SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Nasofan Allergy 50 microgram Nasal Spray

Boots Allergy Relief 50 Microgram Nasal Spray

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 microlitre metered spray contains 50 microgram (mcg) of fluticasone propionate.

For full list of excipients, see 6.1

3 PHARMACEUTICAL FORM

Nasal spray.

The medical product consists of an amber glass multidose bottle fitted with a metering pump.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nasofan Allergy 50 microgram Nasal Spray 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.

Nasofan Allergy 50 microgram Nasal Spray provides symptomatic relief of sneezing, itchy and runny nose, itchy and watery eyes, nasal congestion and associated sinus discomfort.

4.2 Posology and method of administration

Nasofan Allergy 50 microgram Nasal Spray is for administration by the intranasal route only.

Shake the bottle gently before each use. Prior to first use Nasofan Allergy 50 microgram Nasal Spray must be primed by pressing down and releasing the pump six times. If Nasofan Allergy 50 microgram Nasal Spray has not been used for 7 days it must be reprimed by pressing down and releasing the pump a sufficient number of times until a fine mist is produced.

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

Two sprays into each nostril once a day (200 mcg) preferably in the morning is recommended. In some cases two sprays into each nostril twice a day (400 mcg) may be required. Once symptoms are under control a maintenance dose of one spray per nostril once a day (100 mcg) may be used. If symptoms recur the dosage may be increased accordingly. The maximum daily dose should not exceed four sprays into each nostril (400 mcg). The minimum dose at which the effective control of symptoms is maintained should be used.

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:

Should not be used by children and adolescents under 18 years of age.

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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

Administration of treatment may be necessary for several days for the full benefit of Nasofan Allergy 50 microgram Nasal Spray to be achieved.

Upon transferring patients from systemic steroid treatment to Nasofan Allergy 50 microgram Nasal Spray, care must be taken if there is any reason to suppose that their adrenal function is impaired.

Treatment should be stopped or the advice of a doctor sought if an improvement is not seen within 7 days. The advice of a doctor or pharmacist should also be sought if symptoms have improved but are not adequately controlled.

Nasofan Allergy 50 microgram Nasal Spray should not be used for more than 3 months continuously without consulting a doctor.

Medical advice should be sought before using Nasofan Allergy 50 microgram Nasal Spray in the case of;
• concomitant use of other corticosteroid products, such as tablets, creams, ointments, asthma medications, similar nasal sprays or eye/nose drops.
• an infection in the nasal passages or sinuses.
• recent injury or surgery to the nose, or problems with ulceration in the nose.

In most cases Nasofan Allergy 50 microgram Nasal Spray will control seasonal allergic rhinitis, however in the event of an abnormally heavy challenge of summer allergens appropriate additional therapy may be necessitated in certain instances. Such an instance may particularly be to control eye symptoms.

Systemic effects of nasal corticosteroids 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. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Please refer to section 5.1 and 5.2.

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 cause 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.

Adrenal suppression may occur to clinically significant levels as a result of treatment with higher than recommended doses of nasal corticosteroids. 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).

Incidences of significant interactions between fluticasone propionate and potent inhibitors of the cytochrome P450 3A4 system (e.g. ketoconazole and protease inhibitors such as ritonavir) may occur. Increased systemic exposure to fluticasone propionate may result (e.g. Cushing's Syndrome and adrenal suppression have been observed). Therefore concomitant use of fluticasone propionate and ritonavir should be avoided unless the expected benefit exceeds the possible risk of systemic adverse reaction of corticosteroids. (see section 4.5 "Interaction with other medicinal products and other forms of interaction").

In patients who have tuberculosis, any type of untreated infection, ocular herpes or have had a recent surgical operation or injury to the nose or mouth, the possible benefits of the treatment should be weighed against possible hazards.
Local infections: infections of the nasal airways should be appropriately treated but do not constitute a specific contraindication to treatment with Nasofan Allergy 50 microgram Nasal Spray.

Nasofan Allergy 50 microgram Nasal Spray contains benzalkonium chloride. Irritant may cause skin reactions. If used for longer periods, the preservative benzalkonium chloride may cause nasal mucosa swelling. In the case of such a reaction (persistently congested nose) then preservative-free medicinal products for nasal use should be used if possible; however if such preservative-free medicinal products are not available another pharmaceutical form should be taken.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of fluticasone propionate on other drugs
No significant effect of fluticasone propionate on the pharmacokinetics of terfenadine and erythromycin has been shown during drug interaction studies.

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 in the liver. Hence, clinically significant drug interactions mediated by fluticasone propionate are unlikely.

Effects of other drugs on fluticasone propionate

No significant effect of terfenadine and erythromycin on the pharmacokinetics of fluticasone propionate has been shown during drug interaction studies.
(See 4.4 Special Warnings and Precautions for Use).

In an interaction study in healthy subjects with intranasal fluticasone propionate, ritonavir (a highly potent cytochrome P450 3A4 inhibitor) 100mg b.i.d. increased the fluticasone propionate plasma concentration several hundred fold, resulting in markedly reduced serum cortisol concentrations s. Cases of Cushing's syndrome and adrenal suppression have been reported. The combination should be avoided unless the benefit outweighs the increased risk of systemic glucocorticoid side-effects. 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 (see section 4.4).

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. Care is advised when co-administering cytochrome P450 3A4 inhibitors, especially in long-term use and in case of potent inhibitors, as there is potential for increased systemic exposure to fluticasone propionate.

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.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Women of childbearing potential have to use effective contraception during treatment.

Pregnancy
There is inadequate evidence of safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development, including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus. It should be noted, however, that the foetal changes in animals occur after relatively high systemic exposure; direct intranasal application ensures minimal systemic exposure.

As with other drugs the use of Nasofan Allergy 50 microgram Nasal Spray during human pregnancy requires that the possible benefits of the drug be weighed against the possible hazards.

Breast-feeding
The secretion of fluticasone propionate in human breast milk has not been investigated. Subcutaneous administration of fluticasone propionate to lactating laboratory rats produced measurable plasma levels and evidence of fluticasone propionate in the milk. However, following intranasal administration to primates, no drug was detected in the plasma, and it is therefore unlikely that the drug would be detectable in milk. When Nasofan Allergy 50 microgram Nasal Spray is used in breast feeding mothers the therapeutic benefits must be weighed against the potential hazards to mother and baby.

The label will include a warning that medical opinion should be sought, before using Nasofan Allergy Nasal Spray, in the case of pregnancy or breast-feeding.

4.7 Effects on ability to drive and use machines

Nasofan Allergy 50 microgram Nasal Spray has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most frequently reported side effects were epistaxis (> 1/10) followed by headache, unpleasant taste and smell, dryness and irritation of the nose, dryness and irritation of the pharynx (> 1/100 to < 1/10)
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), very rare (<1/10,000) not known (cannot be estimated from the available data).

System Organ Class	Adverse Event	Frequency
Immune system disorders	Hypersensitivity reactions with the following manifestations:	
	Bronchospasm	Rare
	Anaphylactic reactions	Rare
	Anaphylactoid reactions	Rare
	Cutaneous hypersensitivity reactions	Very rare
	Angioedema (mainly facial and oropharyngeal oedema)	Very rare
Nervous system, disorders	Headache, unpleasant taste, unpleasant smell.	Common
Eye disorders	Glaucoma, raised intraocular pressure, cataract These events have been identified from spontaneous reports following prolonged treatment.	Very rare
	Vision, blurred (see also section "Special warnings and precautions for use")	Not Known.
Respiratory, thoracic and mediastinal disorders	Epistaxis	Very common
	Nasal dryness, nasal irritation, throat dryness, throat irritation	Common
	Nasal septal perforation*, mucocutaneous ulceration Usually in patients who have had previous nasal surgery.	Very rare
	Nasal ulcers	Not known

*Cases of perforation of the nasal septal wall have been reported as a result of the use of corticosteroids.

As with other nasal sprays, dryness and irritation of the nose and throat, unpleasant taste and smell, epistaxis and headache have been reported.

Extremely rare cases of nasal ulceration and nasal septal perforation have been reported following the use of intranasal corticosteroids, usually in patients who have had previous nasal surgery.

Systemic effects of some nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods (see section 4.4 “Special warnings and precautions for use”).

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 professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There are no data available on the effects of acute or chronic overdose with Nasofan Allergy 50 microgram Nasal Spray. Intranasal administration of fluticasone propionate at 20 times the recommended starting dose in adults (2 mg twice daily) for seven days to healthy human volunteers has no effect on hypothalamo-pituitary-adrenal (HPA) axis function.

Inhalation or oral administration of high doses of corticosteroids over a long period may lead to suppression of HPA axis function.

In these patients, the dose should be gradually reduced and treatment with Nasofan Allergy 50 microgram Nasal Spray continued at a dosage sufficient to control the symptoms. The adrenal cortex function is restored within a few days, which can be verified by measuring plasma cortisol.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Decongestants and other nasal preparations for topical use
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, (200 microgram/day) no significant change in 24h serum cortisol AUC was found compared to placebo (ratio1.01, 90%CI 0.9-1.14).

Fluticasone propionate has been shown to reduce inflammatory mediators in both the early and late phase reactions of allergic rhinitis.
Once daily dosing with 200µg fluticasone propionate is sufficient to help relieve symptoms (particularly nasal congestion) for up to 24 hours.

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 6.20 cm/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 0.20 cm/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

Absorption: Following intranasal dosing of fluticasone propionate, (200 microgram/day) steady-state maximum plasma concentrations were not quantifiable in most subjects (<0.01ng/mL). The highest Cmax 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%).

Biotransformation: 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 microgram 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

Toxicology and reproduction studies, as well as teratogenic studies, have shown only class effects typical of potent corticosteroids in higher doses than recommended. Fluticasone propionate is without mutagenic activity *in vitro* as well as *in vivo* and exhibits no carcinogenic potential in rodents. It does not irritate or sensitize animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucose
Microcrystalline Cellulose
Carmellose Sodium
Phenylethyl Alcohol
Benzalkonium Chloride
Polysorbate 80
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years, unopened.
3 months after opening.

6.4 Special precautions for storage

Do not store above 25°C
Discard three months after first using the spray.

6.5 Nature and contents of container

Nasofan Allergy 50 microgram Nasal Spray is supplied in an amber glass bottle (Type 3) fitted with an atomising metering pump. Each bottle provides approximately 60 metered sprays.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited,
Ridings Point, Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom

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