

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ventolin Nebules 2.5mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Plastic ampoule containing 2.5 ml of a sterile 0.1% w/v solution of salbutamol (as Salbutamol Sulfate BP) in normal saline.

3. PHARMACEUTICAL FORM

Solution for inhalation via a nebuliser.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Salbutamol is a selective β_2 -agonist providing short-acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Ventolin Nebules are indicated for use in the routine management of chronic bronchospasm unresponsive to conventional therapy, and in the treatment of acute severe asthma.

Ventolin Nebules are indicated in adults, adolescents and children 4 to 11 years. For babies and children under 4 years of age see section 4.2.

4.2 Posology and method of administration

Ventolin Nebules are for inhalation use only, to be breathed in through the mouth, under the direction of a physician, using a suitable nebuliser.

The solution should not be injected or swallowed.

Adults (including the elderly): 2.5 mg to 5mg salbutamol up to four times a day. Up to 40 mg per day can be given under strict medical supervision in hospital.

Paediatric Population

Children aged 12 years and over: Dose as per adult population.

Children aged 4-11 years: 2.5 mg to 5 mg up to four times a day.

Other pharmaceutical forms may be more appropriate for administration in children under 4 years old.

Infants under 18 months old: Clinical efficacy of nebulised salbutamol in infants under 18 months is uncertain. As transient hypoxia may occur supplemental oxygen therapy should be considered.

Ventolin Nebules are intended to be used undiluted. However, if prolonged delivery time (more than 10 minutes) is required, the solution may be diluted with sterile normal saline.

4.3 Contraindications

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

Non-IV formulations of salbutamol must not be used to arrest uncomplicated premature labour or threatened abortion.

4.4 Special warnings and precautions for use

Ventolin Nebules must only be used by inhalation, to be breathed in through the mouth, and must not be injected or swallowed.

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. Physicians should consider using the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients.

Patients receiving treatment at home should seek medical advice if treatment with Ventolin Nebules becomes less effective. The dosage or frequency of administration should only be increased on medical advice.

Patients being treated with Ventolin Nebules may also be receiving other dosage forms of short-acting inhaled bronchodilators to relieve symptoms. Increasing use of bronchodilators, in particular short-acting inhaled β_2 -agonists to relieve symptoms, indicates deterioration of asthma control. The patient should be instructed to seek medical advice if short-acting relief bronchodilator treatment becomes less effective or more inhalations than usual are required. In this situation patients should be assessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid).

Severe exacerbations of asthma must be treated in the normal way.

Salbutamol should be administered cautiously to patients suffering from thyrotoxicosis.

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

Ventolin Nebules should be used with care in patients known to have received large doses of other sympathomimetic drugs.

Potentially serious hypokalaemia may result from β_2 -agonist therapy, mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by hypoxia and by concomitant treatment with xanthine derivatives, steroids and diuretics. Serum potassium levels should be monitored in such situations.

In common with other β -adrenoceptor agonists, salbutamol can induce reversible metabolic changes

such as increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Lactic acidosis has been reported in association with high therapeutic doses of intravenous and nebulised short-acting beta-agonist therapy, mainly in patients being treated for an acute asthma exacerbation (see Section 4.8). Increase in lactate levels may lead to dyspnoea and compensatory hyperventilation, which could be misinterpreted as a sign of asthma treatment failure and lead to inappropriate intensification of short-acting beta-agonist treatment. It is therefore recommended that patients are monitored for the development of elevated serum lactate and consequent metabolic acidosis in this setting.

A small number of cases of acute angle-closure glaucoma have been reported in patients treated with a combination of nebulised salbutamol and ipratropium bromide. A combination of nebulised salbutamol with nebulised anticholinergics should therefore be used cautiously. Patients should receive adequate instruction in correct administration and be warned not to let the solution or mist enter the eye.

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 Nebules should be discontinued and, if necessary a different fast-acting bronchodilator instituted for on-going use.

4.5 Interaction with other medicinal products and other forms of interaction

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

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 fetus. As with the majority of drugs, there is little published evidence of the safety of salbutamol in the early stages of human pregnancy, but in animal studies there was evidence of some harmful effects on the fetus at very high dose levels.

Breast-feeding

As salbutamol is probably secreted in breast milk, its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother is likely to outweigh any potential risk to 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*).

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 ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1000$) and very rare ($< 1/10,000$). Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders

Very rare: Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse

Metabolism and nutrition disorders

Rare: Hypokalaemia.
Potentially serious hypokalaemia may result from beta₂ agonist therapy.

Unknown: Lactic acidosis (see section 4.4)

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)

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.

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

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 Pharmaceutical Services, Ministry of Health, CY-1475 Nicosia, Fax: + 357 22608649, Website: www.moh.gov.cy/phs.

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia and lactic acidosis (see sections 4.4 and 4.8).

Hypokalaemia 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: Adrenergics, inhalants. Selective beta-2-adrenoreceptor agonists
ATC code: R03AC02

Salbutamol is a selective β_2 -agonist providing short-acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction. At therapeutic doses it acts on the β_2 -adrenoceptors of bronchial muscle. With its fast onset of action, it is particularly suitable for the management and prevention of attack in asthma.

5.2 Pharmacokinetic properties

Salbutamol administered intravenously has a half-life of 4 to 6 hours and is cleared partly renally, and partly by metabolism to the inactive 4'-O-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 it 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 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

Sodium chloride
Sulfuric acid if required to adjust pH
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years if unopened.
3 months after removal from the foil overwrap, (see below).

6.4 Special precautions for storage

Ventolin Nebules should be stored below 30°C. The Nebules should be protected from light after removal from the foil tray.

6.5 Nature and contents of container

Low density polyethylene ampoules available in boxes of 20 in strips of 5.

6.6 Special precautions for disposal and other handling

The nebulised solution may be inhaled through a face mask, T-piece or via an endotracheal tube. Intermittent positive pressure ventilation (IPPV) may be used but is rarely necessary. When there is a risk of anoxia through hypoventilation, oxygen should be added to the inspired air.

As many nebulisers operate on a continuous flow basis, it is likely that some nebulised drug will be released into the local environment. Ventolin Nebules should therefore be administered in a well-ventilated room, particularly in hospitals when several patients may be using nebulisers at the same time.

Dilution: Ventolin Nebules may be diluted with sterile normal saline. Solutions in nebulisers should be replaced daily.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

17101

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 January 1998
Date of latest renewal: 12 March 2010

10. DATE OF REVISION OF THE TEXT

2 April 2019