SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE:

FLUTICASONE OTC TEVA (nasal spray)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

FLUTICASONE OTC TEVA: Each metered nasal spray contains 50 µg fluticasone propionate.

Contains sugar (glucose anhydrous 5 mg per spray).

(For the full list of excipients, see **section 6.1**).

3. PHARMACEUTICAL FORM:

Nasal spray, Suspension.

FLUTICASONE OTC TEVA: A white to off-white, opaque aqueous suspension for nasal inhalation via a metering pump.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

FLUTICASONE OTC TEVA is indicated for the short-term (less than 6 months) prophylaxis and treatment of symptoms of allergic rhinitis (hay fever) in adults and children over 12 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 allergic rhinitis (hay fever).

Two sprays into each nostril once a day, preferably in the morning.

Elderly patients:

The normal adult dosage is applicable.

Method of administration:

Shake gently before use.

FLUTICASONE OTC TEVA is for administration by the intranasal route only.

4.3 Contraindications:

Hypersensitivity to fluticasone propionate or to any excipients listed in **section 6.1**.

4.4 Special warnings and precautions for use:

Local infections: infections of the nasal airways should be appropriately treated but do not constitute a specific contraindication to treatment with **FLUTICASONE OTC TEVA**.

The full benefit of **FLUTICASONE OTC TEVA** may not be achieved until treatment has been administered for several days.

Care must be taken while transferring patients from systemic steroid treatment to **FLUTICASONE OTC TEVA** if there is any reason to suppose that their adrenal function is impaired.

Although **FLUTICASONE OTC TEVA** will control seasonal allergic rhinitis in most cases, an abnormally heavy challenge of summer allergens may in certain instances necessitate appropriate additional therapy.

Systemic effects of nasal corticosteroids may occur particularly at high doses prescribed for prolonged periods. 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 some nasal corticosteroids.

Ritonavir can increase the concentration of fluticasone propionate in plasma. Therefore, concomitant use should be avoided. There is also an increased risk of systemic side effects when combining fluticasone propionate with other potent CYP3A inhibitors (see **4.5 Interaction with other medicines and other forms of interaction**).

Visual disturbance:

Visual disturbance may be reported with 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 topical corticosteroids.

FLUTICASONE OTC TEVA contains benzalkonium chloride which may cause irritation or swelling inside the nose, especially if used for a long time.

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.

In an interaction study in healthy subjects with intranasal fluticasone propionate, ritonavir (a highly potent cytochrome P450 3A4 inhibitor) 100 mg twice daily 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.

In a small study using inhaled fluticasone propionate in healthy patients, 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-treatment 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 inhibitors of CYP3A4 produce negligible (erythromycin) and minor (ketoconazole) increases in systemic exposure to fluticasone propionate without notable reductions in serum cortisol concentrations. Combinations should be avoided unless the benefit outweighs the potential 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:

Pregnancy:

Safety during pregnancy has not been established. Corticosteroids have been shown to be teratogenic in animals. As these medicines may be absorbed systemically when administered intra-nasally, teratogenicity cannot be excluded.

There is inadequate evidence of **FLUTICASONE OTC TEVA** safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development, including cleft palate and intra-uterine growth retardation.

Breastfeeding:

Safety during breastfeeding has not been established.

The secretion of fluticasone propionate in human breast milk has not been investigated.

Fertility:

There are no data available for the effect of **FLUTICASONE OTC TEVA** on fertility.

4.7 Effects on ability to drive and use machines:

FLUTICASONE OTC TEVA may cause blurred vision therefore patients should refrain from driving or operating machinery until they are reasonably certain that **FLUTICASONE OTC TEVA** therapy does not adversely affect their ability to engage in such activities.

4.8 Undesirable effects:

SYSTEM ORGAN CLASS:	FREQUENCY:	ADVERSE EVENT:
Immune system disorders:	*Less frequent*	Hypersensitivity reactions with the following manifestations: cutaneous hypersensitivity reactions, angioedema (mainly facial and oropharyngeal oedema), respiratory symptoms (bronchospasm), anaphylactic reactions
Nervous system disorders:	*Frequent*	Headache, unpleasant taste, unpleasant smell
Eye disorders:	*Less frequent*	Glaucoma*, raised intraocular pressure*, cataract*
	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

* These events have been identified from spontaneous reports following prolonged treatment.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after registration of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine.

Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the '**6.04 Adverse Drug Reactions Reporting Form**', found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose:

There are no data from patients available on the effects of acute or chronic overdosage with **FLUTICASONE OTC TEVA**. Inhalation or oral administration of high doses of corticosteroids over a long period may lead to suppression of HPA axis function.

Treatment:

Monitoring of adrenal reserve may be indicated. Further treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

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

ATC Code: R01AD08

Mechanism of action:

Fluticasone propionate has anti-inflammatory activity.

Pharmacodynamic properties:

Following intranasal dosing of fluticasone propionate, (200 mcg/day) no significant change in 24 hour serum cortisol AUC was found compared to placebo (ratio 1,01; 90 % CI 0,9-1,14).

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 C_{max} 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 260 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=1,1 L/min). Peak plasma concentrations are reduced by approximately 98 % within 3-4 hours and only low plasma concentrations were associated with the 3 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 in the bile.

5.3 Preclinical safety data:

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Professional Information.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Excipients: dispersible cellulose, glucose anhydrous, polysorbate 80, purified water.

Preservatives: benzalkonium chloride (40 micrograms per delivered dose) and phenylethyl alcohol 0,25 % m/m.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

2 years.

6.4 Special precautions for storage:

Store at or below 25 °C.

Discard 3 months after opening the bottle.

6.5 Nature and contents of container:

12 ml (60 sprays) or 15 ml (120 sprays) amber glass bottle (Type III) fitted with an atomising metering pump and a nasal adaptor with a dust cap, packed in an outer carton.

Each bottle will provide 60 or 120 sprays respectively with each spray delivering 50 microgram of fluticasone propionate in 100 mg of formulation through the nasal adaptor.

Pack sizes: 60 and 120 metered sprays.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling:

Shake gently before use.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd,

Maxwell Office Park,

Magwa Crescent West,

Waterfall City,

Midrand,

Gauteng,

2090

Tel: 011 055 0200

8. REGISTRATION NUMBER(S):

FLUTICASONE OTC TEVA: 48/21.5.1/0960

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

20 July 2021

10. DATE OF REVISION OF THE TEXT: