FOXAIR® Accuhaler®

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

FOXAIR® 50/100 Accuhaler® Powder for inhalation

FOXAIR® 50/250 Accuhaler® Powder for inhalation

FOXAIR® 50/500 Accuhaler® Powder for inhalation

COMPOSITION:

Each FOXAIR Accuhaler blister contains a mixture of salmeterol xinafoate equivalent to 50 micrograms of salmeterol and microfine fluticasone propionate (100 micrograms, 250 micrograms or 500 micrograms).

Excipient: lactose.

PHARMACOLOGICAL CLASSIFICATION:

A 21.5.4 Corticosteroids - Other combinations

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

FOXAIR Accuhaler contains salmeterol and fluticasone propionate which have differing modes of action.

Salmeterol is a selective beta$_2$-adrenoceptor agonist. Salmeterol has been shown to produce bronchodilatation of at least 12 hours in subjects with reversible airways obstruction.

In vitro tests have shown salmeterol to be an inhibitor of the release, from human lung, of mast cell derived mediators, such as histamine, leukotrienes and prostaglandin D_2. In man salmeterol inhibits the early and late phase response to inhaled allergen and after single dosing attenuates bronchial hyperresponsiveness.

Fluticasone propionate *in vitro* has a glucocorticoid anti-inflammatory action.

Pharmacokinetic properties:

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.

INDICATIONS:

FOXAIR Accuhaler is indicated in the regular prophylactic treatment of atopic asthma in children and adults, who have been stabilised on identical dosages of the components of FOXAIR given concurrently.

Chronic Obstructive Pulmonary Disease (COPD):

FOXAIR Accuhaler is indicated for the regular treatment of chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema.

FOXAIR is indicated for the symptomatic treatment of patients with severe COPD (FEV1 < 50 % predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy.

CONTRA-INDICATIONS:

FOXAIR Accuhaler is contra-indicated in patients with a history of hypersensitivity to any of its components.

WARNINGS AND SPECIAL PRECAUTIONS:

FOXAIR Accuhaler is not for relief of acute symptoms for which a fast and short-acting bronchodilator is required. Patients should be advised to have their relief medication available at all times.

Increasing use of short-acting inhaled beta$_2$-agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient should be reassessed.

Sudden and progressive deterioration in asthma control is potentially life-threatening and may have several causes. Consideration should be given to increasing corticosteroid dosage if not caused by otherwise treatable causes of deterioration.

Patients on corticosteroid therapy may have adrenocortical suppression.

Treatment with FOXAIR Accuhaler should not be stopped abruptly as adrenal insufficiency may be precipitated in this way.

Special care is necessary in patients with active or quiescent pulmonary tuberculosis.

FOXAIR should be administered with caution in patients with thyrotoxicosis.

Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long 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 is maintained.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroid is regularly monitored.

Systemic corticosteroid effects may occur in patients on fluticasone treatment. Patients transferred from other inhaled steroids or oral steroids remain at risk of impaired adrenal reserve for a considerable time after transferring to FOXAIR.

Patients with severe asthma may require high dose inhaled (see DOSAGE AND DIRECTIONS FOR USE) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

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.

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.

Patients in a medical or surgical emergency, who require high doses of inhaled steroids and/or intermittent treatment with oral steroids, are at risk of impaired adrenal reserve.

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. However, the possible effects of previous or intermittent treatment with oral steroids should not be discounted.

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

Paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. FOXAIR Accuhaler should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

INTERACTIONS:

Even though plasma levels of FOXAIR are very low, potential interactions with other substrates or inhibitors of CYP3A4 cannot be excluded.

Both non-selective and selective beta-blockers should be avoided in patients with reversible obstructive airways disease, unless there are compelling reasons for their use.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established.

Fluticasone propionate: Safety during pregnancy and lactation has not been established. Corticosteroids have been shown to be teratogenic in animals. As these agents are absorbed when inhaled, teratogenicity following inhalation cannot be excluded.

Salmeterol: Safety in pregnancy has not been established. There is no experience of the use of salmeterol in breastfeeding mothers.

DOSAGE AND DIRECTIONS FOR USE:

FOXAIR Accuhaler is for oral inhalation use only.

Patients should be made aware that FOXAIR Accuhaler must be used regularly for optimum benefit even when asymptomatic.

Patients should be regularly reassessed by a doctor. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained.

FOXAIR Accuhaler is not for relief of acute symptoms for which a fast and short-acting bronchodilator is required. Patients should be advised to have their relief medication available at all times.

Increasing use of short-acting bronchodilators to relieve asthma symptoms indicates deterioration of asthma control.

Sudden and progressive deterioration in control of asthma is potentially life-threatening and the patient should be reviewed. Consideration should be given to increasing corticosteroid therapy. Also, where the current dosage of FOXAIR Accuhaler has failed to give adequate control of reversible obstructive airways disease, the patient should be reviewed. Consideration should be given to additional corticosteroid therapies, and to including administration of antibiotics if an infection is present.

Recommended Doses:

Adults and adolescents 12 years and older:

One inhalation (FOXAIR 50/100 Accuhaler) twice daily or

One inhalation (FOXAIR 50/250 Accuhaler) twice daily or

One inhalation (FOXAIR 50/500 Accuhaler) twice daily.

Children 4 years and older:

One inhalation (FOXAIR 50/100 Accuhaler) twice daily.

There are no data available for use of FOXAIR Accuhaler in children under 4 years.

Chronic Obstructive Pulmonary Disease (COPD):

For adult patients the recommended dose is one inhalation (FOXAIR 50/250 Accuhaler) to one inhalation (FOXAIR 50/500 Accuhaler) twice daily.

Special patient groups:

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

SIDE EFFECTS:

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥ 1/1 000 and < 1/100), rare
(≥ 1/10 000 and < 1/1 000) and very rare (< 1/10 000) including isolated reports.
As FOXAIR contains salmeterol and fluticasone propionate, the type and severity of adverse reactions associated with each of the compounds may be expected.
Adverse events which have been associated with salmeterol or fluticasone propionate are given below:

<u>Salmeterol</u>:

Clinical trials data:

Immune system disorders:

Hypersensitivity reactions:

Uncommon: rash

Nervous system disorders:

Common: tremor, headache

Cardiac disorders:

Common: palpitations

Musculoskeletal and connective tissue disorders:

Common: muscle cramps.

Post-marketing data:

Immune system disorders:

Hypersensitivity reactions:

Less frequent: oedema and angioedema

Metabolism and nutrition disorders:

Frequency unknown: hypokalaemia

Cardiac disorders:

Less frequent: cardiac arrythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles

Respiratory, thoracic and mediastinal disorders:

Less frequent: oropharyngeal irritation

Musculoskeletal and connective tissue disorders:

Less frequent: arthralgia.

Fluticasone propionate:

Clinical trials data:

Infections and infestations:

Very common: candidiasis of mouth and throat

Candidiasis of the mouth and throat (thrush) may occur. Such patients may find it helpful to gargle with water after using the Accuhaler. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst still continuing with the FOXAIR Accuhaler

Immune system disorders:

Hypersensitivity reactions with the following manifestations have been reported:

Uncommon: cutaneous hypersensitivity reactions

Respiratory, thoracic and mediastinal disorders:

Common: hoarseness

Hoarseness may occur. Such patients may find it helpful to gargle with water after using the Accuhaler.

Post-marketing data:

Endocrine disorders:

Possible systemic effects include (see WARNINGS AND SPECIAL PRECAUTIONS):

Less frequent: adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma

Immune system disorders: angioedema (mainly facial and oropharyngeal oedema), respiratory symptoms (dyspnoea and/or bronchospasm) and anaphylactic reactions

Respiratory, thoracic and mediastinal disorders:

Less frequent: paradoxical bronchospasm

Effects on ability to drive and use machines:

FOXAIR is unlikely to produce an effect.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

The symptoms and signs of salmeterol overdosage are tremor, headache and tachycardia. The preferred antidote for overdosage with salmeterol is a cardio-selective beta-blocking agent. Both non-selective and selective beta-blockers should be avoided in patients with reversible obstructive airways disease, unless there are compelling reasons for their use.

Acute - Inhalation of fluticasone propionate at dosages 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 at doses in excess of those recommended 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.

IDENTIFICATION:

Each blister of FOXAIR 50/100, 50/250 and 50/500 Accuhaler contains a white powder.

PRESENTATION:

FOXAIR Accuhaler is a two-tone purple, circular moulded plastic device containing a foil strip with 60 regularly spaced blisters.

The FOXAIR 50/100 Accuhaler device is labelled with pink lettering.

The FOXAIR 50/250 Accuhaler device is labelled with purple lettering.

The FOXAIR 50/500 Accuhaler device is labelled with black lettering.

The device contains a dose counter which shows the number of doses remaining (60 to 1). To show when the last five doses have been reached, the number appears in red.

A single FOXAIR Accuhaler is packed into a carton.

STORAGE INSTRUCTIONS:

Store in a dry place below 30 ºC.

Keep out of reach of children.

REGISTRATION NUMBER:

FOXAIR 50/100 Accuhaler – 42/21.5.4/0581

FOXAIR 50/250 Accuhaler – 42/21.5.4/0582

FOXAIR 50/500 Accuhaler – 42/21.5.4/0583

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria, 7460

DATE OF PUBLICATION OF THE PACKAGE INSERT:

4 June 2010

GDS-10

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HISTORY:
Registered: 4 June 2010

Amended: 10 December (Notification to bring PI in line with Reg 9 and PIL in line with Reg 10). Implement 11-12-2015