Rinisona

Fluticasone

Spray with dosing valve

MADE IN ARGENTINA
Rx only

FORMULA
Each dose contains:
Fluticasone propionate: 50 mcg
Excipients: anhydrous glucose 5 mg, microcrystalline cellulose +15% sodium carboxymethylcellulose 1.50 mg, phenylethyl alcohol 0.25 mg, benzalkonium chloride (50% sol) 0.020mg, tween 80 0.005 mg, hydrochloric acid (pH 6.3-6.5 qs) 0.1 µl, purified water qs 100 µl.

THERAPEUTIC ACTION
Fluticasone propionate is a corticosteroid for topical action. It has a potent anti-inflammatory activity but when used topically on the nasal mucosa, its bioavailability averages less than 2%. ATC Code: R01AD08.

INDICATIONS
Treatment and prophylaxis of seasonal allergic rhinitis, including hay fever, and perennial rhinitis.
Aqueous nasal Fluticasone propionate is also indicated in patients with allergic rhinitis, for the management of sinus pain and oppression associated with it.

CLINICAL PHARMACOLOGY
Pharmacological action
Fluticasone propionate, after intranasal administration, produces little or no suppression of the hypothalamic-adrenal axis.
After an intranasal dose of Fluticasone propionate (200 mcg/day) no changes were detected in the 24 hours serum cortisol AUC compared with placebo (radio 1.01; CI 90% 0.9-1.14).
Pharmacokinetics
Absorption: After intranasal administration of Fluticasone propionate, (200 mcg/day) maximum plasma concentration at steady state was 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 low water solubility, most of the dose is eventually swallowed.
Distribution: Fluticasone propionate has a large volume of distribution at steady state (approximately 318 l). Binding to plasma proteins is relatively high (91%).
Metabolism: Fluticasone propionate is rapidly cleared from the circulation mainly by hepatic metabolism to an inactive carboxylic acid metabolite by the enzyme cytochrome P450 CYP3A4. Swallowed fluticasone propionate is also subject to extensive first pass metabolism. Caution should be exercised when co-administered with potent CYP3A4 inhibitors such as ketoconazole and ritonavir as there is a potentially increased exposure to fluticasone propionate.
Elimination: The mode of clearance of fluticasone propionate administered intravenously is linear over the dose range of 250-1000 mcg and is characterized by a high plasma clearance (Cl = 1.1 l/min). The peak plasma concentration is reduced by approximately 98% within 3 to 4 hours and only low plasma concentrations were associated with the terminal half-life of 7.8 hours. The renal clearance of fluticasone propionate is negligible (< 0.2%) and less than 5% as the carboxylic acid metabolite. The main route of elimination of fluticasone propionate and its metabolite is excretion in the bile.

DOSAGE AND ADMINISTRATION:
Shake before using.
RINISONA should only be administered intranasally.
Adults: *For prophylaxis and treatment of seasonal allergic rhinitis and perennial rhinitis:*
Two sprays in each nostril once daily, preferably in the morning. The same dosage divided into 100 mcg given twice daily is also effective. Total daily dose: 200 mcg. After the first days, patients can reduce the dose to 100mcg / day: An application in each nostril once daily.
Elderly patients: Use the usual adult dose.
Adolescents and Children 4 Years of Age and Older: For prophylaxis and treatment of seasonal allergic rhinitis and perennial rhinitis, one spray in each nostril once daily, preferably in the morning, is recommended. In some cases, two sprays into each nostril once a day may be needed. Once control is achieved, the dose should be reduced back to one spray in each nostril. To achieve optimal results, it is essential to use the drug regularly. The absence of an immediate effect should be explained to the patient, since the maximum relief can not be obtained until after three to four days of treatment.

CONTRAINDICATIONS
RINISONA is contraindicated in patients with a hypersensitivity to any of its ingredients.

WARNINGS
The concomitant use of intranasal corticosteroids with other inhaled corticosteroids could increase the risk of hypercorticism and/or suppression of the HPA axis. Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals.

PRECAUTIONS
General: Rarely, immediate hypersensitivity reactions or contact dermatitis may occur after the administration of fluticasone. Rare instances of wheezing, nasal septum perforation, cataracts, glaucoma, and increased intraocular pressure have been reported following the intranasal application of corticosteroids, including fluticasone propionate. Use of excessive doses of corticosteroids may lead to signs or symptoms of hypercorticism, suppression of HPA function and/or a reduction in growth velocity in children or adolescents. Physicians should closely follow the growth of children and adolescents taking corticosteroids by any route and weigh the benefits of corticosteroid therapy against the possibility of growth suppression if this appears diminished. Although systemic effects have been minimal with recommended doses of fluticasone, potential risk increases with larger doses. Therefore, larger than recommended doses should be avoided. When used at higher than recommended doses, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of fluticasone should be discontinued slowly consistent with accepted procedures for discontinuing oral corticosteroid therapy. In clinical studies with fluticasone propionate administered intranasally, the development of localized infections of the nose and pharynx with Candida albicans has occurred only rarely. When such an infection develops, it may require treatment with appropriate local therapy and discontinuation of treatment with fluticasone. Patients using fluticasone over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa. Fluticasone should be used with caution in patients with active or quiescent tuberculous infections; systemic viral or parasitic infections; systemic fungal or bacterial infections; or ocular herpes simplex. Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or nasal trauma should not use a nasal corticosteroid until healing has occurred.
Local infection: The nasal tract infections must be treated properly, but they are not a specific contraindication to treatment with fluticasone. The full benefit of the drug will only be achieved after several days of administration. Special care should be taken when transferring patients from systemic corticosteroid therapy to fluticasone treatment in cases of suspected impaired adrenal function. Although fluticasone controls seasonal allergic rhinitis in most patients, an abnormally high exposure to summer allergens may require, in some cases, additional treatment.

During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing syndrome and adrenal suppression. Therefore, coadministration of fluticasone propionate and ritonavir is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. (See Drug Interactions)

Drug Interactions: Under normal circumstances, after intranasal administration very low concentrations of fluticasone propionate are reached , due to the majority first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Because of this, it is unlikely to produce clinically significant interactions mediated by fluticasone propionate. A drug interaction study with fluticasone in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can significantly increase plasma fluticasone propionate exposure, resulting in significantly reduced serum cortisol concentrations. During postmarketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing syndrome and adrenal suppression. Therefore, coadministration of fluticasone propionate and ritonavir is not recommended 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. However, caution is recommended when strong inhibitors of cytochrome P450 3A4 (eg. ketoconazole) are coadministered, due to possible increased systemic exposure to fluticasone propionate.

Pregnancy: There is inadequate evidence of safety in human pregnancy. In animal reproduction studies, adverse events typical of potent corticosteroids are only at high systemic exposure levels; direct intranasal application ensures minimal systemic exposure.
As with any drug, its administration should be considered only if the expected benefit to the mother outweighs any possible risk to the fetus.

Lactation: It has not been studied whether fluticasone passes into breast milk. When measurable plasma levels of fluticasone propionate were obtained after subcutaneous administration in laboratory tests, its presence was detected in the milk of lactating rats. On the other hand, in patients receiving intranasal fluticasone propionate at recommended doses, plasma levels are probably low.

SIDE EFFECTS

Immune System Disorders:
Very rare (<1/10.000): Hypersensitivity reactions, anaphylaxis / anaphylactoid reactions, bronchospasm, rash, facial or tongue edema.
Nervous System Disorders:
Common (≥1/100, <1/10): headache, altered taste, altered sense of smell.
As with other nasal sprays, alterations in taste and smell have been reported .
Respiratory, Thoracic and Mediastinal Disorders:
Very common (≥1/10): Epistaxis.
Common (≥1/100, <1/10): nasal dryness, nasal irritation, dryness and irritation of the throat.
Very rare (<1/10.000): nasal septum perforation.
As with other nasal sprays, dryness and irritation of the nose and throat, and epistaxis have been reported.
Nasal septum perforation has also been reported after use of intranasal corticosteroids.

The following adverse reactions have been reported during the marketing of fluticasone propionate:
In addition to the adverse reactions reported in clinical trials, the following adverse events have been identified during postmarketing use of fluticasone propionate in clinical practice. Because they are reported voluntarily from a population of uncertain size, their frequency can not been estimated. These events have been selected for inclusión because of the seriousness, frequency of reporting or causal connection to fluticasone propionate or a combination of these factors.
Eye Disorders: Glaucoma, increased intraocular pressure, cataract.

OVERDOSE
No data are available on the effects of acute or chronic overdosage with fluticasone. Intranasal administration of 2 mg twice daily for 7 days to healthy volunteers, had no effect on the function of the hypothalamic-pituitary-adrenal axis. In the case of a possible overdose, seek medical attention in the nearest hospital

STORAGE
Store at temperatures below 30 ºC. Keep cool and protected from light.

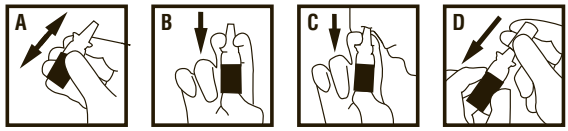
HOW SUPPLIED
Bottles with 120 doses.

KEEP THIS AND ALL MEDICINES AWAY FROM CHILDREN.

HOW TO USE
When you first use the nasal spray, actuate the valve for two or three times to complete the filling and get a full dose.
1. Blow your nose gently.
2. Shake the bottle vigorously and remove the protective cap.
3. Start to breathe in air slowly and as soon as the inspiration starts press firmly the valve of the nasal spray. Complete deep inspiration to allow the air to transport the drug completely.
4. Breathe normally three or four times, and then, according to the dose, apply on the same side or the other nostril.
5. Twice a week remove the valve and wash it under running hot water, let dry and replace.

ADHERING TO THESE INSTRUCTIONS, THE THERAPEUTIC QUALITIES OF THE PRODUCT ARE FULLY TAPPED.

HOW TO USE



Shake | **Position of the fingers to actuate the valve** | **Application** | **Replacement of the protective cap**

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Achrafieh-Chahrouri Street-Attallah Bldg., Beirut, Lebanon. Certificate Nº 195.335/04

"The sale packaging of this product has its trade name embossed in Braille system, in order to allow its identification by blind patients."

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