

# Summary of Product Characteristics

## 1. NAME OF THE MEDICINAL PRODUCT

Flixonase Allergy Relief 50 micrograms per dose Nasal Spray

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each actuation delivers 100 mg of suspension containing 50 micrograms of fluticasone propionate.

Excipients: also includes 20 micrograms of Benzalkonium Chloride per spray.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Nasal spray, suspension

A white, opaque aqueous suspension intended for intranasal administration.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Flixonase Allergy Relief 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 and animal dander.

### 4.2 Posology and method of administration

Flixonase Allergy Relief is for administration by the intranasal route only.

#### ***Adults 18 years and over: for the prophylaxis and treatment of allergic rhinitis:***

Two sprays into each nostril once a day, preferably in the morning. Once control is achieved the dose should be titrated down to the lowest effective dose of 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 to the lowest effective dose (see above).

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

#### ***Elderly patients:***

The normal adult dosage is applicable.

#### ***Children and adolescents under 18 years of age:***

Do not use in those under 18 years of age.

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 (see section 5.1 *Pharmacodynamic Properties*).

When Flixonase Allergy Relief is discontinued, it may be several days before symptoms recur.

### 4.3 Contraindications

Flixonase Allergy Relief is contra-indicated in patients with a hypersensitivity to any of its ingredients.

### 4.4 Special warnings and precautions for use

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

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.

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 effects of nasal corticosteroids (such as Cushing's syndrome, hypertension, adrenal suppression) may occur, particularly at high doses prescribed for prolonged periods. 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 treated with intranasal corticosteroids.

Medical advice should be sought before using Flixonase Allergy Relief 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.

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.

### **Visual Disturbances**

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.

This product contains Benzalkonium Chloride. Long-term use may cause oedema of the nasal mucosa.

### 4.5 Interaction with other medicinal products and other forms of interaction

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.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

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 Fertility, 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**

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 Relief should be avoided during pregnancy unless thought essential by the doctor. Medical advice should be sought before use if pregnant.

### **Lactation**

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**

None reported.

## **4.8 Undesirable effects**

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  and  $< 1/10$ ), uncommon ( $\geq 1/1000$  and  $< 1/100$ ), rare ( $\geq 1/10,000$  and  $< 1/1000$ ) and very rare ( $< 1/10,000$ ) including isolated reports. Very common, common and uncommon events are 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.

System Organ Class	Adverse Event	Frequency
Immune system disorders	Hypersensitivity reactions, anaphylaxis/anaphylactic reactions, bronchospasm, skin rash, oedema of the face or tongue	Very rare
Nervous system, disorders	Headache, unpleasant taste, unpleasant smell	Common
Eye disorders	Glaucoma, raised intraocular pressure, cataract	Very rare
	Blurred Vision	Unknown
Respiratory, thoracic and mediastinal disorders	Epistaxis	Very common
	Nasal dryness, nasal irritation, throat dryness, throat irritation	Common
	Nasal septal perforation Nasal Ulcers	Very rare

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professional are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

**4.9 Overdose**

Administration of doses higher than those recommended over a long period of time may lead to temporary suppression of adrenal function.  
There is no data available on the effects of acute or chronic overdosage with Flixonase Allergy Relief. Intranasal administration of fluticasone propionate at 20 times the recommended dose in adults (2mg twice daily) for seven days to healthy human volunteers had no effect on hypothalamic-pituitary-adrenal axis function.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Nasal preparations, corticosteroids. ATC code: R01AD08

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

Fluticasone propionate has been shown to significantly reduce inflammatory mediators in both the early and late phase reactions of allergic rhinitis. Placebo-controlled clinical studies have demonstrated that intranasal fluticasone propionate significantly reduces the symptoms of allergic rhinitis.

In addition, comparator studies have shown that intranasal fluticasone propionate is more effective in treating nasal symptoms of allergic rhinitis than anti-histamines, but with a similar beneficial effect on eye symptoms.

As with other aqueous nasal sprays, fluticasone propionate has an immediate 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 use. However, most users experience symptomatic relief within 12 hours of starting treatment. Maximum relief may require 3-4 days of continuous treatment in some people.

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, (200mcg/day) steady-state maximum plasma concentrations were not quantifiable in most subjects (<0.01ng/mL). The highest C<sub>max</sub> observed was 0.017ng/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 318L). 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 characterised 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 7.8h 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

No clinically relevant findings were observed in preclinical studies.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Glucose Anhydrous  
Microcrystalline Cellulose and Carboxymethylcellulose (Carmellose) Sodium (Avicel RC591)  
Phenylethyl Alcohol  
Benzalkonium Chloride  
Polysorbate 80  
Dilute Hydrochloric Acid  
Purified Water

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.

**6.4 Special precautions for storage**

Do not store above 30°C. Do not refrigerate.

**6.5 Nature and contents of container**

Flixonase Allergy Relief is supplied in an amber glass Type I or III Ph. Eur. bottle fitted with a metering, atomising pump, nasal adapter and a dust cover.

Each bottle provides approximately 60 metered sprays, when used as recommended.

**6.6 Special precautions for disposal**

Shake gently before use.

**7. MARKETING AUTHORISATION HOLDER**

GlaxoSmithKline Consumer Healthcare (Ireland) Limited,  
12 Riverwalk,  
Citywest Business  
Campus, Dublin 24,  
Ireland

Trading as: Allen & Hanburys

**8. MARKETING AUTHORISATION NUMBER**

PA 0678/095/001

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 02 May 2003

Date of last renewal: 02 May 2008

**10. DATE OF REVISION OF THE TEXT**

May 2019