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 sulfate).
Excipients: Lactose monohydrate (which contains milk protein) 12.26 mg/blister

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Inhalation powder, pre-dispensed.
White powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ventolin Diskus is indicated in adults, adolescents and children over 4 years of age.

Ventolin Diskus is indicated for the treatment or prevention of bronchospasm. It provides short acting (four hours) bronchodilation in reversible airways obstruction due to asthma and chronic obstructive pulmonary disease (COPD) such as chronic bronchitis and emphysema. For patients with asthma salbutamol may be used to relieve symptoms when they occur and to prevent them prior to a known trigger.

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 corticosteroid 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.

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

Adults and Adolescents:

Relief of acute bronchospasm: 200 micrograms as required.

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 Section 4.4).

Prevention of allergen or exercise-induced bronchospasm:
200 micrograms before challenge or exertion.

Chronic therapy:
200 micrograms up to four times daily.

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

Paediatric Population

Relief of acute bronchospasm:
Children aged 4 to 11 years: 200 micrograms as required.

Children aged 12 years and over: 200 micrograms as required.

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 Section 4.4).

Prevention of allergen or exercise-induced bronchospasm:
Children aged 4 to 11 years: 200 micrograms before challenge or exertion.

Children aged 12 years and over: 200 micrograms before challenge or exertion.

Chronic therapy:
Children aged 4 to 11 years: 200 micrograms up to four times daily.

Children aged 12 years and over: 200 micrograms up to four times daily.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Contraindicated in patients with a severe milk-protein allergy.

4.4 Special Warnings and Precautions for Use

The management of asthma should normally follow a stepwise program, and the patient's response should be monitored clinically and by lung function tests.

Patients who are prescribed regular anti-inflammatory therapy (*e.g.*, inhaled corticosteroids) should be advised to continue taking their anti-inflammatory medication even when symptoms decrease, and they do not require Ventolin Diskus.

Increasing use of short-acting inhaled bronchodilators, in particular beta-2-agonists to relieve symptoms indicates deterioration of asthma control, and patients should be warned to seek medical advice as soon as possible. Under these conditions, the patient's therapy plan should be reassessed.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week "as needed" salbutamol, not counting prophylactic use prior to exercise, should be re-evaluated (i.e., daytime symptoms, night-time awakening, and activity limitation due to asthma) for proper treatment adjustment as these patients are at risk for overuse of salbutamol.

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 now failing to give rapid medical relief with a duration of at least three hours following administration,, the patient should be advised to promptly seek medical advice in order that any necessary additional steps may be taken.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalemia may result from beta-2-agonist therapy mainly from parenteral and nebulized 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 persistent asthma. In patients with persistent asthma unresponsive to salbutamol, treatment with inhaled corticosteroids is recommended to achieve and maintain control. Failing to respond to treatment with salbutamol may signal a need for urgent medical advice or treatment.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of myocardial ischemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischemic 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 dyspnea and chest pain, as they may be of either respiratory or cardiac origin.

As with other inhalation therapy, paradoxical bronchospasm may occur, resulting in an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator, if immediately available. The specific salbutamol presentation should be discontinued, and if necessary a different fast-acting bronchodilator instituted for ongoing use.

In common with other beta-adrenoceptor agonists, salbutamol can induce reversible metabolic changes, for example increased blood sugar levels. Caution is advised when administering this product to patients with a history of diabetes mellitus or hyperglycaemia.

This product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 anesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents.

4.6 Fertility, pregnancy and lactation

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 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.

Breast-feeding

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.

Fertility
There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals (*see section 5.3, Pre-clinical safety data*).

4.7 Effects on the Ability to Drive and Use Machines

Ventolin Diskus has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable Effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000) including isolated reports. Very common and common reactions were generally determined from clinical trial data. Rare and very rare reactions 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: Hypokalemia

Potentially serious hypokalemia 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 ischemia* (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

Gastrointestinal disorders
Uncommon: Mouth and throat irritation

Musculoskeletal and connective tissue disorders
Uncommon: Muscle cramps

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed below:
ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events (see section 4.4 and section 4.8).

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

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Selective beta-2-adrenoreceptor agonists, ATC Code - R03AC02.

Salbutamol is a selective $beta_2$-adrenoceptor agonist. At therapeutic doses it acts on the $beta_2$-adrenoceptors of bronchial muscle providing short acting (4 to 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-sulfate (phenolic sulfate) 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 sulfate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulfate. 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.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofetal development, litter size, birth weight or growth rate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Lactose monohydrate (which contains milk protein)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special Precautions for Storage

Do not store above 30°C.
Protect from frost and sunlight.

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

No special requirements for disposal.
Any unused medicinal product or waster material should be disposed of in accordance with local

requirements.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24

8. MARKETING AUTHORISATION NUMBER

MA192/03303

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11th December 2017

10. DATE OF REVISION OF THE TEXT

7th October 2026