AUSTRALIAN PRODUCT INFORMATION

FLIXOTIDE (fluticasone propionate) NEBULES

1 NAME OF THE MEDICINE

Fluticasone propionate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluticasone propionate Nebules (plastic ampoules) 0.5 mg/2 mL and 2 mg/2 mL contain an aqueous white, opaque suspension of micronised fluticasone propionate in an isotonic phosphate buffer.

List of excipients with known effect

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

3 PHARMACEUTICAL FORM

Conventional inhalation

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Adults and adolescents over 16 years of age

Prophylactic management in severe asthma (patients requiring high dose inhaled or oral corticosteroid therapy).

Children and adolescents from 4 to 16 years of age

Treatment of mild to moderate acute exacerbations of asthma in an outpatient setting.

4.2 DOSE AND METHOD OF ADMINISTRATION

FLIXOTIDE Nebules should be administered by inhalation as an aerosol produced by a jet nebuliser, as directed by a physician. As drug delivery can be affected by a wide range of criteria, please refer to the directions recommended by the manufacturer of the nebuliser equipment. Fluticasone propionate for nebulisation is intended for oral inhalation, and use of a mouthpiece is recommended. If use of a face mask is necessary, nasal inhalation will occur.

Use of FLIXOTIDE Nebules with ultrasonic nebulisers is not generally recommended.

Fluticasone propionate for nebulisation should not be injected.

Patients should be made aware of the prophylactic nature of therapy with inhaled fluticasone propionate and that it should be taken regularly for optimal benefit. Maximal improvement in asthma may be achieved within 4 to 7 days of starting treatment. However, fluticasone propionate has been shown to have a therapeutic effect as soon as 24 hours after starting treatment, in patients who have not previously received inhaled steroids.

If patients find that relief with short-acting bronchodilator treatment becomes less effective or they need more inhalations than usual, medical attention must be sought.

To aid administration of small volumes of the suspension, or if a prolonged delivery time is desirable, fluticasone propionate suspension for nebulisation may be diluted immediately before use with sodium chloride injection BP.

As many nebulisers operate on a continuous flow basis, it is likely that nebulised drug will be released in the local environment. FLIXOTIDE Nebules should therefore be administered in a well ventilated room, particularly in hospitals when several patients may be using nebulisers at the same time.

The Australian Asthma Handbook provides an additional source of reference information for prescribers.

Dosage

Adults and adolescents over 16 years (prophylactic management in severe asthma):

The recommended initial dose is 2 mg twice daily. The dosage should then be adjusted until control is achieved or reduced to the minimum effective dose according to the individual response.

Children and adolescents 4 to 16 years of age (treatment of acute exacerbations of asthma):

1 mg twice daily. The maximum duration of treatment used in the clinical trials was 7 days.

Subsequent maintenance dosing may be more conveniently accomplished using a pressurised metered-dose inhaler or powder inhalation.

Special patient groups

There is no need to adjust the dose in elderly patients or in those with hepatic or renal impairment.

Instructions for Use/Handling

Refer to the manufacturer's instructions for nebuliser use.

It is important that the contents of your Nebule are well mixed before use. While holding the Nebule horizontally by the labelled tab, ‘flick’ the other end a few times and shake. Repeat this process several (at least three) times until the entire contents of the Nebule are completely mixed.

To open - twist tab at the top of the Nebule.

Dilution: If required, dilute with Sodium Chloride Injection BP.

Discard unused suspension remaining in bowl of nebuliser.

It is advisable to administer via a mouth piece.

If using a face mask, protect the skin exposed to the nebuliser mist with barrier cream, and wash face thoroughly after treatment.

4.3 CONTRAINDICATIONS

FLIXOTIDE Nebules are contraindicated in patients with a history of hypersensitivity to any component of the preparation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

FLIXOTIDE Nebules should not be used for the treatment of severe acute exacerbations of asthma in children and adolescents as efficacy in this situation has not been established.

The management of asthma should follow a stepwise programme, and patient response should be monitored clinically and by lung function tests. Increasing use of short-acting inhaled beta-2 agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to increasing corticosteroid dosage. In patients considered at risk, daily peak flow monitoring may be instituted.

FLIXOTIDE Nebules are intended for regular daily treatment, and for short-term anti-inflammatory therapy in acute exacerbations of asthma. They are not for use alone for the relief of symptoms arising from acute bronchospasms when a short-acting bronchodilator (e.g. Ventolin) is also required.

Lack of response or severe exacerbations of asthma may be an indication for review of the patient. Treatment options may include increasing the dose of inhaled fluticasone propionate and, if necessary, giving a systemic steroid and/or an antibiotic if there is an infection.

Severe asthma requires regular medical assessment, as it could be life-threatening. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical attention.

FLIXOTIDE Nebules are not a substitute for injectable or oral corticosteroids in an emergency situation.

Patients receiving treatment with nebulised fluticasone propionate must be warned that if their clinical condition deteriorates, or if a dose fails to give the usual relief, they should not increase the dose or the frequency of administration, but should seek medical advice.

It is advisable to inhale via a mouthpiece rather than a face mask. If a face mask is used, the skin exposed to the nebulised mist should be protected by use of barrier cream and by thorough washing of face after nebulisation.

Prolonged therapy with inhaled FLIXOTIDE Nebules should be reduced gradually and not stopped abruptly, and this should be done under medical supervision.

There have been very rare reports of increases in blood glucose levels (See Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and this should be considered when prescribing to patients with a history of diabetes mellitus.

As with all inhaled corticosteroids, special care is necessary in patients with active or quiescent pulmonary tuberculosis.

A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects

including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects.

As with other inhalation therapy, paradoxical bronchospasm may occur rarely, with an immediate increase in wheezing after dosing. This should be treated immediately with a fast and short-acting inhaled bronchodilator. FLIXOTIDE should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted if necessary.

Possible systemic effects, including Adrenocortical function, Bone density and Growth

Inhaled steroids are designed to direct glucocorticoid delivery to the lungs in order to reduce overall systemic glucocorticoid exposure and side effects. With sufficient doses however, all inhaled steroids can have adverse effects; possible systemic effects include Cushing's syndrome, Cushingoid features, depression of the hypothalmic-pituitary adrenal (HPA) axis (See Section 4.9 OVERDOSE), reduction of bone density, retardation of growth rate, cataract, glaucoma and central serous chorioretinopathy. If a patient presents with a change in vision, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes.

The lowest doses of inhaled corticosteroids that cause suppression of the HPA axis (as indicated by the 24 hour urinary cortisol concentrations), effects on bone mineral density or growth retardation in children has not yet been established. Some depression of plasma cortisol may occur in a small number of adult patients receiving inhaled FP at recommended and higher doses but it is not possible to predict which patients are at risk based solely on dose, previous history or length of exposure to inhaled or oral steroids. Adrenal function and adrenal reserve usually remain within normal range on recommended doses of inhaled fluticasone propionate therapy. To minimise the systemic effects of orally inhaled corticosteroids, including fluticasone propionate, each patient should be titrated down to the lowest dose that effectively controls his/her asthma.

Medical Emergency

Patients in a medical or surgical emergency, who in the past have required high doses of other inhaled steroids and/or intermittent treatment with oral steroids, remain at risk of impaired adrenal reserve for a considerable time after transferring to inhaled fluticasone propionate. The extent of the adrenal impairment may require specialist advice before elective procedures. The possibility of residual impaired adrenal response should always be borne in mind in emergency and elective situations likely to produce stress and appropriate corticosteroid treatment must be considered.

Transfer of patients being treated with oral corticosteroids

Because of the possibility of impaired adrenal response, patients transferring from oral steroid therapy to inhaled fluticasone propionate should be treated with special care and adrenocortical function regularly monitored.

Following introduction of inhaled fluticasone propionate, withdrawal of systemic therapy should be gradual and patients whose adrenocortical function is still impaired should carry a steroid warning card indicating that they may need supplementary systemic steroid during periods of stress, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

In rare cases inhaled therapy may unmask underlying eosinophilic conditions (e.g. Churg Strauss syndrome). These cases have usually been associated with reduction or withdrawal of oral corticosteroid therapy. A direct causal relationship has not been established.

Similarly, replacement of systemic steroid treatment with inhaled therapy sometimes unmasks allergies such as allergic rhinitis or eczema previously controlled by the systemic drug. These allergies should be symptomatically treated with antihistamine and/or topical preparations, including topical steroids.

Use in the elderly

There are no special precautions for use in the elderly.

Paediatric use

The growth of paediatric patients receiving corticosteroids, including fluticasone propionate, should be monitored. The potential growth effects of prolonged treatment should be weighed against the clinical benefits obtained.

In children taking recommended doses of inhaled fluticasone propionate, adrenal function and adrenal reserve usually remain within the normal range. However, the possible effects of previous or intermittent treatment with oral steroids should not be discounted. Nevertheless, the benefits of inhaled fluticasone propionate should minimise the need for oral steroids.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 drug interactions mediated by fluticasone propionate are unlikely.

A drug interaction study in healthy subjects has shown that ritonavir (a highly potent cytochrome P450 3A4 inhibitor) can greatly increase fluticasone propionate plasma concentrations, resulting in markedly reduced serum cortisol concentrations. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects.

Studies have shown that 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. Nevertheless, care is advised when co-administering potent cytochrome P450 3A4 inhibitors (e.g. ketoconazole) as there is potential for increased systemic exposure to fluticasone propionate.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There are no data on human fertility. No effects of fluticasone propionate on male or female fertility were observed in rats at subcutaneous doses up to 50 micrograms/kg/day.

Use in pregnancy

(Pregnancy Category B3)

There are limited data in pregnant women. Administration of fluticasone propionate during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

An observational retrospective epidemiological cohort study utilising electronic health records from the United Kingdom was conducted to evaluate the risk of major congenital malformations (MCMs) following first trimester exposure to inhaled fluticasone propionate alone and salmeterol-fluticasone propionate combination relative to non-fluticasone propionate containing inhaled corticosteroids. No placebo comparator was included in this study.

Within the asthma cohort of 5,362 first trimester inhaled corticosteroid-exposed pregnancies, 131 diagnosed MCMs were identified: 1,612 (30%) were exposed to fluticasone propionate or salmeterol-fluticasone propionate of which 42 diagnosed MCMs were identified. The adjusted odds ratio for MCMs diagnosed by 1 year was 1.1 (95%CI: 0.5 – 2.3) for fluticasone propionate exposed vs non-fluticasone propionate inhaled corticosteroid exposed women with moderate asthma and 1.2 (95%: 0.7 – 2.0) for women with considerable to severe asthma. No difference in the risk of MCMs was identified following first trimester exposure to fluticasone propionate alone versus salmeterol-fluticasone propionate combination. Absolute risks of MCM across the asthma severity strata ranged from 2.0 to 2.9 per 100 fluticasone propionate-exposed pregnancies which is comparable to results from a study of 15,840 pregnancies unexposed to asthma therapies in the General Practice Research Database (2.8 MCM events per 100 pregnancies).

Results from the retrospective epidemiological study did not find an increased risk of MCMs following exposure to fluticasone propionate when compared to other inhaled corticosteroids, during the first trimester of pregnancy.

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. Teratology studies with fluticasone propionate in mice and rats have shown the expected fetotoxic and teratogenic effects at SC doses of 100 to 150 micrograms/kg/day and above. In an inhalational teratology study in rats, fluticasone propionate was not teratogenic at inhalational doses up to 68.7 micrograms/kg/day, but reduced foetal bodyweight and delayed foetal development were noted at maternal doses of 25.7 micrograms/kg/day and greater. Mean foetal weight, retardation of ossification, and decreased postnatal viability were observed in rats receiving fluticasone propionate at 50 micrograms/kg/day SC. As for previous compounds of this class, these effects are unlikely to be relevant to human therapy.

Use in lactation

The excretion of fluticasone propionate into human breast milk has not been investigated. Subcutaneous administration of titrated drug to lactating rats resulted in measurable radioactivity in both plasma and milk (levels in milk were 3-7 times plasma levels) 1-8 hours post-dosing.

However, the amount of fluticasone propionate ingested by the newborn is estimated to be very small as a consequence of very low maternal plasma concentration of fluticasone propionate.

Administration during lactation should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Fluticasone propionate is unlikely to produce an effect.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

In the pivotal study (FLTB3001), the overall incidence of adverse events was similar in all three groups; most were either respiratory in nature or were predictable adverse events.

Table 1. Most Common Adverse Events (%) in Trials FLTB3001 and 3002 (regardless of causality)

	FLTB3001 (prophylactic management of asthma, adults, t=12 weeks)			**FLTB3002** (acute exacerbation, children, t=7 days)	
Event	**Placebo N=96**	**FP 0.5mg twice daily N=102**	**FP 2mg twice daily N=103**	**FP 0.5mg twice daily N=165**	**Prednisolone *N=156**
Asthma	41.7	34.3	21.4	4	4
Candidiasis	8.3	13.7	11.7	8	3
Upper Respiratory Tract Infection	13.5	9.8	16.5	<1	2
Cough	6.3	9.8	7.8	-	-
Lower Respiratory Tract Infection	9.4	6.9	8.7	-	-
Headache	2.1	2.9	6.8	-	-
Hoarseness	1.0	2.9	5.8	-	-
Bronchitis	5.2	2.0	4.9	-	-
Malaise	2.1	1.0	4.9	-	-
Nausea & Vomiting	-	-	-	4	5
Throat Irritation	-	-	-	1	-
Skin Rash	-	-	-	-	<1
Abdominal discomfort	-	-	-	-	<1
At Least One Event	77.1	76.5	78.6	35	28

* 2 mg/kg/day [max. 40 mg/day] prednisolone soluble tablets for 4 days followed by 1mg/kg/day [max. 40 mg/day] for 3 days.

General experience with fluticasone propionate

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000) including isolated reports. Very common, common and uncommon events were generally determined from clinical trial data. Rare and very rare events were generally determined from spontaneous data.

Infections and infestations

Very common: Candidiasis (thrush) of the mouth and throat

Candidiasis of the mouth and throat (thrush) occurs in some patients. Patients may find it helpful to rinse out their mouth with water after inhalation. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst still continuing with the fluticasone propionate.

Rare: Oesophageal candidiasis

Immune system disorders

Hypersensitivity reactions with the following manifestations have been reported:

Uncommon: Cutaneous hypersensitivity reactions.

Rare: Angioedema (mainly facial and oropharyngeal oedema), respiratory symptoms (dyspnoea and/or bronchospasm)

Very rare: Anaphylactic reactions.

Skin and subcutaneous tissue disorders

Common: Contusions.

Endocrine Disorders

Possible systemic effects include (See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

Rare: Adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma.

There have also been reports of Cushing's syndrome and Cushingoid features.

Psychiatric disorders

Very rare: Anxiety, sleep disorders and behavioural changes, including hyperactivity and irritability (predominantly in children).

Metabolism and nutrition disorders

Very rare: Hyperglycaemia.

Respiratory, thoracic and mediastinal disorders

Common: Hoarseness

In some patients FLIXOTIDE may cause hoarseness. It may be helpful to rinse out the mouth with water immediately after inhalation.

Rare: Paradoxical bronchospasm (See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

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

Acute inhalation of fluticasone propionate doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not need emergency action as adrenal function is recovered in a few days, and can be verified by plasma cortisol measurements. However, if higher than recommended dosage is continued over prolonged periods, some degree of adrenal suppression may result. Monitoring of adrenal reserve may be necessary. In cases of fluticasone propionate overdose, therapy may still be continued at a suitable dosage for symptom control.

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 propionate given by inhalation at recommended doses has potent glucocorticoid activity in the airway. The potent anti-inflammatory action improves the symptomatic control of asthma. It allows reduction of other drugs, such as rescue bronchodilators, and may limit the risk of decline in lung function over time. The low systemic bioavailability of fluticasone propionate provides a better risk: benefit outcome without the adverse effects that accompany systemically administered corticosteroids.

Clinical trials

Prophylactic management of asthma in adults
A multicentre, randomised, double-blind, parallel trial (FLTB3001) examined the oral corticosteroid sparing effect of nebulised fluticasone propionate (FP) in asthmatic adult patients aged 17 to 83 years, dependent on oral corticosteroids. Of 301 patients randomised, four were excluded due to lack of follow-up and nine due to irregularities at one study site. Of the evaluable patients, 90 received placebo, 98 received FP 0.5 mg twice daily and 100 received FP 2 mg twice daily.

In an analysis of covariance adjusted for age, sex, country and nebuliser type, the mean reduction in oral corticosteroid dose from baseline to last recorded dose was 1.20 mg/day in the placebo group, 2.16 mg/day in the FP 0.5 mg twice daily group and 4.44 mg/day in the FP 2 mg twice daily group, after 12 weeks treatment. The reduction in the FP 2 mg/day group was significantly better than placebo. The difference from placebo in the FP 0.5 mg twice daily group was 0.95 mg/day [95% CI: -1.27,3.18] and in the FP 2 mg twice daily group, 3.23 mg/day [95% CI: 1.02,5.45].

Acute exacerbation of asthma in children
In a double-blind parallel study (FLTB3002), 321 patients aged 4-16 years with an established diagnosis of asthma, and suffering a mild to moderate acute exacerbation, received either 1 mg twice daily nebulised FP, or 2mg/kg/day [max. 40mg/day] prednisolone soluble tablets for 4 days followed by 1mg/kg/day [max. 40mg/day] for 3 days in an outpatient setting.

Improvement for patients in the FP group was comparable to the prednisolone group according to clinical endpoints such as cough, sputum, wheeze, dyspnoea and bronchodilator use.

In asthmatic children aged 4 to 14, 7 days of 1000 micrograms nebulised FP twice daily were associated with less effect on HPA axis (as measured by 24-hour urinary cortisol

excretion) when compared with oral prednisolone therapy of 2 mg/kg/day for 4 days followed by 1 mg/kg/day for 3 days.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Systemic absorption of FP occurs mainly through the lungs and is initially rapid then prolonged. Following inhaled dosing, systemic bioavailability of nebulised fluticasone propionate in healthy volunteers is estimated as 8%.

Distribution

Following one nebulised dose of 4000 micrograms FP in healthy adults, median peak plasma FP concentrations (geometric mean 0.39 ng/mL) were observed 0.5 hours (range 0.33 to 0.83 hours) post-dose, with an apparent terminal half-life of 11.4 hours.

Metabolism / Excretion

Following oral administration 87-100% of the dose is excreted in the faeces, up to 75% as parent compound depending on the dose. There is a non-active major metabolite. Following intravenous administration there is rapid plasma clearance suggestive of extensive hepatic extraction. The plasma elimination half-life is approximately 3 hours. The volume of distribution is approximately 250 litres.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

There was no evidence of mutagenic or clastogenic activity for fluticasone propionate in the standard battery of genotoxicity assays.

Carcinogenicity

No evidence of a tumorigenic effect was observed in either a 2 year study in rats receiving doses of fluticasone propionate up to 57 micrograms/kg/day by inhalation or in an 18 month study in mice receiving oral doses of fluticasone propionate up to 1 mg/kg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Polysorbate 20, sodium chloride, dibasic sodium phosphate, monobasic sodium phosphate, sorbitan monolaurate and water for injection.

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.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

Protect from light. Do not freeze. Store upright.

Once Nebules have been removed from their flow wrap pack, they should be protected from light and used within 28 days.

Once opened, Nebules should be used immediately.

6.5 NATURE AND CONTENTS OF CONTAINER

FLIXOTIDE Nebules are plastic ampoules containing 0.5 mg or 2 mg of fluticasone propionate (micronised) as a 2 mL buffered isotonic saline suspension, for inhalation by nebulisation.

The Nebules are provided as strips of Nebules in a foil flow wrap. Each pack contains 10 Nebules.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

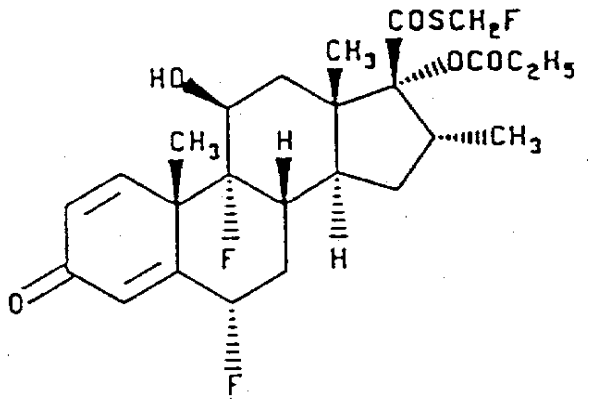
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical name: S-Fluoromethyl 6α, 9α-difluoro-11ß-hydroxy-16α-methyl-3-oxo-17 α-propionyloxy-androsta-1, 4-diene-17ß-carbothioate.

Molecular formula: $C_{25}H_{31}F_3O_5S$

Chemical structure



CAS number

80474-14-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

Level 4, 436 Johnston Street,

Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

21 May 1999

10 DATE OF REVISION

02 March 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
6.4	Update to Storage conditions for opened Nebules

Version 9.0