Professional Information for

FLUTICASONE 50 µg NASAL SPRAY UNICORN

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

FLUTICASONE 50 µg NASAL SPRAY UNICORN metered-dose nasal spray (aqueous suspension)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

FLUTICASONE 50 µg NASAL SPRAY UNICORN contains fluticasone propionate 0,05 % *w/w* per actuation. Each actuation contains 0,050 mg of fluticasone propionate.

Preservatives: benzalkonium chloride (50 %) 0,04 % *w/w*.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Nasal Spray (aqueous suspension)

White homogenous aqueous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

FLUTICASONE 50 µg NASAL SPRAY UNICORN is indicated for the prophylaxis and treatment of seasonal and perennial allergic rhinitis including hay fever in adults and children over 12 years old, and the short-term treatment of seasonal allergic rhinitis in children 4 - 11 years old.

4.2 Posology and method of administration

Posology

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 to 4 days of treatment.

Adults and children over 12 years of age:

For the prophylaxis and treatment of perennial and seasonal allergic rhinitis: Two sprays in each nostril once a day, preferably in the morning. In certain cases two sprays in each nostril twice a day may be required. The maximum daily dose is two sprays in each nostril twice a day.

Special populations

Use in elderly: The normal adult dose is applicable.

Paediatric population:

Children aged 4 to 11 years:

For the prophylaxis and treatment of seasonal allergic rhinitis in children aged 4 - 11 years a dose of one spray into each nostril once daily is recommended. The maximum daily dose should not exceed two sprays into each nostril.

Safety and efficacy has not been studied for periods longer than 4 weeks.

For the prophylaxis and treatment of perennial allergic rhinitis in children of this age (4 - 11 years), there are insufficient clinical data at present to recommend the use of FLUTICASONE 50 µg NASAL SPRAY UNICORN.

Method of administration

Shake gently before use.

FLUTICASONE 50 µg NASAL SPRAY UNICORN is for administration by the intranasal route only.

4.3 Contraindications

Hypersensitivity to fluticasone proprionate or any of the excipients of FLUTICASONE 50 µg NASAL SPRAY UNICORN (see Section 6.1).

4.4 Special warnings and precautions for use

Infections in the nasal cavity should be treated appropriately but do not constitute a specific contra-indication to treatment with FLUTICASONE 50 µg NASAL SPRAY UNICORN.

The full benefit of FLUTICASONE 50 µg NASAL SPRAY UNICORN may not be achieved until treatment has been administered for several days.

Caution is advised when transferring patients from systemic corticosteroid treatment to FLUTICASONE 50 µg NASAL SPRAY UNICORN, if there is any reason to suspect that the patient’s adrenal function is compromised.

FLUTICASONE 50 µg NASAL SPRAY UNICORN may cause hypothalamic-pituitary-adrenal (HPA) axis suppression following intranasal administration at dosages higher than recommended.

Excessive summer allergens may require additional but appropriate therapy, particularly to control eye symptoms.

High doses prescribed for prolonged periods of nasal corticosteroids may have systemic effects. These effects are less likely to occur than with oral administration of corticosteroids and may vary

in individual patients and between different corticosteroids preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Growth retardation has been reported in children receiving certain nasal corticosteroids at appropriate doses. It is strongly 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 goal of reducing the dose of nasal corticosteroid to the lowest dose required for maintenance of effective control of symptoms. Consideration should also 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 higher than recommended doses is administered then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

Concomitant use with ritonavir should be avoided, as ritonavir can greatly increase the concentration of fluticasone propionate in plasma. There is also an increased risk of systemic side effects when combining fluticasone propionate with other potent CYP3A inhibitors.

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient experiences 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 diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

This medicine contains 0,040 mg benzalkonium chloride in each 100 g actuation which is equivalent to 0,040 % *w/w*.

Long-term use may cause oedema of the nasal mucosa.

Benzalkonium chloride may cause wheezing and breathing difficulties (bronchospasm), especially if you have asthma.

4.5 Interaction with other medicines and other forms of interaction

Under normal circumstances, low plasma concentrations of fluticasone propionate are achieved after inhaled dosing, due to extensive first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Hence, clinically significant medicine interactions mediated by fluticasone propionate are unlikely.

Interaction studies have demonstrated ritonavir (a highly potent cytochrome P450 3A4 inhibitor) 100 mg twice a day increased the fluticasone propionate plasma concentrations several hundred fold, resulting in markedly reduced serum cortisol concentrations. Cases of Cushing's syndrome and adrenal suppression have been reported. Unless the benefit outweighs the increased risk of systemic glucocorticoid side effects this combination should be avoided.

The slightly less potent CYP3A inhibitor ketoconazole increased the exposure of fluticasone propionate after a single inhalation by 150 %. This resulted in a greater reduction of plasma cortisol as compared with fluticasone propionate alone. Co-administration with other potent CYP3A inhibitors, such as itraconazole, is also expected to increase the systemic fluticasone propionate exposure and the risk of systemic side effects.

Caution is recommended and long term treatment with such medicines should if possible be avoided.

Co-treatment with other potent CYP3A inhibitors, including cobicistat-containing medicines, is expected to increase the risk of systemic side effects.

Other CYP3A4 inhibitors produce insignificant (erythromycin) and minor (ketoconazole) increases in systemic exposure to fluticasone propionate without notable reductions in serum cortisol concentrations. Combinations should be avoided, in which case patients should be monitored for systemic corticosteroid side effects.

4.6 Fertility, pregnancy and lactation

The safety of FLUTICASONE 50 µg NASAL SPRAY UNICORN in pregnancy and lactation has not been established.

Pregnancy

Corticosteroids have been shown to be teratogenic (such as abnormalities of foetal development, including cleft palate and intrauterine growth retardation) in animals. Therefore, a very small risk of such effects in the human foetus may occur.

Teratogenicity cannot be excluded, as these medicines may be absorbed systemically when administered intra-nasally. However, it should be noted, that the foetal changes in animals occur after elatively high systemic exposure; direct intranasal administration ensures minimal systemic exposure.

The use of FLUTICASONE 50 µg NASAL SPRAY UNICORN during human pregnancy requires that the possible benefits of the medicine be weighed against the possible hazards.

Breastfeeding

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 fluticasone propioate was detected in the plasma, and it is therefore unlikely that the medicine would be detectable in breast milk. When FLUTICASONE 50 µg NASAL SPRAY UNICORN is used in breastfeeding mothers the therapeutic benefits must be weighed against the potential hazards to mother and baby.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

The most frequently reported undesirable effect was nausea.

System Organ Class	**Frequency**	**Adverse reaction**
Immune system disorders	Less frequent	Hypersensitivity reactions with the following manifestations: cutaneous hypersensitivity reactions, angioedema (mainly facial and oropharyngeal oedema), respiratory symptoms (bronchospasm) and anaphylactic reactions
Nervous system disorders	Frequent	Headache, unpleasant taste, unpleasant smell
Eye disorders	Less frequent	Glaucoma, raised intraocular pressure, cataract

System Organ Class	Frequency	Adverse reaction
		These events have been identified from spontaneous reports following prolonged treatment
	Frequency unknown	Blurred vision
Respiratory, Thoracic & Mediastinal disorders	Frequent	Epistaxis, nasal dryness, nasal irritation, throat dryness, throat irritation
	Less frequent	Nasal septal perforation
	Frequency unknown	Nasal ulcers

Description of selected adverse reactions

There have been reports of unpleasant taste and smell and headache, as well as 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. Systemic side effects of some nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Side effects must also be reported to Unicorn Pharmaceuticals (Pty) Ltd to vigilance@unicornpharma.co.za.

4.9 Overdose

There is no data available from patients on the effects of acute or chronic overdosage with fluticasone proprionate.

Chronic administration of FLUTICASONE 50 µg NASAL SPRAY UNICORN in excess of the recommended daily dosage and / or in conjunction with other corticosteroid formulations may lead to suppression of the hypothalamic-pituitary- adrenal (HPA) function. Monitoring of adrenal reserve may be required.

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

Further treatment would be supportive and symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Decongestants and other nasal preparations for topical use Corticosteroids.

ATC code: R01AD08

Pharmacological classification: A 21.5.1 Corticosteroids and analogues

Fluticasone propionate has potent anti-inflammatory activity and has no detectable systemic activity when used topically on the nasal mucosa. Following intranasal administration, fluticasone propionate causes little or no hypothalamic-pituitary-adrenal axis suppression.

5.2 Pharmacokinetic properties

Absorption: Following intranasal administration of fluticasone propionate (200mcg/day), steady-

state maximum plasma concentrations were not measurable in most subjects (< 0,01 ng/ml). The highest C_{max} detected 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 insignificant.

Distribution: The volume of distribution of fluticasone propionate is large at steady-state (approximately 260 L). Plasma protein binding is moderately high (91 %).

Metabolism: Hepatic metabolism clears fluticasone propionate rapidly from the systemic circulation to an inactive carboxylic acid metabolite, by the cytochrome P450 enzyme CYP3A4. Swallowed fluticasone propionate is may also undergo extensive first pass metabolism. Caution is advised 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=1,1 L/min). Peak plasma levels are reduced by approximately 98 % within 3 – 4 hours and only low plasma concentrations accompanied the 7,8 hour 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 via bile.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate, dextrose monohydrate, disodium hydrogen phosphate, microcrystalline cellulose and sodium carboxymethyl cellulose (Avicell RC 591) and polysorbate 80.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 ºC.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

FLUTICASONE 50 µg NASAL SPRAY UNICORN is contained in white HDPE bottle, metered dose micro pump with nasal actuator and dust protective cap, with 120 actuations in each plastic (HDPE) bottle.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER(S)

53/21.5.1/0609

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 November 2023

10 DATE OF REVISION OF THE TEXT

08 April 2025