replacement for oral or inhaled corticosteroids. Its use is complementary to them. Patients must be warned not to stop steroid therapy and not to reduce it without medical advice even if they feel better on Serevent.

Serevent is not designed to relieve acute asthmatic symptoms, for which an inhaled short-acting bronchodilator (e.g. salbutamol) is required. Patients should be advised to have such relief medication available. If patients find that short-acting relief bronchodilator treatment becomes less effective or they need more inhalations than usual, medical attention must be sought. In this situation patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroids or a course of oral corticosteroids). Severe exacerbations of asthma must be treated in the normal way.

Potentially serious hypokalaemia may result from beta-2 agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Salmeterol should be administered with caution in patients with thyrotoxicosis.

Pregnancy:
In animal studies, some effects on the foetus, typical for a beta-2 agonist, occurred at exposure levels substantially higher than those that occur with therapeutic use. Extensive experience with other beta-2 agonists has provided no evidence that such effects are relevant for women receiving clinical doses. As yet, experience of the use of salmeterol during pregnancy is limited. As with any medicine, use during pregnancy should be considered only if the expected benefit to the mother is greater than any possible risk to the foetus.

Lactation:
Plasma levels of salmeterol after inhaled therapeutic doses are negligible and therefore levels in milk should be correspondingly low. Nevertheless, as there is no experience of the use of salmeterol in nursing mothers, its use in such circumstances should only be considered if the expected benefit to the mother is greater than any possible risk to the infant.

Studies in lactating animals support the view that salmeterol is likely to be secreted in only very small amounts into breast milk.

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The pharmacological side-effects of beta-2 agonist treatment, such as tremor, subjective palpitations and

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Side-effects:
The pharmacological side-effects of beta-2 agonist treatment, such as tremor, subjective palpitations and headache, have been reported, but tend to be transient and to reduce with regular therapy. Tachycardia may occur in some patients.

Potentially serious hypokalaemia may result from beta-2 agonist therapy.

As with other inhalational therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. Serevent Diskus should be discontinued immediately, the patient assessed, and if necessary, an alternative therapy instituted.

There have been reports of cutaneous hypersensitivity reactions and arthralgia. There have been very rare reports of muscle cramps.

There have been no reports of ability to drive and operate machinery being affected.

Drug Interactions

Both non-selective and selective beta-blockers should be avoided in patients with reversible obstructive airways disease, unless there are compelling reasons for their use.

Overdosage

The symptoms and signs of salmeterol overdosage are tremor, headache and tachycardia. The preferred antidote for overdosage with Serevent Diskus is a cardio-selective beta-blocking agent. Cardio-selective beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

Pharmaceutical Precautions

Serevent Diskus should not be exposed to extreme temperatures and should be stored in a dry place below 30°C.

Further Information

Mode of action: Salmeterol is a selective long-acting (12 hour) beta-2 adrenoceptor agonist with a long side-chain which binds to the exosite of the receptor. These pharmacological properties of salmeterol offer more effective protection against histamine-induced bronchoconstriction and produce a longer duration of bronchodilatation, lasting for at least 12 hours, than recommended doses of conventional short-acting beta-2 agonists.

In vitro tests have shown that salmeterol is a potent and long-lasting inhibitor of the release, from the human lung, of mast cell mediators, such as histamine, leukotrienes and prostaglandin D2. In man, salmeterol inhibits the early and late phase response to inhaled allergen: the latter persisting for over 30 hours after a single dose when the bronchodilator effect is no longer evident. Single dosing with salmeterol attenuates bronchial hyper-responsiveness. These properties indicate that Serevent modulates the inflammatory process in the lung, but the full clinical significance is not yet clear. The mechanism is different from the anti-inflammatory effect of corticosteroids, which should not be stopped or reduced when Serevent is prescribed.

Pharmacokinetic Properties

Salmeterol acts locally in the lung, therefore, plasma levels are not predicative of therapeutic effect. In addition, there are only limited data available on the pharmacokinetics of salmeterol because of the technical difficulty of assaying the drug in plasma because of the very low plasma concentrations (approximately 200 pg/ml or less) achieved after inhaled dosing. After regular dosing with salmeterol xinafoate, hydroxynaphthoic acid can be detected in the systemic circulation, reaching steady state concentrations of approximately 100 ng/ml. These concentrations are up to 1000 fold lower than steady state levels observed in toxicity studies and in long term regular dosing (more than 12 months) in patients with airways obstruction, have been shown to produce no ill effects.

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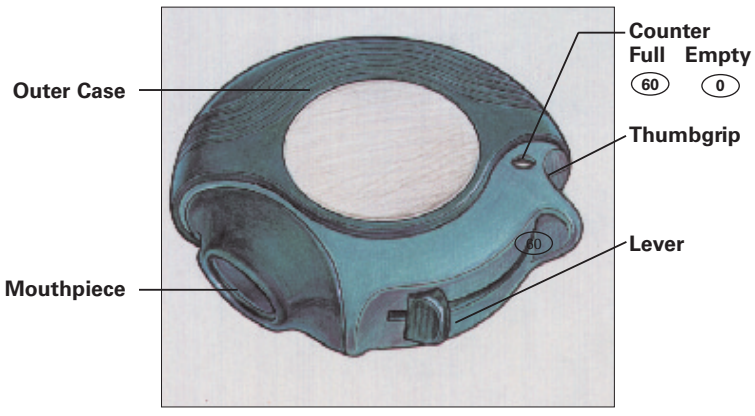
SEREVENT™ DISKUS™

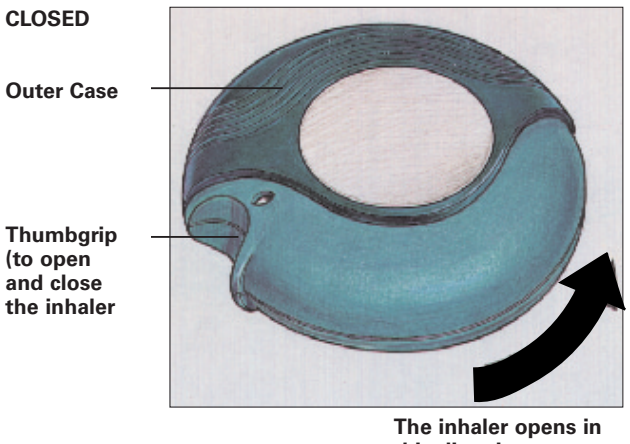


WHAT IS A SEREVENT DISKUS INHALER?

Serevent Diskus is a plastic inhaler device containing a foil strip with 60 blisters. Each blister contains 50 micrograms of the active ingredient salmeterol xinafoate and lactose which acts as the 'carrier'. The blisters protect the powder for inhalation from the effects of the atmosphere. The device has a counter which tells you the number of blisters remaining. It counts down from 60 to 0. To show when the last five blisters have been reached the numbers appear in red. When the counter shows 0 your inhaler is empty and should be disposed of.

HOW TO USE YOUR DISKUS INHALER

When you take your Diskus out of its box, it will be in the closed position.



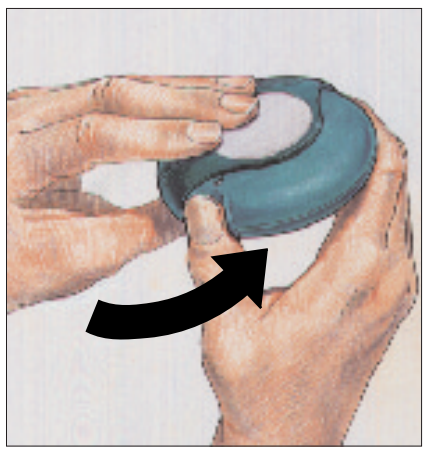
The inhaler opens in this direction

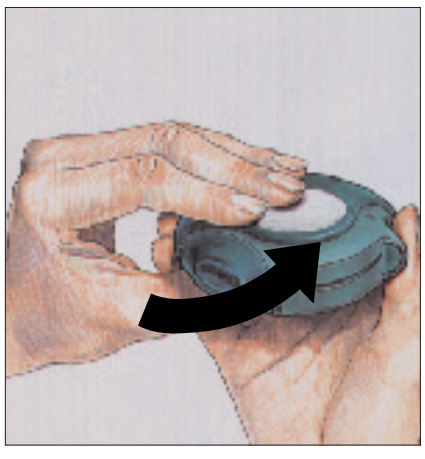
A new Diskus contains 60 individual blisters containing your medicine in powder form.
The contents of each blister are accurately measured and hygienically protected.
The Diskus requires no maintenance and no refilling.
The counter on top of your Diskus tells you how many blisters are left. Numbers 5 to 0 will appear in RED, to warn you when there are only a few blisters left.

HOW YOUR DISKUS WORKS
Sliding the lever of your Diskus opens a small hole in the mouthpiece and opens a blister in a foil strip, ready for you to inhale the powder. When you close the Diskus, the lever automatically moves back to its original position. The outer case protects your Diskus when it is not in use.

The Diskus is easy to use. When you need to use it, just follow these four simple steps:

1 OPEN 2 SLIDE 3 INHALE 4 CLOSE



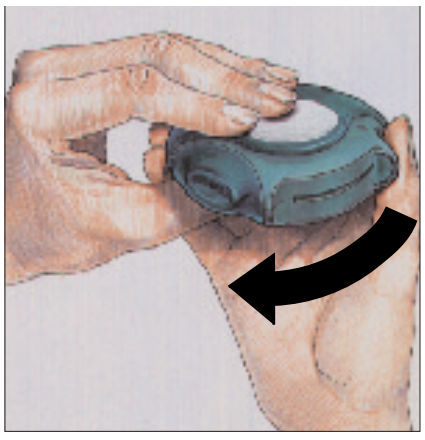


1 OPEN

To open your Diskus, hold the outer case in one hand and put the thumb of your other hand on the thumbgrip. Push your thumb away from you as far as it will go until you hear a click.

2 SLIDE

Hold your Diskus with the mouthpiece towards you. You can hold it in either your right or left hand. Slide the lever away from you, as far as it will go - until it clicks. Your Diskus is now ready to use.
Every time the lever is pushed back a blister is opened and the power made available for inhaling. This is shown by the counter. Do not play with the lever because this opens the blisters and wastes the medicine.



3 INHALE

BEFORE YOU START TO INHALE READ THROUGH THIS SECTION CAREFULLY.

* Hold the Diskus away from your mouth. Breathe out as far as is comfortable. Remember - never breathe into your Accuhaler.
* Put the mouthpiece to your lips. Suck in steadily and deeply through the Accuhaler.
* Remove the Diskus from your mouth.
* Hold your breath for about 10 seconds, or as long as is comfortable.
* Breathe out slowly.

4 CLOSE

To close your Diskus, put your thumb in the thumbgrip, and slide the thumbgrip back towards you, as far as it will go.
When you close the Diskus, it clicks shut. The lever automatically returns to its original position and is reset.
Your Diskus is now ready for you to use again.
If you have been instructed to take two blisters you must repeat steps 1 to 4.

CLEANING
Wipe the mouthpiece of the Diskus with a dry tissue to clean it.