Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Flixonase Aqueous 50 micrograms per metered dose, nasal spray, suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered spray contains 50 micrograms of fluticasone propionate.

Excipients: also contains Benzalkonium chloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nasal spray, suspension.

Product imported from Poland:
White opaque aqueous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Fluticasone Propionate Aqueous Nasal Spray is indicated for the prophylaxis and treatment of seasonal allergic rhinitis including hay fever, and perennial rhinitis. Fluticasone propionate has potent anti-inflammatory activity but when used topically on the nasal mucosa has no detectable systemic activity.

4.2 Posology and method of 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 Patients:
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 or 4 days of treatment.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Systemic effects of nasal corticosteroids may occur particularly at high doses prescribed for prolonged periods. These effects vary between patients and different corticosteroids (please refer to Sections 5.1 and 5.2).

Growth retardation has been reported in children receiving some nasal corticosteroids at licensed doses. It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should be given to referring the patient to a paediatric specialist.

Treatment with higher than recommended doses of nasal corticosteroids may result in clinically significant adrenal suppression. If there is evidence for higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery (see section 5.1 for data on intranasal fluticasone propionate).

In some patients hoarseness or throat irritation may occur.

Particular care should be taken to minimise use of topical corticosteroids in patients with immunosuppression.

Transfer of patients from other therapies for rhinitis is preferably done when patients are reasonably stable. Following introduction of Flixonase it may be possible to reduce the other therapy. Particularly in those on systemic corticosteroids it is essential to carry out such decrements slowly and with great care in view of the possibility of induced impairment of adrenocortical function.

It is important to be on the look-out for intercurrent infections including local monilial infections, and to treat these appropriately.

Extremely rare cases of nasal septal perforation have been reported following the use of intranasal aerosol corticosteroids. Usually in patients who have had previous nasal surgery.

Occasionally sneezing attacks may follow use.

Local Infection: Infections of 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.

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, particularly to control eye symptoms.

During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systematic 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 systematic corticosteroid side effects. (see Section 4.5).

Fluticasone Propionate Aqueous Nasal Spray contains benzalkonium chloride which is an irritant. May cause skin reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Under normal circumstances, 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 intranasal or inhaled fluticasone propionate and ritonavir, resulting in systematic 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 systematic corticosteroid side effects.

Studies have shown that other inhibitors of cytochrome P450 3A4 produce negligible (erythromycin) and minor (ketoconazole) increase 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

Pregnancy:
There is inadequate evidence of safety in human pregnancy. In animal reproduction studies adverse effects typical of potent corticosteroid 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.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Adverse events are listed 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 form 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.

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 have also been reported following the use of intranasal corticosteroids.

4.9 Overdose

There is no data available on the effects of acute or chronic overdosage with Fluticasone Propionate Aqueous Nasal Spray. Intranasal administration of 2mg fluticasone propionate 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

Fluticasone propionate causes little or no hypothalamic-pituitary-adrenal axis suppression following intranasal or topical (dermal) administration, and only causes overt HPA axis suppression after very high oral doses (10mg qds-four times a day - i.e. 40mg daily and above). Plasma fluticasone propionate levels after intranasal doses of up to and including 1mg are low, around the limit of quantitation of the assay (0.05 nanograms/ml).

In a 1-year randomised, double blind, placebo-controlled parallel group growth study in pre-pubescent children aged 3 to 9 years (56 patients receiving intranasal fluticasone propionate and 52 receiving placebo,) no statistically significant difference in growth velocity was observed in patients receiving intranasal fluticasone propionate(200 micrograms per day nasal spray) compared to placebo. The estimated growth velocity over one year of treatment was 6.20cm/year (SE=0.23) in the placebo group and 5.99 cm/year (SE=0.23) in the fluticasone propionate group; the mean difference between treatments in growth velocity after one year was 0.20cm/year (SE=0.28,95%CI=-0.35,0.76). No evidence of clinically relevant changes in HPA axis function or bone mineral density was observed as assessed by 12-hour urinary cortisol excretion and dual-energy x-ray absorptiometry, respectively.

5.2 Pharmacokinetic properties

Following oral administration 87-100% of the dose is excreted in the faeces, up to 75% as unabsorbed parent compound depending on the dose. After 6mg oral 64% excreted as parent. There is a non active major metabolite. Following intravenous administration there is high plasma clearance suggestive of extensive hepatic extraction. From limited early data the terminal plasma half-life was estimated at 3h and the associated volume of distribution, over 3 times body weight. This is consistent with rapid elimination and extensive tissue distribution.

5.3 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrose anhydrous
Microcrystalline cellulose and carboxymethylcellulose
Phenylethyl Alcohol
Benzalkonium Chloride
Polysorbate 80
Dilute hydrochloric Acid (to pH 6.3-6.5)
Purified Water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The shelf-life expiry date of this product is the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 30°C

Do not refrigerate

6.5 Nature and contents of container

Flixonase Aqueous Nasal Spray suspension is supplied in an amber glass bottle fitted with a metering, atomising pump, nasal adapter and a dust cover, in an overlabelled carton.

Each bottle provides approximately 120 metered sprays, when used as recommended.

6.6 Special precautions for disposal and other handling

Shake gently before use.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

PCO Manufacturing
Unit 10, Ashbourne Business Park
Rath
Ashbourne
Co Meath
Ireland

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 465/285/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20th January 2012

10 DATE OF REVISION OF THE TEXT