FLIXOTIDE INHALER

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Trade Mark

PRESENTATION

Flixotide Inhaler is a pressurised metered dose inhaler delivering 25, 50, 125 or 250 micrograms of fluticasone propionate with each actuation. Each canister provides either 60 or 120 actuations.

USES

Fluticasone propionate has a marked anti-inflammatory effect in the lungs. It reduces symptoms and exacerbations of asthma in patients previously treated with bronchodilator alone or with other prophylactic therapy. In the majority of patients it has no effect on adrenal function or reserve at the recommended doses.

Severe asthma requires regular medical assessment as death may occur. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and PEF values below 60% predicted at baseline with greater than 30% variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled (see dosage instructions) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

THERAPEUTIC INDICATIONS

Adults

Prophylactic management in:-

Mild asthma (PEF values greater then 80% predicted at baseline with less than 20% variability):

Patients requiring intermittent symptomatic bronchodilator asthma medication on more than an occasional basis.

Moderate asthma (PEF values 60-80% predicted at baseline with 20-30% variability):

Patients requiring regular asthma medication and patients with unstable or worsening asthma on currently available prophylactic therapy or bronchodilator alone.

Severe asthma (PEF values less than 60% predicted at baseline with greater than 30% variability):

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

Children

Any child who requires preventive asthma medication, including patients not controlled on currently available prophylactic medication.

Posology and Method of Administration

Fluticasone Propionate Inhaler is administered by the inhaled route only.

Patients should be made aware of the prophylactic nature of therapy with inhaled fluticasone propionate and that it should be taken regularly even when they are asymptomatic. The onset of therapeutic effect is within 4 to 7 days.

The dosage of fluticasone propionate should be adjusted according to the individual response.

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.

It is intended that each prescribed dose is given by a minimum of 2 inhalations

Adults and Children Over 16 Years of Age

100 to 1000 micrograms twice daily.

Patients should be given a starting dose of inhaled fluticasone propionate which is appropriate for the severity of their disease:

Mild asthma:	100 to 250 micrograms twice daily.
Moderate asthma:	250 to 500 micrograms twice daily.
Severe asthma:	500 to 1000 micrograms twice daily.

The dose may then be adjusted until control is achieved or reduced to the minimum effective dose, according to the individual response.

Alternatively, the starting dose of fluticasone propionate may be gauged at half the total daily dose of beclomethasone dipropionate or equivalent as administered by metered-dose inhaler.

Children Over 4 Years of Age:

50 to 100 micrograms twice daily.

Children should be given a starting dose of inhaled fluticasone propionate which is appropriate for the severity of their disease, this may be 50 or 100 micrograms twice daily.

The dose may then be adjusted until control is achieved or reduced to the minimum effective dose according to the individual response.

Special Patient Groups

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

Contra-indications

Fluticasone Propionate Inhaler is contra-indicated in patients with a history of hypersensitivity to any of its components

Special Warnings and Special Precautions for Use

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.

Fluticasone Propionate Inhaler is not for use in acute attacks but for routine long-term management. Patients will require a fast-and short-acting inhaled bronchodilator to relieve acute asthmatic symptoms.

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

Adrenal function and adrenal reserve usually remain within the normal range on inhaled fluticasone propionate. However, some systemic effects may occur in a small proportion of adult patients after prolonged treatment at the maximum recommended daily dose. Patients transferred from other inhaled steroids or oral steroids remain at risk of impaired adrenal reserve for a considerable time after transferring to inhaled fluticasone propionate.

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.

In children taking recommended doses of inhaled fluticasone propionate adrenal function and adrenal reserve usually remain within the normal range. No systemic side-effects and, in particular, no stunting of growth has been observed in children on inhaled fluticasone propionate. However, the possible effects of previous or intermittent treatment with oral steroids should not be discounted. Nevertheless, the benefits of inhaled fluticasone propionate should minimize the need for oral steroids.

necessary, by giving a systemic steroid and/or an antibiotic if there is an infection.

For the transfer of patients being treated with oral corticosteroids:

- The transfer of oral steroid-dependent patients to Fluticasone Propionate Inhaler 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 1mg per day, at not less than weekly intervals. For maintenance doses of prednisolone in excess of 10 mg daily, it may be appropriate to employ cautiously, larger decrements in dose at weekly intervals.

- Some patients feel unwell in a non-specific way during the withdrawal phase despite maintenance or even improvement of the 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 may need supplementary systemic steroid during periods of stress, e.g. worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma etc.

- 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.

Treatment with Fluticasone Propionate Inhaler should not be stopped abruptly

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

Interaction with Other Medicaments and other Forms of Interaction

No specific drug interaction studies have been performed. However, because of the very low plasma drug concentrations achieved after inhaled dosing, there are unlikely to be any implications for displacement drug interactions.

There were no reports of suspected drug interactions in the clinical programme.

Pregnancy and Lactation

There is inadequate evidence of safety of fluticasone propionate in human pregnancy. Reproductive studies in animals have shown only those effects characteristic of glucocorticosteroids at systemic exposure greatly in excess of the recommended inhaled therapeutic dose. Tests of genotoxicity have shown no mutagenic potential. However, as with other drugs the 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.

It is not known whether fluticasone propionate is excreted in human breast milk, nor are any data available from animal studies. However, in view of its pharmacokinetic profile, transfer of fluticasone propionate into milk is unlikely.

Effects on Ability to Drive and Use Machines

Fluticasone propionate is unlikely to produce an effect.

Undesirable Effects

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 with the Fluticasone Propionate Inhaler.

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

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. Fluticasone Propionate Inhaler should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

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 dose sufficient 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 2 milligrams over prolonged periods may lead to some degree of adrenal suppression. Monitoring of adrenal reserve may be indicated. Treatment with inhaled fluticasone propionate should be continued at a dose sufficient to control asthma.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Mechanism of Action

Fluticasone propionate given by inhalation at recommended doses has a potent glucocorticoid anti-inflammatory action within the lungs, resulting in reduced symptoms and exacerbations of asthma, without adverse effects observed when corticosteroids are administered systemically.

Pharmacokinetic Properties

Following oral administration 87-100% of the dose is excreted in the faeces, up to 75% as unabsorbed 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.

Adrenocortical Function

Daily output of adrenocortical hormones remain within the normal range during chronic treatment with inhaled fluticasone propionate, even at the highest recommended doses in children and adults. After transfer from other inhaled steroids to inhaled fluticasone propionate, the daily output gradually improves despite past and present intermittent use of oral steroids, thus demonstrating return of normal adrenal function on inhaled fluticasone propionate. The adrenal reserve also remains normal during chronic treatment with inhaled fluticasone propionate, as measured by a normal increment on a stimulation test. However, any residual impairment of adrenal reserve from previous treatments may persist for a considerable time and should be borne in mind (see Special warnings and special precautions for use).

Pre-clinical 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.

PHARMACEUTICAL PRECAUTIONS

Fluticasone Propionate Inhalers should be stored between 2 degrees C and 30 degrees C.

Protect from frost and direct sunlight.
As with most inhaled medications 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.

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