AUSTRALIAN PRODUCT INFORMATION
VYMAZE (fluticasone furoate) NASAL SPRAY

1 NAME OF THE MEDICINE

Fluticasone furoate.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each spray of the suspension delivers approximately 27.5 micrograms of micronised fluticasone furoate as an ex-device dose.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Nasal spray suspension.

VYMAZE Nasal Spray is a white to off white, opaque, thixotropic suspension of micronised fluticasone furoate for topical administration to the nasal mucosa by means of a metering atomising spray pump.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the treatment of seasonal allergic rhinitis and perennial allergic rhinitis in adults and children of ages 2 years and older.

4.2 DOSE AND METHOD OF ADMINISTRATION

VYMAZE Nasal Spray is for administration by the intranasal route only.

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

Patients should be instructed that the device must be primed:

- before first use, and
- if the cap is left off
- if the device does not seem to be working
- if the nasal spray has not been used for 30 days or more.

To prime the device, the nasal spray needs to be shaken vigorously for about 10 seconds with the cap on. This is important as fluticasone furoate is a thick suspension that becomes liquid when vigorously shaken. It will only spray when it becomes liquid.

The patient must then press the actuator firmly all the way down, approximately 6 times until a fine mist is seen, (to ensure a full dose is delivered).

Once primed, the patient must shake the nasal spray vigorously each time before use.

The cap must be replaced after use to keep the nozzle clean and to prevent the need for re-priming.

Patients must follow the step by step instruction in the consumer medicine information for use and handling.

For seasonal allergic rhinitis and perennial allergic rhinitis

Adults and Adolescents (12 years and over)

The recommended starting dosage is 2 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 once daily (total daily dose, 55 micrograms) may be effective for maintenance.

Children (2 to 11 years of age)

The recommended starting dosage is 1 spray (27.5 micrograms of fluticasone furoate per spray) in each nostril once daily (total daily dose, 55 micrograms).

Patients not adequately responding to 1 spray in each nostril once daily (total daily dose, 55 micrograms) may use 2 sprays in each nostril once daily (total daily dose, 110 micrograms).

Once adequate control of symptoms is achieved, dose reduction to 1 spray in each nostril once daily (total daily dose, 55 micrograms) is recommended.

Children under 2 years of age

There is no experience in children under the age of 2 years.

Special patient groups

Elderly patients

No dosage adjustment required (see Section 5.2 PHARMACOKINETIC PROPERTIES, Special patient populations).

Patients with renal impairment

No dosage adjustment required (see Section 5.2 PHARMACOKINETIC PROPERTIES, Special patient populations).

Patients with hepatic impairment

No dosage adjustment is required (see Section 5.2 PHARMACOKINETIC PROPERTIES, Special patient populations).

4.3 CONTRAINDICATIONS

VYMAZE is contraindicated in patients with a history of hypersensitivity to any components of the preparations (see Section 2 QUALITATIVE AND QUANTITATIVE COMPOSITION and Section 6.1 LIST OF EXCIPIENTS).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with all intranasal corticosteroids, the total systemic burden of corticosteroids should be considered whenever other forms of corticosteroids are prescribed concurrently.

Local infection

Infection of the nasal airways should be appropriately treated but does not constitute a contraindication to treatment with fluticasone furoate. After nasal surgery, healing must have occurred before use.

Nasopharyngeal candidiasis can occur in patients treated with intranasal steroids, as a class effect. Special care should be taken when treating patients who may be susceptible to candida infections (e.g. diabetics).

Systemic effects/adrenocortical function

Systemic effects with nasal corticosteroids have been reported, 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. Intranasal steroid products are designed to deliver drug directly to the nasal mucosa to minimise overall systemic glucocorticoid exposure and side effects.

Topical corticosteroids may be absorbed in amounts that can have systemic effects. Use of excessive doses may cause suppression of HPA function, reduction in bone density and retardation of growth rate in adolescents and children.

The lowest dose of fluticasone furoate that causes suppression of the HPA axis, effects on bone mineral density or growth retardation has not yet been established. However, the systemic bioavailability of fluticasone furoate is low (estimated at 0.50%) and this limits the potential for systemic side effects. Measurement of serum cortisol concentrations in clinical studies did not suggest any HPA axis suppression with recommended doses.

Ocular effects

As with other intranasal corticosteroids, physicians should be alert for evidence of systemic effects including ocular changes. Rare instances of glaucoma and increased intraocular pressure have been reported following the administration of intranasal corticosteroids, as a class effect. Therefore, close monitoring is warranted in patients with a history of increased intraocular pressure, glaucoma and/or cataracts.

If a patient presents with a change in vision, 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).

Paediatric use

Growth retardation has been reported in children receiving some nasal corticosteroids 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 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and Section 5.1 PHARMACODYNAMIC PROPERTIES). Therefore, children should be maintained on the lowest dose which delivers adequate symptom control (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

The potential growth effects of treatment should be weighed against the clinical benefits and availability of safe and effective non-corticosteroid alternatives.

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.

Use in the elderly

No dosage adjustment required (see Section 5.2 PHARMACOKINETIC PROPERTIES – Special patient populations).

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Fluticasone furoate is rapidly cleared by extensive first pass metabolism mediated by the cytochrome P450 3A4. In a drug 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 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 fluticasone furoate on other drugs (see Section 5.2 PHARMACOKINETIC PROPERTIES).

Based on data with another glucocorticoid metabolised by CYP3A4, co-administration with ritonavir is not recommended because of the potential risk of increased systemic exposure to fluticasone furoate.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There were no effects on mating performance or fertility of male or female rats in which systemic exposure to fluticasone furoate was achieved by inhalational administration.

Use in pregnancy

(Category B3)

There is insufficient evidence of safety of fluticasone furoate in human pregnancy. Systemically absorbed corticosteroids are known to induce fetotoxic and teratogenic effects in rodent studies. However, equivalent effects have not been reported when these compounds have been given to humans during pregnancy. Following intranasal administration of fluticasone furoate at the maximum recommended human dose (110 micrograms per day), plasma concentrations were typically non-quantifiable (see Section 5.2 PHARMACOKINETIC PROPERTIES). Fetal exposure and therefore potential for reproductive toxicity is expected to be very low. As with other compounds of this class, the use of VYMAZE during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus.

Use in lactation

The excretion of fluticasone furoate into human breast milk has not been investigated. Related drugs are known to be excreted in the milk of lactating rats. However, plasma levels in patients following intranasal application of fluticasone furoate at recommended doses are low, and therefore the amount of fluticasone furoate ingested by the newborn is likely to be very small.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Fluticasone furoate is unlikely to produce an effect.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Fluticasone furoate nasal spray was well tolerated in adult, adolescent and paediatric subjects 2 years of age and older with seasonal allergic rhinitis and/or perennial allergic rhinitis over two- and six-week treatment periods. The compound was also well tolerated in longer term use over a period of 12 weeks in paediatric subjects and over a period of one year in adult and adolescent subjects**.**

Adverse Events

A summary of the adverse events occurring at an incidence of ≥ 3% and more frequently in the fluticasone furoate than placebo group in the adult and adolescent perennial allergic rhinitis long-term safety study (FFR102123) is provided below:

Adverse Event	Number (%) of subjects	
	Placebo (N = 201)	Fluticasone furoate 110 microgram (N = 605)
Nasopharyngitis	51 (25)	157 (26)
Epistaxis	17 (8)	123 (20)
Back pain	12 (6)	39 (6)
Cough	7 (3)	29 (5)
Toothache	5 (2)	29 (5)
Nausea	6 (3)	20 (3)
Pharyngitis	5 (2)	18 (3)
Diarrhoea	5 (2)	17 (3)
Bronchitis	4 (2)	17 (3)
Conjunctivitis	3 (1)	18 (3)
Nasal dryness	1 (< 1)	17 (3)

Adverse Reactions

Data from large clinical trials were used to determine the frequency of adverse reactions. The following convention has been used for the classification of frequency:

- Very common ≥ 1/10
- Common ≥ 1/100 and < 1/10
- Uncommon ≥ 1/1,000 and < 1/100
- Rare ≥ 1/10,000 and < 1/1000
- Very rare < 1/10,000

Respiratory, thoracic and mediastinal disorders

Very Common: 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 six weeks) than in short term use (up to six weeks). In paediatric clinical studies of up to 12 weeks duration the incidence of epistaxis was similar between fluticasone furoate and placebo.

Common: Nasal ulceration

Children

Not known: Growth retardation

In a one-year clinical study assessing growth in pre-pubescent children receiving 110 micrograms of fluticasone furoate once daily, an average treatment difference of -0.27 cm per year (95% confidence interval (CI): -0.48, -0.06 cm) in growth velocity was observed compared to placebo (see Section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical Trials).

Post-marketing Data

Immune system disorders

Rare: Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria.

Nervous system disorders

Common: Headache.

Respiratory, thoracic and mediastinal disorders

Uncommon: Rhinalgia, nasal discomfort (including nasal burning, nasal irritation, and nasal soreness), nasal dryness.

Very rare: Nasal septum perforation.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

In a bioavailability study, intranasal doses of up to 2640 micrograms per day were administered over three days with no adverse systemic effects observed (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Acute overdose is unlikely to require any therapy other than observation.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Fluticasone furoate is a synthetic trifluorinated corticosteroid that possesses a very high affinity for the glucocorticoid receptor and when administered intranasally, has a potent anti-inflammatory action in the airway).

Clinical trials

Seasonal and Perennial Allergic Rhinitis in Adults and Adolescents (12 years and over)

Five randomised, double blind, parallel group, placebo-controlled trials have investigated the safety and efficacy of fluticasone furoate nasal spray 110 micrograms once daily in adults and adolescents 12 years of age and older with symptoms of seasonal or perennial allergic rhinitis. The five trials include one 2-week dose-ranging trial in patients with seasonal allergic rhinitis (FFR20001), three 2-week efficacy trials in patients with seasonal allergic rhinitis (FFR30003, FFR103184, FFR104861), and one 4-week efficacy trial in patients with perennial allergic rhinitis (FFR30002).

The primary efficacy variable for all studies was based on the daily assessment of four nasal symptoms (rhinorrhoea, nasal congestion, nasal itching and sneezing) using a four-point (0 [none] to 3 [severe]) categorical scoring scale, with the maximum score being 12, called the total nasal symptom score (TNSS). The reflective TNSS (rTNSS) requires the patient to record symptom severity over the previous 12 hours; the instantaneous TNSS (iTNSS) requires the patient to record symptom severity at the time immediately prior to the next dose. Morning and evening rTNSS scores were averaged over the treatment period and the difference in placebo in the change from baseline rTNSS was the primary efficacy variable.

Additional key secondary efficacy variables were assessed, including mean change from baseline over the entire treatment period in AM pre-dose iTNSS, mean change from baseline over the entire treatment period in daily reflective total ocular symptom score (rTOSS) (applicable to the seasonal allergic rhinitis trials only, excluding FFR20001) and the patients' perception of overall response to therapy. The total ocular symptom score (TOSS) was calculated on the daily assessment of three ocular symptoms (itching/burning, tearing/watering, and redness) using a four-point (0 [none] to 3 [severe]) categorical scoring scale, with the maximum score being 9.

In the four seasonal allergic rhinitis trials, fluticasone furoate nasal spray 110 micrograms once daily significantly improved nasal symptoms (comprising rhinorrhea, nasal congestion, sneezing and nasal itching) and ocular symptoms (comprising itching/burning, tearing/watering and redness of the eyes) compared with placebo (see Table 1). The improvement was maintained over the full 24 hours after once daily administration as evaluated by AM predose iTNSS (treatment effect ranged from, -0.902 to -1.898, $p < 0.001$ across the four studies). Similar improvement was observed for AM rTNSS and PM rTNSS and AM rTOSS and PM rTOSS suggesting consistent day time and nighttime relief of nasal and ocular symptoms.

Table 1: Seasonal Allergic Rhinitis – primary and secondary key endpoints

Study	Primary Endpoint: Daily rTNSS		Secondary Endpoint: Daily rTOSS	
	LS Mean Difference (95% CI)	p-value	LS Mean Difference (95% CI)	p-value
FFR20001	-2.012 (-2.58, -1.44)	< 0.001	–	–
FFR30003	-0.777 (-1.28, -0.27)	0.003	-0.546 (-0.95, -0.14)	0.008
FFR103184	-1.757 (-2.28, -1.23)	< 0.001	-0.741 (-1.14, -0.34)	< 0.001
FFR104861	-1.473 (-2.01, -0.94)	< 0.001	-0.600 (-1.01, -0.19)	0.004

rTNSS = reflective Total Nasal Symptom Scores (comprising rhinorrhea, nasal congestion, sneezing and nasal itching);

rTOSS = reflective Total Ocular Symptom Scores (comprising itching/burning, tearing/watering and redness of the eyes);

LS = Least square; LS Mean Difference = LS mean change from baseline in active – LS mean change from baseline in placebo;

CI = Confidence Interval.

Onset of action was experienced as early as eight hours after initial administration. Significant improvement in symptoms was observed in the first 24 hours in all studies and continued to improve over several days.

Fluticasone furoate nasal spray significantly improved the patients' perception of overall response to therapy. Additionally, the patients' quality of life (assessed by the Rhinoconjunctivitis Quality of Life Questionnaire – RQLQ), was significantly improved from baseline with fluticasone furoate nasal spray compared to placebo (Minimum Important Difference in all studies = improvement of at least -0.5 over placebo; treatment difference ranged from -0.572 to -1.000, $p < 0.001$, across the four studies).

In the perennial allergic rhinitis trial, fluticasone furoate nasal spray 110 micrograms once daily significantly improved nasal symptoms compared to placebo (mean change from baseline in daily rTNSS, LS mean difference = -0.706, $p = 0.005$, 95% CI: -1.20, -0.21). The improvement in nasal symptoms was maintained over the full 24 hours after once daily administration. The patients' perception of overall response to therapy was significantly improved compared to placebo. Although numerical improvements in overall RQLQ scores with fluticasone furoate

nasal spray 110 micrograms were noted, these were not statistically significant when compared to placebo.

In a two-year study designed to assess the ocular safety of fluticasone furoate (110 micrograms once daily) nasal spray, adults and adolescents with perennial allergic rhinitis received either fluticasone furoate nasal spray (n = 367) or placebo (n = 181). The primary outcomes [time to increase in posterior subcapsular opacity (≥ 0.3 units from baseline in Lens Opacities Classification System, Version III (LOCS III grade, a visual comparison classification system)) and time to increase in intraocular pressure (IOP; ≥ 7 mmHg from baseline)] were not statistically significant between the two groups. Increases in posterior subcapsular opacity (≥ 0.3 units from baseline) were more frequent in subjects treated with fluticasone furoate nasal spray 110 micrograms [14 (4%)] versus placebo [4 (2%)] and were transient in nature for ten subjects in the fluticasone furoate nasal spray group and two subjects in the placebo group. Increases in IOP (≥ 7 mmHg from baseline) were more frequent in subjects treated with fluticasone furoate nasal spray 110 micrograms: 7 (2%) for fluticasone furoate nasal spray 110 micrograms once daily and 1 (< 1%) for placebo. These events were transient in nature for four subjects in the fluticasone furoate nasal spray group and one placebo subject; for two additional subjects in the fluticasone furoate group the finding occurred at the final visit and it could not be determined whether the event was transient or not. At weeks 52 and 104, 95% of subjects in both treatment groups had posterior subcapsular opacity values within ± 0.1 of baseline values for each eye and, at week 104, ≤ 1% of subjects in both treatment groups had ≥ 0.3 increase from baseline in posterior subcapsular opacity. At weeks 52 and 104, the majority of subjects (> 95%) had IOP values of within ± 5mmHg of the baseline value. Increases in posterior subcapsular opacity or IOP were not accompanied by any adverse events of cataracts or glaucoma.

Seasonal and Perennial Allergic Rhinitis in Children (2 to 11 years of age)

The paediatric dose is based on assessment of the efficacy data across the allergic rhinitis population in children.

Two randomised, double blind, parallel group, placebo-controlled trials have investigated the safety and efficacy of fluticasone furoate nasal spray 55 micrograms and 110 micrograms once daily in the treatment of children 2 to < 12 years of age with symptoms of seasonal or perennial allergic rhinitis.

In the seasonal allergic rhinitis trial (FFR100010) of two weeks duration, fluticasone furoate nasal spray 110 micrograms once daily was effective on primary (daily rTNSS, LS mean difference = -0.616, p = 0.025, 95% CI: -1.15, -0.08) and all secondary nasal endpoints, except the individual reflective score for rhinorrhea. No significant differences were observed between fluticasone furoate nasal spray 55 micrograms and placebo on any endpoint.

In the perennial allergic rhinitis trial (FFR30008) of twelve weeks duration, with the primary endpoint assessed over the first 4 weeks, fluticasone furoate nasal spray 55 micrograms once daily was effective on daily rTNSS (LS mean difference = -0.754, p = 0.003, 95% CI: -1.24, -0.27). Although there was a trend towards improvement in rTNSS with fluticasone furoate nasal spray 110 micrograms this did not reach statistical significance (LS mean difference = -0.452, p = 0.073, 95% CI: -0.95, 0.04).

The above efficacy results are based on children 6 to < 12 years of age. Efficacy in children 2 to < 6 years of age was supported by a numerical decrease in the rTNSS.

A randomised, double-blind, parallel-group, multicenter, one-year placebo-controlled clinical growth study (FFR101782) evaluated the effect of fluticasone furoate nasal spray 110 micrograms daily on growth velocity in 474 prepubescent children (5 to 7.5 years of age for girls and 5 to 8.5 years of age for boys) with stadiometry. Mean growth velocity over the 52-week treatment period was lower in the patients receiving fluticasone furoate nasal spray (5.19 cm/year) compared to placebo (5.46 cm/year). The mean treatment difference was -0.27 cm per year [95% CI: -0.48, to -0.06].

At baseline, mean daily 24-h rTNSS as reported by subjects in the placebo group was similar to rTNSS reported by the fluticasone furoate nasal spray group (6.099 and 6.118, respectively).

Daily 24-h rTNSS decreased in both the placebo and fluticasone furoate nasal spray groups over 1-52 weeks of treatment. This reduction in nasal symptom scores was consistently equal or greater for the fluticasone furoate nasal spray treated group (mean change from baseline -1.23) over treatment weeks 1–52 compared with the placebo treated group (mean change from baseline -0.99). Study treatment compliance based on daily e-diary recordings was high and similar between the treatment groups, and was supported by changes in nasal spray device weights.

These findings may have been due to several factors including the naturally occurring increase and decrease in frequency and severity of the symptoms of PAR; the subjective nature of symptom ratings; variations in the maturity of the patients; the need for parental assistance in rating symptoms; and the availability of the study supplied loratadine syrup. Mean loratadine syrup rescue medication use was approximately 0.5 teaspoon per day for both treatment groups over the 52-week treatment period. There was little change from baseline in the percentage of rescue-free days for both treatment groups (-2.23%, placebo; -2.96%, fluticasone furoate nasal spray).

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Fluticasone furoate undergoes extensive first-pass metabolism and incomplete absorption 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 picograms/mL). Fluticasone furoate has a low (0.50%) systemic bioavailability at intranasal doses of up to 2,640 micrograms per day.

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

Metabolism

Fluticasone furoate is rapidly cleared (total plasma clearance of 58.7L/h) from systemic circulation principally by hepatic metabolism to an inactive 17β-carboxylic metabolite, 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.

Excretion

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.

Special patient populations

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 to the younger subjects).

Children

Fluticasone furoate is typically not quantifiable (< 10 picograms/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).

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 is no data on intranasal fluticasone furoate in subjects 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 microgram 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 (up to 3-fold as measured by $AUC_{(0–24)}$) in subjects with hepatic impairment (Child-Pugh A, B or C) compared with healthy subjects. The increase in fluticasone furoate systemic exposure (fluticasone furoate/vilanterol 200/25 micrograms) in subjects with moderate hepatic impairment (Child-Pugh B) was associated with an average 34% reduction in serum cortisol compared with healthy subjects. In subjects with severe hepatic impairment (Child-Pugh C) that received a lower dose of 100/12.5 micrograms there was no reduction in serum cortisol. 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 clinically significant suppression of cortisol.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

There was no evidence of a genotoxicity potential of fluticasone furoate in a standard battery of genotoxicity assays.

Carcinogenicity

No evidence of a tumorigenic effect was observed in two-year inhalational studies of fluticasone furoate in mice receiving doses of up to 18.8 microgram/kg/day or in rats receiving up to 8.6 microgram/kg/day. These doses were approximately 8.5 and 4-fold the human adult dose based on mg/kg, respectively.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

VYMAZE Nasal Spray also contains the following excipients: Glucose, Dispersible Cellulose, Polysorbate 80, Benzalkonium Chloride, Disodium Edetate and Purified Water.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Discard 3 months after first opening.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not refrigerate or freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

VYMAZE Nasal Spray is a white to off white, opaque, thixotropic suspension contained in an amber glass bottle fitted with a metering atomising spray pump consisting of PP, rubber/EVA, aluminium, stainless steel, LDPE and PE components with a dip tube. Each spray of the suspension delivers approximately 27.5 micrograms of micronised fluticasone furoate as an ex-device dose.

VYMAZE Nasal Spray is available in 60 and 120 spray packs.

Not all pack sizes may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

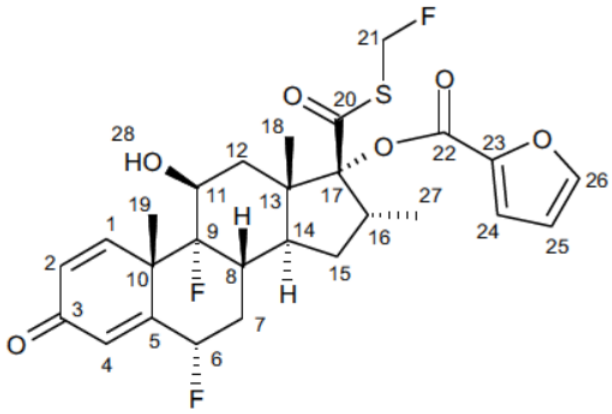
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Description

Fluticasone furoate is practically insoluble or insoluble in water, and slightly soluble in acetone, dimethylsulfoxide and ethanol.

Chemical structure



CAS number

397864-44-7

Chemical Name: Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methyl-3-oxo-,*S*-(fluoromethyl) ester, (6α,11β,16α,17α)

Molecular formula: $C_{27}H_{29}F_3O_6S$

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

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AUSTRALIA
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9 DATE OF FIRST APPROVAL

01 July 2026

10 DATE OF REVISION

N/A

Summary Table of Changes

Section Changed	Summary of new information
All	New PI