Flixonase ™

Aqueous Nasal Spray

To the Medical and Pharmaceutical Professions.

Presentations

Not all presentations are registered in every, country.

Nasal spray, suspension.

Indications

Fluticasone Propionate Aqueous Nasal Spray is indicated for the prophylaxis and treatment of seasonal allergic rhinitis including hay fever, and perennial rhinitis. In patients with allergic rhinitis, fluticasone propionate aqueous nasal spray is also indicated for the management of associated sinus pain and pressure. Fluticasone propionate has potent anti-inflammatory activity but when used topically on the nasal mucosa has no detectable systemic activity.

Dosage and Administration

Fluticasone Propionate Aqueous Nasal Spray is for administration by the, intranasal route only.

Adults and children over 12 years of age: For the prophylaxis and treatment of seasonal allergic rhinitis and perennial rhinitis:

Two sprays into each nostril once a day, preferably in the morning. In some cases two sprays into each nostril twice daily may be required. The maximum daily dose should not exceed four sprays into each nostril.

Elderly:

The normal adult dosage is applicable.

Children under 12 years of age: For the prophylaxis and treatment of seasonal allergic rhinitis and perennial rhinitis in children aged 4-11 years:

One spray into each nostril once a day, preferably in the morning. In some cases one spray into each nostril twice daily may be required. The maximum daily dose should not exceed two sprays into each nostril.

For full therapeutic benefit regular usage is essential. The absence of an immediate effect should be explained to the patient as maximum relief may not be obtained until after 3 to 4 days of treatment.

Contra-indications

Fluticasone Propionate Aqueous Nasal Spray is contra-indicated in patients with a hypersensitivity to any of its ingredients.

Precautions and Warnings

Local infection: Infections of the nasal airways should be appropriately treated but do not constitute a specific contra-indication to treatment with Fluticasone Propionate Aqueous Nasal Spray.

The full benefit of Fluticasone Propionate Aqueous Nasal Spray may not be achieved until treatment has been administered for several days. Care must be taken while transferring patients from systemic steroid treatment to Fluticasone Propionate Aqueous Nasal Spray if there is any reason to suppose that their adrenal function is impaired.

Although Fluticasone Propionate Aqueous Nasal Spray will control seasonal allergic rhinitis in most cases, an abnormality heavy challenge of summer allergens may in certain instances necessitate appropriate additional therapy. A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 Inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects.

Drug Interactions

Under normal circumstances, very low plasma concentrations of fluticasone propionate are achieved after intranasal dosing, due to extensive first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Hence, clinically significant drug interactions mediated by fluticasone propionate are unlikely.

A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. Studies have shown that other inhibitors of cytochrome P450 3A4 produce negligible (erythromycin) and minor (ketoconazole) increases in systemic exposure to fluticasone propionate without notable reductions in serum cortisol concentrations. Nevertheless, care is advised when co-administering potent cytochrome P450 3A4 inhibitors (e.g. ketoconazole), as there is potential for increased systemic exposure to fluticasone propionate.

Pregnancy and lactation

Pregnancy: There is inadequate evidence of safety in human pregnancy. In animal reproduction studies, adverse effects typical of potent corticosteroids are only seen at high systemic exposure levels; direct intranasal application ensures minimal systemic exposure.

However, as with other drugs, the use of Fluticasone Propionate Aqueous Nasal Spray during human pregnancy requires that the benefits be weighed against the possible risks associated with the product or with any alternative therapy.

lactation: The excretion of fluticasone propionate into human breast milk has not been investigated. When measurable plasma levels were obtained in lactating laboratory rats following subcutaneous administration, there was evidence of fluticasone propionate in the breast milk. However, plasma levels in patients following intranasal application of fluticasone propionate at recommended doses are likely to be low.

Adverse Reactions

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (.1/10), common (.1/100 and .1/10), uncommon (.1/1000 and .1/100), rare (.1/10,000 and .1/1000) and very rare (.1/10,000) including isolated reports. Very common, common and uncommon events-were generally determined from clinical trial data.

Rare and very rare events were generally determined from spontaneous data. In assigning adverse event frequencies, the background rates in placebo groups were not taken into account, since these rates were generally comparable to those in the active treatment group.

Immune system disorders:

Very rare: Hypersensitivity reactions, anaphylaxis/anaphylactic reactions, bronchospasm, skin rash, oedema of the face or tongue.

Nervous system disorders:

Common: Headache, unpleasant taste, unpleasant smell.

As with other nasal sprays, unpleasant taste and smell and headache have been reported.

Eye disorders:

Very rare: Glaucoma, raised intraocular pressure, cataract.

A very small number of spontaneous reports have been identified following prolonged treatment. However, clinical trials of up to one year duration have shown that intranasal fluticasone propionate is not associated with an increased incidence of ocular events including cataract, increased intraocular pressure or glaucoma.

Respiratory, thoracic and mediastinal disorders:
Very common: Epistaxis.
Common: Nasal dryness, nasal irritation, throat dryness, throat irritation.
Very rare: Nasal septal perforation.
As with other nasal sprays, dryness and irritation of the nose and throat, and epistaxis have been reported. *Nasal septal perforation has also been reported following the use of intranasal corticosteroids.

Overdosage
There are no data available on the effects of acute or chronic overdosage with Fluticasone Propionate Aqueous Nasal Spray. Intranasal administration of 2 mg fluticasone propionate twice daily for seven days to healthy human volunteers had no effect on hypothalamic-pituitary-adrenal axis function.

Pharmacodynamic Properties
Fluticasone propionate causes little or no hypothalamic-pituitary-adrenal axis suppression following intranasal administration.
Following intranasal dosing of fluticasone propionate, (200 mcg/day) no significant change in 24 h serum cortisol AUC was found compared to placebo (ratiol.01, 90%CI 0.9-1.14).

Pharmacokinetic Properties
Absorption: Following intranasal dosing of fluticasone propionate, (200 mcg/day) steady-state maximum plasma concentrations were not quantifiable in most subjects (<0.01 ng/ml). The highest Cmax observed was 0.017 ng/ml. Direct absorption in the nose is negligible due to the low aqueous solubility with the majority of the dose being eventually swallowed. When administered orally the systemic exposure is <1% due to poor absorption and pre-systemic metabolism. The total systemic absorption arising from both nasal and oral absorption of the swallowed dose is therefore negligible.

Distribution: Fluticasone propionate has a large volume of distribution at steady-state (approximately 318 1). Plasma protein binding is moderately high (91%).

Metabolism: Fluticasone propionate is cleared rapidly from the systemic circulation, principally by hepatic metabolism to an inactive carboxylic acid metabolite, by the cytochrome P450 enzyme CYP3A4. Swallowed fluticasone propionate is also subject to extensive first pass metabolism. Care should be taken when Co-administering potent CYP3A4 inhibitors such as ketoconazole and ritonavir as there is potential for increased systemic exposure to fluticasone propionate.

Elimination: The elimination rate of intravenous administered fluticasone propionate is linear over the 250-1000 mcg dose range and are characterized by a high plasma clearance (CL=1.1 I/min). Peak plasma concentrations are reduced by approximately 98% within 3-4 hours and only low plasma concentrations were associated with the 7.8 h terminal half-life. The renal clearance of fluticasone propionate is negligible (<0.2%) and less than 5% as the carboxylic acid metabolite. The major route of elimination is the excretion of fluticasone propionate and its metabolites in the bile.

Further Information
Preclinical Safety Data:
Toxicology has shown only those class effects typical of a potent corticosteroid, and these only at doses greatly in excess of those proposed for therapeutic use. No novel effects were identified in repeat dose toxicity tests, reproductive toxicology studies or teratology studies. Fluticasone propionate is devoid of mutagenic activity in vitro and in vivo and showed no tumorigenic potential in rodents. It is both non irritant and non sensitising in animal models.

Pharmaceutical Precautions and Recommendations
Do not store above 30°C.

List of Excipients
Dextrose (anhydrous), Microcrystalline cellulose and carboxymethylcellulose sodium (Avicel RC591), Phenylethyl alcohol, Benzalkonium chloride, Polysorbate 80, Dilute hydrochloric acid, purified water.

Nature and Contents of Container
Fluticasone Propionate Aqueous Nasal Spray is supplied in an amber glass bottle fitted with a metering, atomising pump, nasal adaptor and a dust cover. Each bottle provides approximately 60 or 120 metered sprays, when used as recommended.

Instructions for Use
Shake gently before use.

Patient Information leaflet for Flixonase Aqueous Nasal Spray
(fluticasone propionate)
Your doctor has decided to prescribe Flixonase Aqueous Nasal Spray as part of your treatment.
This leaflet tells you about Flixonase and how to use it. Please read it carefully and keep it until you have finished the medicine.

What is Flixonase?
Flixonase Aqueous Nasal Spray contains 50 micrograms of the active ingredient fluticasone propionate in each spray. It also contains other substances needed to make a stable suspension which will not go off. These are microcrystalline cellulose, sodium carboxymethylcellulose, dextrose, polysorbate 80, dilute hydrochloric acid, purified water and the preservatives benzalkonium chloride and phenylethyl alcohol. Each bottle of Flixonase provides 60 sprays or 120 sprays.

How your medicine works?
Fluticasone propionate is a corticosteroid (steroid for short) which has an anti-inflammatory action. The tiny amounts sprayed into your nose help to reduce swelling and irritation.
Fluticasone propionate should not be confused with anabolic steroids misused by some athletes and taken as tablets or injection.

Uses
Flixonase is used to prevent and treat seasonal allergic rhinitis (e.g. hayfever) and perennial rhinitis in adults and children aged 4 years and over.
When you have rhinitis the inside of your nose becomes swollen and itchy. This often occurs during the early summer when it is caused by breathing in pollens from grasses or trees and is called hayfever. Some people get problems all the year round and this is called perennial rhinitis. It is often due to house dust mites or animals such as cats or, dogs.
When you spray Flixonase into your nose it helps to relieve the itching, sneezing and blocked or runny nose.

Make sure that this medicine is suitable for you
Tell your doctor before starting to take this medicine
if you are pregnant (or intending to become pregnant), if you are breast feeding a baby, if you have ever had an operation on your nose, if you have recently been treated with injected steroids or if you have been taking oral steroids for a long time, if you have ever had to stop taking this or another medicine for this illness because you were allergic to it or it caused problems, if you have, or recently had an infection, n your nose, if you are having other regular treatment, such as certain medicines used to treat fungal infections (e.g. ketoconazole) or a type of antiviral medicine known as protease inhibitor (e.g. ritonavir). Check with your pharmacist or doctor if you are not sure.

Sometimes this medicine may not be suitable and your doctor may want to give you something different. Make sure that your doctor knows what other medicines you are taking, including those you have bought from the chemist.
Remember to take this medicine with you if you have to go into hospital.

Using your nasal spray
Follow the instructions shown later in the leaflet. If you have any problems tell your doctor or pharmacist.
Make sure you know **how**, **when** and **how many** sprays you should use. Your doctor should have told you and the instructions should be on the pharmacist's label. If they are not, or you are not sure, ask your doctor or pharmacist.
Only use in your nose.

Dose
For adults and children aged 12 and over: the usual starting dose is 2 sprays into each nostril once daily, preferably in the morning. Your doctor may advise you to increase this to a maximum of 2 sprays twice daily.
As your symptoms become better, your doctor may advise you to use a lower dose of one spray into each nostril once a day. If your symptoms get worse again, your dose may be increased back again to the starting dose.
For children aged 4-11 years: the usual dose is one spray into each nostril once daily, preferably in the morning. Your doctor may advise you to increase this to one spray into each nostril twice daily. Your doctor will prescribe the lowest dose of Flixonase Aqueous Nasal Spray that will best control your symptoms.
Do not take a larger dose or use your nasal spray more often than your doctor advises.
It takes a few days or this medicine to work and it is **very important that you use it regularly. Do not stop treatment** even if you feel better unless told t do so by your doctor.
If you also have itchy, watery eyes you should tell your doctor. He or she may give you an extra medicine to treat your eyes. Be careful not to confuse them, particularly if the second medicine is eye drops.

If you miss a dose
If you miss a dose just take the next dose when it is due.

If you take too much
Tell your doctor if you accidentally take more than you were told to.

After using your nasal spray
You may sometimes sneeze a little after using this spray but this soon stops. Very occasionally you may experience an unpleasant taste or smell. If you are using high doses of Flixonase, you may require extra steroids in times of extreme stress, or during admission to hospital after a serious accident or injury, or before a surgical operation. Your doctor may decide to give you extra steroid medication during this period as tablets or injection if you are in hospital.

Side effects
Most people do not have any problems after using this spray. Some people occasionally have a headache after using the nasal spray. If your nose or throat becomes painful or if you have a bad nose bleed after using the nasal spray, tell your doctor as soon as possible.
There have been very rare reports of a severe allergic reaction to this medicine. If you suddenly develop a rash, swelling (usually of the face, lips or tongue) or difficulty with your breathing, stop using your Flixonase spray and contact your doctor **immediately**.
In very rare instances, treatment with some nasal corticosteroids may affect the normal production of steroids in the body. This is more likely to happen if high doses are being used over a long period of time. One of the rare effects is that children may grow more slowly than others.
Children who are receiving treatment over a long period of time will have their height checked regularly by their doctor. Your doctor will help prevent this happening by prescribing the lowest dose of steroid at which your symptoms are well-controlled.

If you feel unwell or have any other problems, tell your doctor and follow his or her advice.

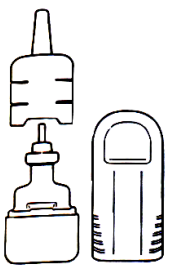
Storing your medicine
Keep the nasal spray in a safe place **where children cannot reach it**.
Do not store above 30°C.
Do not use this nasal spray after the date shown as 'EXP' on the label and carton.
If you are told to stop taking this medicine, **return any unused Flixonase to your pharmacist** to be destroyed.

Further information
Remember: This medicine is for **You**. Only a doctor can prescribe it for you. Never give it to someone else. It may harm them even if their symptoms are similar.
This leaflet does not tell you everything about your medicine. If you have any questions or are not sure about anything, ask your doctor or the pharmacist.
You will be able to find out more information about prescribed medicines from books in public libraries.
The information in this leaf1et only applies to Flixonase Aqueous Nasal Spray. Flixonase is a trade mark of the GlaxoSmithKline group of companies.

About your nasal spray
Your Flixonase Aqueous Nasal Spray has a dust cap which protects the nozzle and keeps it clean. Remember to take this off before using the spray. Replace the dust cap after use.
A new spray, or one which has not been used for a few days, may not work the first time. You may need to 'prime' the bottle by pumping the spray a few times until a fine mist is produced. To do this hold the bottle as shown. Put your forefinger and middle finger on the collar either side of the nozzle and your thumb underneath the bottle. Keeping your thumb still, press down with your fingers to pump the spray.
Hold the nozzle pointing away from you while you are doing this.
If the spray still doesn't work and you think it may be blocked, clean it as follows.
Never try to unblock it or enlarge the tiny spray hole with a pin or other sharp object because this will destroy the spray mechanism.

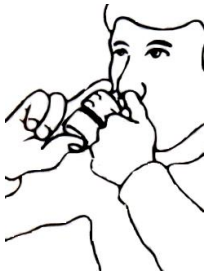
To clean the spray
1. Take the dust cap off by gently squeezing the ribbed sides between your finger and I thumb and lifting it off. Do not twist it off.
2. Pull upwards on the white collar to remove the nozzle.
3. Soak the nozzle and dust cap in warm water for a few minutes, and then rinse under a running tap.
4. Shake off the excess water and allow to dry in a warm, not hot, place.
5. Re-fit the nozzle.
6. 'Prime' the bottle if necessary by pumping the spray a few times until the fine mist is produced.

Your nasal spray should be cleaned at least once a week, or more often if it gets blocked.



Using the spray

1. Shake the bottle and remove the dust cap.
2. Blow your nose gently.
3. Close one nostril as shown and put the nozzle in the other nostril. Tilt your head forward slightly and keep the bottle upright. Hold the bottle as shown.
4. Start to breathe in slowly through your nose. **While you are breathing in** squirt a spray of fine mist into your nostril by pressing down firmly on the collar with your fingers.
5. Breathe out through your mouth. Repeat step 4 to take a second spray, in the same nostril.
6. Remove the nozzle from this nostril and breathe out through your mouth.



7. Repeat steps 3 to 6 for the other nostril.

After using the spray

Wipe the nozzle carefully with a clean tissue or handkerchief, and replace the dust cap.

GlaxoSmithKline

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