Applicant: Teva Pharmaceuticals (Pty) Ltd	Product name: Mysteva OTC (nasal spray, suspension)
	Each spray actuation delivers 27,5 micrograms of fluticasone furoate.
Registration date: 21.10.2025 **Reg No:** 58/21.5.1/0117	

APPROVED PROFESSIONAL INFORMATION:

PROFESSIONAL INFORMATION:

SCHEDULING STATUS:

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1. NAME OF THE MEDICINE:

MYSTEVA OTC (27,5 micrograms/spray, nasal spray suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each spray actuation delivers 27,5 micrograms of fluticasone furoate.

Preservative: benzalkonium chloride 0,015 % w/w.

Excipient(s) with known effect:

One actuation delivers 8,25 micrograms of benzalkonium chloride.

For a full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM:

Nasal spray, suspension

Milky white suspension with no agglomerates.

The suspension is homogenous, re-dispersible and free of visible foreign particulate matter.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Adults and children over 12 years of age:

MYSTEVA OTC nasal spray is indicated in the short-term (less than 6 months) prophylaxis and treatment of the symptoms of seasonal allergic rhinitis (hay fever) in adults and children over 12 years of age.

4.2 Posology and method of administration:

Posology:

For full therapeutic benefit regular scheduled usage is recommended. Onset of action has been observed as early as 8 hours after initial administration. It may take several days of treatment to achieve maximum benefit. An absence of an immediate effect should be explained to the patient.

Adults and children over 12 years of age:

The recommended starting dosage is two sprays (27,5 micrograms of fluticasone furoate per spray) in each nostril once daily (total daily dose: 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to one spray in each nostril (total daily dose: 55 micrograms) may be effective for maintenance.

Special populations:

Elderly patients:

The normal adult dosage is applicable.

Renal patients:

The normal adult dosage is applicable.

Hepatic patients:

No dose adjustment is required in patients with hepatic impairment (see **section 5.2**).

Paediatric population:

MYSTEVA OTC nasal spray is not intended for children under 12 years of age.

Method of administration:

MYSTEVA OTC nasal spray is for administration by the intranasal route only.

Shake the nasal spray before use.

The intranasal device should be shaken before use and the protective cap removed afterwards. Prior to first use the device must be primed by pressing down and release the pump for at least ten spray actuations (until a fine mist is seen), whilst holding the bottle upright.

Re-priming (approximately 10 sprays until a fine mist is seen) is only necessary if the cap is left off for 5 days or the intranasal device has not been used for 30 days or more.

The device should be cleaned after each use and the protective cap to be replaced.

4.3 Contraindications:

- Hypersensitivity to fluticasone furoate or to any of the excipients of MYSTEVA OTC nasal spray listed in **section 6.1**.

4.4 Special warnings and precautions for use:

Systemic corticosteroid effects:

If there is any reason to suppose that adrenal function is impaired, care must be taken when transferring patients from systemic steroid treatment to MYSTEVA OTC.

Systemic effects of nasal corticosteroid may occur, particularly at high doses prescribed for prolonged periods. These effects are less likely to occur than with oral corticosteroids and may vary between patients

and different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and less frequently, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

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.

Fluticasone furoate 110 micrograms once daily was not associated with hypothalamic-pituitary-adrenal (HPA) axis suppression in adult, adolescent or paediatric subjects. However, the dose of intranasal MYSTEVA OTC should be reduced to the lowest dose at which effective control of the symptoms of rhinitis are maintained. The total systemic burden of corticosteroids should be considered whenever other forms of corticosteroid treatment are prescribed concurrently.

Visual disturbance:

Medical practitioners should be alert to the risk that potential systemic steroid effects including ocular changes.

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.

Growth retardation:

Growth retardation has been reported in children receiving nasal corticosteroids, such as fluticasone furoate as contained in MYSTEVA OTC, at licensed doses. A reduction in growth velocity has been

observed in children treated with fluticasone furoate 110 micrograms daily for one year (see **section 4.8**). Therefore, children should be maintained on the lowest dose which delivers adequate symptom control (see **section 4.2**).

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 MYSTEVA OTC, 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. MYSTEVA OTC is not indicated in children under 12 years of age (see **section 4.2**).

Patients on ritonavir:

Concomitant administration with ritonavir is not recommended because of the risk of increased systemic exposure of fluticasone furoate (see **section 4.5**).

Excipients:

MYSTEVA OTC contains benzalkonium chloride (see **section 6.1**). Long-term use may cause oedema of the nasal mucosa.

4.5 Interaction with other medicines and other forms of interaction:

Interaction with CYP3A inhibitors:

Fluticasone furoate is rapidly cleared by extensive first pass metabolism mediated by the cytochrome P450 3A4.

Based on data with another glucocorticoid (fluticasone propionate), that is metabolised by CYP3A4, coadministration with ritonavir is not recommended because of the risk of increased systemic exposure of fluticasone furoate.

Caution is recommended when co-administering MYSTEVA OTC with potent CYP3A inhibitors including cobicistat-containing products as an increase in the risk of systemic side effects is expected. Co-administration 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. In an interaction study of intranasal fluticasone furoate with the potent CYP3A4 inhibitor ketoconazole there were more subjects with measurable fluticasone furoate concentrations in the ketoconazole group (6 of the 20 subjects) compared to placebo (1 out of 20 subjects). This small increase in exposure did not result in a statistically significant difference in 24 hour serum cortisol levels between the two groups.

The enzyme induction and inhibition data suggest that there is no theoretical basis for anticipating metabolic interactions between fluticasone furoate and the cytochrome P450 mediated metabolism of other compounds at clinically relevant intranasal doses. Therefore, no clinical studies have been conducted to investigate interactions of MYSTEVA OTC on other medicines.

4.6 Fertility, pregnancy and lactation:

Pregnancy:

Safety and efficacy of MYSTEVA OTC in pregnancy has not been established.

Breastfeeding:

It is unknown whether nasal administered fluticasone furoate is excreted in human breast milk.

Safety and efficacy of MYSTEVA OTC in lactation has not been established.

Fertility:

There are no fertility data in humans.

4.7 Effects on ability to drive and use machines:

Based on the pharmacodynamic and pharmacokinetic profile, MYSTEVA OTC has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects:

Summary of the safety profile:

The most frequently reported adverse reactions during treatment with MYSTEVA OTC are epistaxis, nasal ulceration and headache. The most serious undesirable effects are less frequent reports of hypersensitivity reactions, including anaphylaxis.

TABULATED LIST OF ADVERSE REACTIONS:

MedDRA System organ class:	
Immune system disorders:	
Less frequent:	Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria
Nervous system disorders:	
Frequent:	Headache
Eye disorders:	
Unknown frequency:	Transient ocular changes, vision blurred (see also **section 4.4**)
Respiratory, thoracic and mediastinal disorders:	
Frequent:	Epistaxis*, nasal ulceration, dyspnoea**
Less frequent:	Rhinalgia, nasal discomfort (including nasal burning, nasal irritation, and nasal soreness),

	nasal dryness, nasal septum perforation
Unknown frequency:	Bronchospasm
Musculoskeletal and connective tissue disorders:	
Unknown frequency:	Growth retardation

Description of selected adverse reactions:

Epistaxis:

*Epistaxis was generally mild to moderate in intensity. In adults and adolescents, the incidence of epistaxis was higher in longer-term use (more than 6 weeks) than in short-term use (up to 6 weeks).

Systemic effects:

Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods (see **section 4.4**). Growth retardation has been reported in children receiving nasal corticosteroids, such as MYSTEVA OTC.

**Dyspnoea cases were reported in more than 1 % of patients during clinical trials with fluticasone furoate; similar rates were also observed in placebo groups.

Paediatric population:

MYSTEVA OTC is not indicated in children under 12 years of age.

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. Healthcare providers are requested 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 the SAHPRA website.

4.9 Overdose:

In a bioavailability study, intranasal doses of up to 2 640 micrograms per day were administered over three days with no adverse systemic reactions observed (see **section 5.2**). Acute overdose is unlikely to require any therapy other than observation.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

Category and class: A 21.5.1 Corticosteroids and analogues.

Pharmacotherapeutic group: Nasal preparations, corticosteroids.

ATC code: R01AD12.

Mechanism of action:

Fluticasone furoate is a synthetic trifluorinated corticosteroid that possesses a high affinity for the glucocorticoid receptor and has a potent anti-inflammatory action.

5.2 Pharmacokinetic properties:

Absorption:

Fluticasone furoate undergoes incomplete absorption and extensive first-pass metabolism in the liver and gut resulting in negligible systemic exposure. The intranasal dosing of 110 micrograms once daily does not typically result in measurable plasma concentrations (< 10 pg/ml). The absolute bioavailability for intranasal fluticasone furoate is 0,50 %, such that less than 1 microgram of fluticasone furoate would be systemically available after administration of 110 micrograms (see **section 4.9**).

Distribution:

The plasma protein binding of fluticasone furoate is greater than 99 %. Fluticasone furoate is widely distributed with volume of distribution at steady state of, on average, 608 L.

Biotransformation:

Fluticasone furoate is rapidly cleared (total plasma clearance of 58,7 L/h) from systemic circulation principally by hepatic metabolism to an inactive 17β-carboxylic metabolite (GW694301X), by the cytochrome P450 enzyme CYP3A4. The principal route of metabolism was hydrolysis of the S-fluoromethyl carbothioate function to form the 17β-carboxylic acid metabolite. *In vivo* studies have revealed no evidence of cleavage of the furoate moiety to form fluticasone.

Elimination:

Elimination was primarily via the faecal route following oral and intravenous administration indicative of excretion of fluticasone furoate and its metabolites via the bile. Following intravenous administration, the elimination phase half-life averaged 15,1 hours. Urinary excretion accounted for approximately 1 % and 2 % of the orally and intravenously administered dose, respectively.

Specific patient groups:

Elderly:

Only a small number of elderly subjects (n = 23/872; 2,6 %) provided pharmacokinetic data. There was no evidence for a higher incidence of subjects with quantifiable fluticasone furoate concentrations in the elderly, when compared with the younger subjects.

Renal impairment:

Fluticasone furoate is not detectable in urine from healthy volunteers after intranasal dosing. Less than 1

% of dose-related material is excreted in urine and therefore renal impairment would not be expected to affect the pharmacokinetics of fluticasone furoate.

Hepatic impairment:

There are no data on intranasal fluticasone furoate in participants with hepatic impairment. Data are available following inhaled administration of fluticasone furoate (as fluticasone furoate or fluticasone furoate/vilanterol) to subjects with hepatic impairment that are also applicable for intranasal dosing. A study of a single 400 micrograms dose of oral inhaled fluticasone furoate in patients with moderate hepatic impairment (Child-Pugh B) resulted in increased C_{max} (42 %) and AUC $(_{0-\infty})$ (172 %) compared to healthy subjects. Following repeat dosing of orally inhaled fluticasone furoate/vilanterol for 7 days, there was an increase in fluticasone furoate systemic exposure (on average two-fold as measured by AUC $(_{0–24})$) in subjects with moderate or severe hepatic impairment (Child-Pugh B or C) compared with healthy subjects. The increase in fluticasone furoate systemic exposure in subjects with moderate hepatic impairment (fluticasone furoate/vilanterol 200/25 micrograms) was associated with an average 34 % reduction in serum cortisol compared with healthy subjects. There was no effect on serum cortisol in subjects with severe hepatic impairment (fluticasone furoate/vilanterol 100/12,5 micrograms). Based on these findings the average predicted exposure for 110 micrograms of intranasal fluticasone furoate in this patient population would not be expected to result in suppression of cortisol.

Paediatric population:

Fluticasone furoate is typically not quantifiable (< 10 pg/ml) following intranasal dosing of 110 micrograms once daily. Quantifiable levels were observed in < 16 % of paediatric patients following intranasal dosing of 110 micrograms once daily and only < 7 % of paediatric patients following 55 micrograms once daily. There was no evidence for a higher incidence of quantifiable levels of fluticasone furoate in younger children (less than 6 years of age).

At 110 micrograms, median concentrations in those subjects with quantifiable levels were 14,3 pg/ml and 14,4 pg/ml for 2 to 5 years and 6 to 11 years, respectively. The values are similar to those seen in adults (12+) where median concentrations in those subjects with quantifiable levels were 15,4 pg/ml and 21,8 pg/ml at 55 micrograms and 110 micrograms, respectively.

MYSTEVA OTC is not indicated for children under 12 years of age (see **section 4.2**).

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Benzalkonium chloride

Disodium edetate

Glucose

Microcrystalline cellulose and carmellose sodium

Polysorbate 80

Water for injections

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

24 months.

In-use shelf life: 2 months.

6.4 Special precautions for storage:

Store at or below 25 ºC.

Do not refrigerate or freeze.

Store upright.

Always keep the cap on after use.

6.5 Nature and contents of container:

12 ml Type III amber bottle (glass) fitted with a metering spray pump, a white nasal applicator (actuator) and a clear cap.

MYSTEVA OTC is available in one pack size: 1 bottle of 120 sprays.

6.6 Special precautions for disposal and other handling:

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd.

Maxwell Office Park

Magwa Crescent West

Waterfall City, Midrand

Gauteng, South Africa

2090

8. REGISTRATION NUMBER(S):

58/21.5.1/0117

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

21 October 2025

10. DATE OF REVISION OF THE TEXT: