Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ventolin Diskus 200 micrograms Inhalation Powder, pre-dispensed.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each blister contains 200 micrograms of salbutamol (as sulphate).

Excipient with a known effect: lactose monohydrate

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Inhalation powder, pre-dispensed.

Product imported from the UK:
White powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Salbutamol is a selective beta-2-adrenoceptor agonist. At therapeutic doses it acts on the beta-2-adrenoceptors of bronchial muscle, with little or no action on the beta-1- adrenoceptors of the heart. With its fast onset of action, it is particularly suitable for the management and prevention of attacks in mild asthma and for the treatment of acute exacerbations in moderate and severe 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 to normal after a bronchodilator. These patients will require high dose inhaled (e.g. >1mg/day beclomethasone dipropionate) or oral corticosteroid therapy. With this primary background corticosteroid treatment, Ventolin 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.

Salbutamol provides short-acting (4-hour) bronchodilation with fast onset (within 5 minutes) in reversible airways obstruction due to asthma, chronic bronchitis and emphysema. It is suitable for long-term use in the relief and prevention of asthmatic symptoms.

Ventolin should be used to relieve symptoms when they occur and to prevent them in those circumstances recognised by the patient to precipitate an asthmatic attack (e.g. before exercise or unavoidable allergen exposure).

Ventolin is of particular value as rescue medication in mild, moderate or severe asthma, provided that reliance on them does not delay the introduction and use of regular inhaled corticosteroid therapy.

4.2 Posology and method of administration

Ventolin Diskus is administered by the inhaled route only, to be breathed in through the mouth.

Increasing use of beta-2-agonists may be a sign of worsening asthma. Under these conditions a reassessment of the patient’s therapy plan may be required and concomitant glucocorticosteroid therapy should be considered.

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

Salbutamol has a duration of action of 4 to 6 hours in most patients.

Relief of acute bronchospasm:
Adults: 200mcg as required.
Children: 200mcg as required.

Prevention of allergen or exercise-induced bronchospasm:
Adults: 200mcg before challenge.
Children: 200mcg before challenge

Chronic therapy:
Adults: 200mcg up to four times daily.
Children: 200mcg up to four times daily.

Elderly: There is no need to adjust the dose in the elderly.

On demand use of Ventolin Diskus should not exceed four times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see *Special Warnings and Special Precautions for Use*).

Patients' inhaler technique should be checked to ensure that the device is used at maximum efficiency.

4.3 Contraindications

Ventolin Diskus is contra-indicated in patients with a history of hypersensitivity to any of its components *(see Pharmaceutical Particulars – List of Excipients).*

Although intravenous salbutamol and occasionally salbutamol tablets are used in the management of premature labour uncomplicated by conditions such as placenta praevia, ante-partum haemorrhage or toxaemia of pregnancy, inhaled salbutamol preparations are not appropriate for managing premature labour. Salbutamol presentations should not be used for threatened abortion.

4.4 Special warnings and precautions for use

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 beta-2-agonists to relieve 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.

In the event of a previously effective dose of inhaled salbutamol failing to give medical relief lasting at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalaemia may result from beta-2-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.

Patients requiring long-term management with bronchodilators should be kept under regular surveillance.

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

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment including lung-function testing as patients are at risk of severe attacks and even death.

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

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature 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 salbutmaol 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

Salbutamol and non-selective beta-blocking drugs, such as propranolol, should not be prescribed together.

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.

Caution should be exercised during the concurrent use of anaesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents.

4.6 Fertility, pregnancy and lactation

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 world-wide 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.

As salbutamol is probably secreted in breast milk its use in nursing mothers is not recommended unless the expected benefits outweigh the 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 reported.

4.8 Undesirable 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 (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports. Very common and common events were generally determined from clinical trial data. Rare and very rare events were generally determined from spontaneous data.

Immune System Disorders
Very rare: Hypersensitivity reactions including angioedema and urticaria, bronchospasm, hypotension and collapse.

Metabolism and nutrition disorders
Rare: Hypokalaemia

Potentially serious hypokalaemia may result from beta-2-agonist therapy.

Nervous system disorders
Common: Tremor, headache

Very rare: Hyperactivity

Cardiac disorders
Common: Tachycardia

Uncommon: Palpitations

Very rare: Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles.

Unknown: Myocardial ischaemia* *(see section 4.4).*

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

Vascular disorders
Rare: Peripheral vasodilatation

Respiratory, thoracic and mediastinal disorders
Very Rare: Paradoxical bronchospasm

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

Gastrointestinal disorders
Uncommon: Mouth and throat irritation

Musculoskeletal and connective tissue disorders
Uncommon: Muscle cramps

4.9 Overdose

Symptoms and Signs
The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events *(see Special Warnings and Precautions and Adverse Reactions).*

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

Treatment
Consideration should be given to discontinuation of treatment and appropriate symptomatic therapy such as cardio-selective beta-blocking agents in patients presenting with cardiac symptoms (e.g. tachycardia, palpitations).

Beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Salbutamol is a selective beta-2-adrenoceptor agonist. At therapeutic doses it acts on the beta-2-adrenoreceptors of bronchial muscle, with little or no action on the beta-1- adrenoreceptors of cardiac muscle.

Salbutamol is a selective beta-2-agonist providing short-acting (4-6 hours) 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 the 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

In common with other potent selective beta-2 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 2.5mg/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 a 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

Lactose monohydrate

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 30°C.

6.5 Nature and contents of container

A blister strip consisting of a formed base foil with a peelable foil laminate lid. The foil strip is contained within the Diskus device. Each Diskus provides 60 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

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

LTT Pharma Limited
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Worcestershire B98 0RE
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1562/002/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24th August 2012

10 DATE OF REVISION OF THE TEXT