SUMMARY OF PRODUCT CHARACTERISTICS

FLIXOTIDE™ suspension for inhalation in pressurised can 50mcg

PRODUCT SUMMARY

1. Trade Name of the Medicinal Product

Flixotide™ suspension for inhalation in pressurised can 50 micrograms.

2. Qualitative and Quantitative Composition

Flixotide suspension for inhalation in pressurised can is a pressurised metered-dose inhaler, delivering 50 micrograms of fluticasone propionate per actuation.

3. Pharmaceutical Form

Pressurised Inhalation, suspension.
Flixotide suspension for inhalation in pressurised can contains a new propellant and does not contain any chlorofluorocarbons (CFCs).

4. Clinical Particulars

4.1 Therapeutic indications

Fluticasone propionate given by inhalation offers prophylactic treatment for asthma. At recommended doses it has a potent glucocorticoid anti-inflammatory action within the lungs, with a lower incidence and severity of adverse effects than those observed when corticosteroids are administered systemically.

Adults: Prophylactic management in:

Mild asthma: Patients requiring intermittent symptomatic bronchodilator asthma medication on a regular daily basis.

Moderate asthma: Patients with unstable or worsening asthma despite prophylactic therapy or bronchodilator alone.

Severe asthma: Patients with severe chronic asthma and those who are dependent on systemic corticosteroids for adequate control of symptoms. On introduction of inhaled fluticasone propionate many of these patients may be able to reduce significantly or to eliminate their requirement for oral corticosteroids.

Children: Any child who requires prophylactic medication, including patients not controlled on currently available prophylactic medication.

4.2 Posology and method of administration

Flixotide suspension for inhalation in pressurised can is for oral inhalation use only. A Volumatic™ spacer device may be used in patients who find it difficult to synchronise aerosol actuation with inspiration of breath.
Patients should be made aware of the prophylactic nature of therapy with Flixotide suspension for inhalation in pressurised can and that it should be taken regularly even when they are asymptomatic. The onset of therapeutic effect is within 4 to 7 days.

Adults and children over 16 years
100 to 1,000 micrograms twice daily, usually as two twice daily inhalations. Patients should be given a starting dose appropriate to the severity of their disease. The prescriber should be aware that the dose required for disease control with fluticasone propionate may be lower than that required with some other inhaled steroids.

Typical starting doses are:
Mild asthma: 100 to 250 micrograms twice daily,
Moderate asthma: 250 to 500 micrograms twice daily,
Severe asthma: 500 to 1,000 micrograms twice daily.

Children over 4 years of age
50 to 100 micrograms twice daily.

The starting dose should be appropriate to the severity of the disease.

Should this particular Flixotide presentation not offer the exact paediatric dose prescribed by the physician, please see data sheets of alternative Flixotide presentation (Diskus, Diskhaler, Inhaler)

Administration of doses above 1000 micrograms (500 micrograms twice daily) should be via a spacer device to help reduce side-effects in the mouth and throat.

Special patient groups
There is no need to adjust the dose in elderly patients or those with hepatic or renal impairment.
The dose should be titrated to the lowest dose at which effective control of asthma is maintained.

4.3 Contra-indications

Hypersensitivity to any ingredient of the preparation.

4.4 Special warnings and precautions for use

Patients' inhaler technique should be checked regularly to make sure that inhaler actuation is synchronised with inspiration to ensure optimum delivery of the drug to the lungs.

Flixotide suspension for inhalation in pressurised can is not designed to relieve acute symptoms, for which an inhaled short-acting bronchodilator is required. Patients should be advised to have such rescue medication available.

Severe asthma requires regular medical assessment, including lung-function testing, as patients are at risk of severe attacks and even death. Increasing use of short-acting inhaled β_2-agonists to relieve symptoms indicates deterioration of asthma control. If patients find that short-acting relief bronchodilator treatment becomes less effective, or they need more inhalations than usual, medical attention must be sought. In this situation patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroids or a course of oral corticosteroids). Severe exacerbations of asthma must be treated in the normal way.

Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important therefore that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of inhaled corticosteroid, if possible, to the lowest dose at which effective control of asthma is maintained. In addition, consideration should be given to referring the patient to a paediatric respiratory specialist.

Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

The benefits of inhaled fluticasone propionate should minimise the need for oral steroids. However, patients transferred from oral steroids, remain at risk of impaired adrenal reserve for a considerable time after transferring to inhaled fluticasone propionate. The possibility of adverse effects may persist for some time. These patients may require specialised advice to determine the extent of adrenal impairment before elective procedures. The possibility of residual impaired adrenal response should always be considered in emergency (medical or surgical) and elective situations likely to produce stress, and appropriate corticosteroid treatment considered.

Lack of response or severe exacerbations of asthma should be treated by increasing the dose of inhaled fluticasone propionate and, if necessary, by giving a systemic steroid and/or an antibiotic if there is an infection.

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.

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

Treatment with Flixotide suspension for inhalation in pressurised can should not be stopped abruptly.

For the transfer of patients being treated with oral corticosteroids: The transfer of oral steroid-dependent patients to Flixotide suspension for inhalation in pressurised can, and their subsequent management, needs special care as recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy, may take a considerable time.

Patients who have been treated with systemic steroids for long periods of time, or at a high dose, may have adrenocortical suppression. With these patients adrenocortical function should be monitored regularly and their dose of systemic steroid reduced cautiously.

After approximately a week, gradual withdrawal of the systemic steroid is commenced. Decrements in dosages should be appropriate to the level of maintenance systemic steroid, and introduced at not less than weekly intervals. For maintenance doses of prednisolone (or equivalent) of 10mg daily or less, the decrements in dose should not be greater than 1 mg per day, at not less than weekly intervals. For maintenance doses of prednisolone in excess of 10mg daily, it may be appropriate to employ cautiously, larger reductions in dose at weekly intervals.

Some patients feel unwell in a non-specific way during the withdrawal phase despite maintenance or even improvement of respiratory function. They should be encouraged to persevere with inhaled fluticasone propionate and to continue withdrawal of systemic steroid, unless there are objective signs of adrenal insufficiency.

Patients weaned off oral steroids whose adrenocortical function is still impaired should carry a steroid warning card indicating that they need supplementary systemic steroid during periods of stress, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

Significant interactions between fluticasone propionate and potent inhibitors of the cytochrome P450 3A4 system, e.g. ketoconazole and protease inhibitors, such as ritonavir, may occur. This may result in increased systemic exposure to fluticasone propionate.

4.5 Interaction with other medicaments and other forms of interaction

Effects of fluticasone propionate on other drugs.
Drug interaction studies have shown no significant effect of fluticasone propionate on the pharmacokinetics of terfenadine and erythromycin.

Effects of other drugs on fluticasone propionate
Drug interaction studies have shown no significant effect of terfenadine or erythromycin on the pharmacokinetics of fluticasone propionate.

The use of fluticasone propionate in patients taking concurrent drugs which are potent inhibitors of the cytochrome P450 3A4 system, e.g. ketoconazole and protease inhibitors such as ritonavir, may be associated with increased systemic exposure of fluticasone propionate. There have been reports of suppression of the hypothalmic-pituitary-adrenal axis in patients receiving fluticasone propionate with ritonavir.

4.6. Pregnancy and Lactation

There is inadequate evidence of safety of fluticasone propionate in human pregnancy. Data on a limited (200) of exposed pregnancies indicate no adverse effects of Flixotide suspension for inhalation in pressurised can on pregnancy or the health of the foetus/new born child. To date no other relevant epidemiological data are available. Administration of corticosteroids to pregnant animals can cause abnormalities of fetal development, including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human fetus. It should be noted, however, that the fetal changes in animals occur after relatively high systemic exposure. Because Flixotide suspension for inhalation in pressurised can delivers fluticasone propionate directly to the lungs by the inhaled route it avoids the high level of exposure that occurs when corticosteroids are given by systemic routes. 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 fetus.

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 plasma levels in humans after inhalation at recommended doses are likely to be low. When fluticasone propionate is used in breast-feeding mothers the therapeutic benefits must be weighed against the potential hazards to mother and baby.

4.7 Effect on ability to drive and use machines

Fluticasone propionate is unlikely to produce an effect.

4.8 Undesirable effects

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

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

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

Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These may include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma.

There have been rare reports of peripheral oedema and cutaneous hypersensitivity reactions such as skin rash.

There have been very rare reports of dyspepsia and arthralgia although a causal link with fluticasone propionate has not been established.

4.9 Overdose

Acute: Inhalation of the drug in doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not necessitate emergency action being taken. In these patients treatment with fluticasone propionate by inhalation should be continued at a reduced dose to control asthma; adrenal function recovers in a few days and can be verified by measuring plasma cortisol.

Chronic: Use of inhaled fluticasone propionate in daily doses in excess of 2mg over prolonged periods may lead to adrenal suppression. Monitoring of adrenal reserve may be indicated. Treatment with Flixotide suspension for inhalation in pressurised can should be continued at a dose sufficient to control asthma.

5. Preclinical safety data

Toxicology has shown only those class effects typical of potent corticosteroids, and these only at doses greatly in excess of that proposed for therapeutic use. No novel effects were identified in repeat dose toxicity tests, reproductive studies or teratology studies. Fluticasone propionate is devoid of mutagenic activity in vitro and in vivo and showed no tumorigenic potential in rodents. It is both non-irritant and non-sensitising in animal models. The non-CFC propellant, HFA 134a, has been shown to have no toxic effect at very high vapour concentrations, far in excess of those likely to be experienced by patients, in a wide range of animal species exposed daily for periods of two years.
The use of HFA 134a as a propellant has not altered the toxicity profile of fluticasone propionate compared to that using the conventional CFC propellant.

6 Pharmaceutical Particulars

6.1 List of Excipients

HFA 134a

6.2 Special Precautions for Storage

Do not store above 30°C (86°F). Do not refrigerate or freeze. Protect from frost and direct sunlight.

As with most medicines in pressurised canisters, the therapeutic effect of this medication may decrease when the canister is cold.

The canister should not be punctured, broken or burnt even when apparently empty.

7. Date of (Partial) Revision of Text

16 March 2000

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