Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Salamol Easi-Breathe CFC-Free Inhaler 100 micrograms Pressurised Inhalation, Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each actuation contains salbutamol sulphate equivalent to 100 micrograms salbutamol per metered dose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Pressurised inhalation, suspension
Product imported from the UK:
Pressurised container fitted with a metering valve and breath-operated actuator.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Salamol Easi-Breathe CFC-Free Inhaler provides short-acting (4 to 6 hour) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction (asthma, chronic bronchitis, emphysema).

Salamol Easi-Breathe CFC-Free Inhaler should be used in the management of asthma symptoms. For relief of wheezing and shortness of breath, Salamol Easi-Breathe CFC-Free Inhaler should be used on an as required basis. It is also useful to prevent asthma attacks induced by exercise or exposure to allergens.

Salamol Easi-Breathe CFC-Free Inhaler can be used to manage mild, moderate and severe asthma, provided its use does not delay the introduction and regular use of corticosteroid therapy, where necessary.

4.2 Posology and method of administration

Adults (including the Elderly):
For the relief of acute asthma, including wheeze, breathlessness and tightness of the chest, one inhalation (100 micrograms), increasing to two (200 micrograms) if necessary, may be administered as a single dose.

For the prevention of exercise- or allergen-induced asthma, two inhalations (200 micrograms) should be taken 10-15 minutes before challenge.
For chronic therapy, two inhalations (200 micrograms) should be administered up to four times daily.

Children:
For the relief of acute asthma symptoms including wheeze, breathlessness and tightness of the chest, or before allergen exposure or exercise, one inhalation (100 micrograms), or two (200 micrograms) if necessary, should be administered.

For chronic therapy in children, two inhalations (200 micrograms) should be administered up to four times daily.

For all patients, four hours should be allowed between each dose. No more than a maximum of eight inhalations (800 micrograms) should be taken in any 24 hours.

Patients with Hepatic or Renal Impairment
No need to adjust the dose.

Method of Administration:

Oral Inhalation

4.3 Contraindications

In spite of the fact that salbutamol has been used intravenously and orally in the management of uncomplicated premature labour, Salamol Easi-Breathe CFC-Free Inhaler should not be used for managing premature labour or for threatened abortion.

Salamol Easi-Breathe CFC-Free Inhaler is contra-indicated in patients with a history of hypersensitivity to any of its components.

4.4 Special warnings and precautions for use

Patients should be instructed in the proper use of the inhaler and their technique checked, to ensure that the drug reaches the target areas within the lungs.

Salbutamol should be administered cautiously to patients with thyrotoxicosis, coronary insufficiency, hypertrophic obstructive cardiomyopathy, arterial hypertension, tachyarrhythmias, in concomitant use of cardiac glycosides or diabetes mellitus.

The management of asthma should normally follow a stepwise programme, and the patient's response should be monitored clinically and by lung function tests. Increasing use of short-acting inhaled bronchodilators, in particular ß$_2$-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 starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

Asthmatic patients whose condition deteriorates despite salbutamol therapy, or where a previously effective dose fails to give relief for at least three hours, should seek medical advice in order that any necessary additional steps may be taken. Severe exacerbations of asthma must be treated in the normal way.

The dosage or frequency of administration should only be increased on medical advice.

Patients requiring long term management with Salamol Easi-Breathe CFC-Free Inhaler should be kept under regular surveillance.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. 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 steroid treatment (e.g.>1mg/day beclomethasone dipropionate) or oral corticosteroid therapy. With this primary background corticosteroid treatment, Salbutamol provides essential rescue medication for a severe asthmatic in treating acute exacerbations. Failure to respond promptly or fully to such rescue medication, signals a need for urgent medical advice and treatment.

A responsible adult should supervise the use of the inhaler in children.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

Potentially serious hypokalaemia may result from ß2-agonist therapy mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant

treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

As with other inhalation therapy, the potential for paradoxical bronchospasm should be considered. If it occurs the preparation should be discontinued immediately and alternative therapy given. Solutions which are not of neutral pH may rarely cause paradoxical bronchospasm in some patients. Salbutamol and non-selective beta blocking drugs such as propranolol should not usually be prescribed together.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurances of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease.

Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

4.5 Interaction with other medicinal products and other forms of interaction

Propranolol and other non-cardioselective ß-adrenoreceptor blocking agents antagonise the effects of salbutamol.

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs). However, the effects of salbutamol may be altered by guanethidine, reserpine, methyldopa and tricyclic antidepressants.

Digoxin: risk of increased cardiovascular effects.

Caution should be exercised during the concurrent use of anaesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents. Patients should be instructed to discontinue salbutamol at least 6 hours before an intended anaesthesia with halogenic anaesthetics, wherever possible.

Salbutamol and beta-blockers should not usually be prescribed together.

Hypokalaemia occurring with ß2-agonist therapy may be exacerbated by treatment with xantines, steroids, diuretics and long-term laxatives.

Because of the content of ethanol, there is a theoretical potential for interaction in patients taking disulfiram or metronidazole.

4.6 Fertility, pregnancy and lactation

Salbutamol:
Pregnancy
Administration of drugs during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

During worldwide marketing experience, rare cases of various congenital anomalies, including cleft palate and limb defects have been reported in the offspring of patients being treated with salbutamol. Some of the mothers were taking multiple medications during their pregnancies.

Because no consistent pattern of defects can be discerned, and baseline rate for congenital anomalies is 2-3%, a relationship with salbutamol use cannot be established.

High systemic doses at the end of pregnancy can cause inhibition of labour and may induce ß2-specific foetal/neonatal effects like tachycardia and hypoglycaemia. Inhalation therapy at recommended doses is not expected to induce these harmful side effects at the end of pregnancy.

Salbutamol inhalation is contraindicated in treatment of threatened abortion or premature labour.

Breastfeeding
As salbutamol is probably secreted in breast milk, its use in nursing mothers is not recommended unless the expected benefits outweigh any potential risk. It is not known whether salbutamol in breast milk has a harmful effect on the neonate.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

List of adverse reactions
The frequencies of adverse events are ranked according to the following: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000; including isolated reports), not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Hypersensitivity including angioedema, urticaria, bronchospasm, hypotension and collapse

Metabolism and nutrition disorders
Rare: Hypokalaemia (especially in combination with xanthine derivatives, corticosteroids and diuretics), increased serum lactate levels and acidosis lactic (following prolonged therapy)

Psychiatric disorders
Common: Tenseness (in the beginning of treatment)
Very rare: Insomnia

Nervous system disorders
Common: Tremor muscle, headache (both especially in the beginning of treatment), dizziness

Cardiac disorders
Rare: Palpitations (especially in the beginning of treatment), tachycardia
Very rare: Cardiac arrhythmia including atrial fibrillation, supraventricular tachycardia and extrasystoles – especially if used concomitantly with other ß2-agonists
Not known: Myocardial ischaemia* (see section Special Warnings and Special Precautions

Vascular disorders
Rare: Peripheral vasodilatation

Respiratory, thoracic and mediastinal disorders
Rare: Throat irritation
Very rare: Paradoxical bronchospasm (with an immediate increase in wheezing after dosing)

Gastrointestinal disorders
Rare: Mouth irritation, nausea, vomiting, dry mouth, sore mouth

Musculoskeletal and connective tissue disorders
Rare: Muscle cramps
Paediatric population:
Nervous system disorders:
Rare: hyperactivity

* reported spontaneously in post-marketing data therefore frequency regarded as unknown

4.9 Overdose

Overdosage may result in skeletal muscle tremor, tachycardia, tenseness, headache and peripheral vasodilatation.

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Hyperglycaemia and agitation have also been reported following overdose with salbutamol.

The preferred antidote for overdosage with salbutamol is a cardioselective ß-adrenoceptor blocking agent. Beta-blocking drugs should be used with caution in patients with a history of bronchospasm, as these drugs are potentially life-threatening.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Salbutamol is a selective β_2-adrenoceptor agonist. At therapeutic doses it acts on the β_2-adrenoceptors of bronchial muscle with little or no action on the β_2-adrenoceptors of the heart. Salbutamol thus provides short acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

5.2 Pharmacokinetic properties

Salbutamol administered intravenously has a half-life of 4-6 hours and is cleared partly renally and partly by metabolism to the inactive 4'-0- sulphate (phenolic sulphate) which is also excreted primarily in the urine.

The faeces are a minor route of excretion. Most of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours. Salbutamol is bound to plasma proteins to the extent of 10%.

After administration by the inhaled route between 10 and 20% of the dose reaches the lower airways. The remainder is retained in the delivery system or is deposited in the oropharynx from where it is swallowed. The fraction deposited in the airways is absorbed into the pulmonary tissues and circulation but is not metabolised by the lung. On reaching systemic circulation, salbutamol becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged drug and as the phenolic sulphate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulphate. Both unchanged drug and conjugate are excreted primarily in the urine.

5.3 Preclinical safety data

Salamol Easi-Breathe CFC-Free Inhaler:
Toxicological studies in rats and dogs with salbutamol formulated in propellant HFA-134a have shown a comparative safety profile to the current CFC-containing products. Few adverse effects were noted at high doses which were consistent with the known effects of salbutamol inhalation.

Propellant HFA-134a:
Toxicological effects of propellant HFA-134a consisted of narcosis and a relatively weak cardiac sensitising potential at very high exposure concentrations only. Safety margins of 2200, 1314 and 381 for mouse, rat and dog with respect to humans have been observed.

Salbutamol:
In common with other potent selective ß receptor agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of foetuses were found to have cleft palate, at 2.5 mg/kg, 4 times the maximum human oral dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout

pregnancy resulted in no significant foetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. A reproductive study in rabbits revealed cranial malformations in 37% of foetuses at 50mg/kg/day, 78 times the maximum human oral dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol, anhydrous
Norflurane (Propellant HFA-134a)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date for this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze. Protect from frost, direct sunlight and heat.
The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C.
Do not puncture, break or burn the canister even when apparently empty.
As with most inhaled medication in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

6.5 Nature and contents of container

A pressurised aluminium container with a metering valve and breath-operated actuator. Each pack contains a single inhaler which supplies 200 metered doses.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Any unused product or waste material should be disposed in accordance with local requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

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8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1151/074/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 8th December 2008

10 DATE OF REVISION OF THE TEXT

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