New Zealand Data Sheet

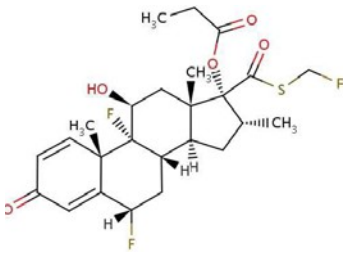
1 PRODUCT NAME

Fluticasone propionate (50 mcg per actuation) Aqueous Nasal Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Fluticasone propionate 50 mcg per actuation. CAS:

80474-14-2



Flixonase MW 500.57

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Aqueous suspension of microfine fluticasone propionate. Each 100 mg of spray contains 50 micrograms of fluticasone propionate. Nasal spray, suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Flixonase Allergy & Hayfever 24 Hour is indicated for the prophylaxis and treatment of allergic rhinitis including hay fever and that caused by other airborne allergens such as house dust mite, mould spores and animal dander.

During treatment Flixonase Allergy & Hayfever 24 Hour provides symptomatic relief of sneezing, itchy and runny nose, congestion including associated sinus discomfort and pressure around the nose and eyes. Flixonase Allergy & Hayfever 24 Hour also provides relief of ocular symptoms associated with allergic rhinitis.

4.2 Dose and method of administration

Flixonase Allergy & Hayfever 24 Hour is for administration by the intranasal route only.

Adults 18 years and over: For the prophylaxis and treatment of allergic rhinitis:-

The recommended dose is two sprays into each nostril once a day, preferably in the morning. Once control is achieved the dose should be titrated down to one spray in each nostril once a day (100 micrograms per day).

In some cases two sprays into each nostril twice daily may be required for short periods to achieve control of symptoms, after which the dose should be titrated down.

The maximum daily dose should not exceed four sprays into each nostril.

Onset of action in the treatment of allergic rhinitis has been observed in some patients as early as 2-4 hours after use, with most users achieving symptomatic relief within 12 hours of treatment.

Prophylaxis of allergic rhinitis requires treatment before contact with allergen.

For full therapeutic benefit regular usage is recommended.

Maximum benefit may require 3-4 days of continuous treatment in some people (Pharmacodynamic Properties).

Adolescents 12-17 years: Use only on medical advice. Do

not use in children under 12 years of age.

Elderly:-

The normal adult dosage is applicable

4.3 Contraindications

FLIXONASE Allergy & Hayfever 24 Hour is contra-indicated in patients with a hypersensitivity to fluticasone propionate or any other of the ingredients.

4.4 Special warnings and precautions for use

If improvement is not seen within 7 days of continuous use treatment should be stopped and the advice of a doctor sought.

If after 7 days of continuous use, symptoms have improved but are not adequately controlled then the advice of a pharmacist or doctor should be sought.

The nasal spray should not be used for more than 6 months continuously without consulting a doctor.

Local infection: Infections of the nasal airways should be appropriately treated but do not constitute a specific contraindication to treatment with intranasal fluticasone propionate

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Care must be taken when withdrawing patients from systemic steroid treatment, and commencing therapy with intranasal fluticasone propionate, particularly if there is any reason to

suspect that their adrenal function is impaired.

Systemic physiological and behavioural effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods and in children. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations.

Reduced growth velocity has been observed in children with intranasal corticosteroids.

Medical advice should be sought before using Flixonase Allergy & Hayfever 24 Hour in the case of:

- Concomitant use of other corticosteroid products, such as tablets, creams, ointments, asthma medications, similar nasal sprays or eye/nose drops.
- Fever or an infection in the nasal passages or sinuses.
- Recent injury or surgery to the nose, or problems with ulceration in the nose.

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 (*see Interaction with other medicines and other forms of interaction*).

The full benefit of fluticasone propionate aqueous nasal spray may not be achieved until treatment has been administered for several days.

Although fluticasone propionate aqueous nasal spray will control seasonal allergic rhinitis in most cases, an abnormally heavy challenge of summer allergens may in certain instances necessitate appropriate additional therapy.

Candidiasis of the throat can occur in patients treated with intranasal steroids. Special care should be taken when treating patients who may be susceptible to candida infections (eg diabetics).

Because of the inhibitory effect of these drugs on wound healing, patients with recent nasal septal ulcers, nasal surgery or nasal trauma should not use intranasal corticosteroids until healing has occurred.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicines and other forms ofinteraction

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.

4.6 Pregnancy and lactation

As with other drugs, the use of intranasal fluticasone propionate during pregnancy and lactation requires that the benefits be weighed against possible risks associated with the product or with any alternative therapy.

Pregnancy **(Category B3)**

There is inadequate evidence of the safety of fluticasone propionate 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. The use of Flixonase Allergy & Hayfever 24 Hour should be avoided during pregnancy unless thought essential by the doctor. Medical advice should be sought before use if pregnant.

Breast-feeding

Medical advice should be sought before use if breast-feeding.

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 very low.

4.7 Effects on ability to drive and use machines

Fluticasone propionate is unlikely to produce an effect.

4.8 Undesirable effects

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.
Not Known Vision Blurred.

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, Nasal ulcer.

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.

4.9 Overdose

Administration of doses higher than those recommended over a long period of time may lead to temporary suppression of adrenal function.

Symptoms and Signs

There are no data from patients available on the effects of acute or chronic overdosage with intranasal fluticasone propionate. In healthy volunteers, intranasal administration of 2 mg fluticasone propionate twice daily for seven days had no effect on hypothalamic-pituitary-adrenal *(HPA)* axis function (this equates to 20 times the recommended dose).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other Nasal preparations for Topical Use. Corticosteroids. ATC code: R01A D08

Mechanism of action

Fluticasone propionate is a glucocorticosteroid which has potent anti-inflammatory activity by acting via the glucocorticoid receptor. It has no detectable systemic activity and causes little or no hypothalamic pituitary adrenal (HPA) axis suppression. Following intranasal dosing of fluticasone propionate (200 mcg/day) no significant change in 24h serum cortisol AUC was found compared to placebo (ratio 1.01,90%CI 0.9-1.14).

Pharmacodynamic Effects

Fluticasone propionate has been shown to significantly reduce inflammatory mediators in both the early and late phase reactions of allergic rhinitis. As with other aqueous nasal sprays, Flixonase Allergy & Hayfever 24 Hour has an immediate soothing and cooling lavage effect in the nose, and onset of action has been observed in clinical trials to be as early as 2-4 hours after first use. Symptom relief (particularly of nasal congestion) is sustained for 24 hours following once daily administration of 200 mcg doses.

Quality of life studies have shown fluticasone propionate, when compared with placebo and antihistamine, to improve patient's routine functioning, including physical and social functioning, and sense of well-being as exemplified by effects on indicators of emotional health, mental health, and energy. In addition, patients receiving fluticasone propionate report superior impact (as compared to placebo and antihistamine) on work and school attendance and performance, and home and leisure/recreation activities affected as a result of symptoms of allergic rhinitis.

5.2 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 L). 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=1.1L/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.

5.3 Preclinical safety data

Toxicology studies in animals, including reproductive and development toxicology studies, have shown 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. Fluticasone propionate is devoid of mutagenic activity in vitro and in vivo and showed no tumorigenic potential in rodents. It is both non irritating and non sensitising in animal models.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Fluticasone propionate (50 mcg per actuation) Aqueous Nasal Spray contains the following excipients:

Dextrose (anhydrous)
Microcrystalline cellulose
Carboxymethylcellulose sodium
Phenylethyl alcohol Benzalkonium
chloride Polysorbate 80
Dilute hydrochloric acid Purified
water

6.2 Incompatibilities

Not applicable

6.3 Shelf life
24 Months

6.4 Special precautions for storage
Store at or below 30°C.
Protect from light. Do not freeze.

6.5 Nature and contents of container
FLIXONASE ALLERGY & HAYFEVER 24 HOUR 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/Handling:
Shake gently before use.

6.6 Special precautions for disposal
No special requirements.

7 MEDICINE SCHEDULE
Pharmacy Only Medicine.

8 SPONSOR
Haleon New Zealand ULC

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9 DATE OF FIRST APPROVAL
07 November 1991

10 DATE OF REVISION OF THE TEXT
November 2022
Issue: 26

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Transferred to new data sheet template
3.0	Addition of statement for pharmaceutical form section.
4.4	Addition of a statement in precautions sections for Candidiasis, Wound Healing and visual disturbances.
4.8	Addition of a statement under Eye disorders for- blurred vision and under Respiratory, thoracic and mediastinal disorders- nasal ulcer.
8	Update sponsor details to Haleon