

Salbutamol

Ventolin® Nebules®

1mg/mL Solution for Inhalation
Anti-asthma

PRODUCT DESCRIPTION

Salbutamol (*Ventolin® Nebules®*) Solution for Inhalation 1mg/mL is in a plastic ampoule containing a concentration of salbutamol of 0.1% (1mg salbutamol, as the sulphate, in 1mL). Each Salbutamol (*Ventolin® Nebules®*) Solution for Inhalation contains 2.5mL of solution equivalent to 2.5mg salbutamol.

PHARMACOLOGIC PROPERTIES

Pharmacodynamics

Salbutamol is a selective beta2-adrenoceptor agonist. At therapeutic doses it acts on the beta2-adrenoceptors of bronchial muscle providing short acting (4 to 6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Pharmacokinetics

Absorption

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.

Distribution

Salbutamol is bound to plasma proteins to the extent of 10%.

Metabolism

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 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.

Elimination

Salbutamol administered intravenously has a half-life of four to six hours and is cleared partly renally and partly by metabolism to the inactive 4'-O-sulphate (phenolic sulphate) which is also excreted primarily in the urine. The faeces are a minor route of excretion. The majority of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours.

Pre-clinical Safety Data

In common with other potent selective beta2 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. 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.

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.

INDICATIONS

Salbutamol is a selective beta2 adrenoceptor agonist indicated for the treatment or prevention of bronchospasm. It provides short acting (four hours) bronchodilation in reversible airways obstruction due to asthma, 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.

Bronchodilators should not be the only or main treatment in patients with persistent asthma. In patients with persistent asthma unresponsive to Salbutamol (*Ventolin*®), treatment with inhaled corticosteroids is recommended to achieve and maintain control. Failing to respond to treatment with Salbutamol (*Ventolin*®) may signal a need for urgent medical advice or treatment.

Salbutamol (*Ventolin*® *Nebules*®) are indicated for the routine management of chronic bronchospasm (unresponsive to conventional therapy) and treatment of acute severe asthma (status asthmaticus).

DOSAGE AND ADMINISTRATION

Salbutamol (*Ventolin*®) has a duration of action of 4 to 6 hours in most patients.

Salbutamol (*Ventolin*® *Nebules*®) are intended to be used undiluted. However, if prolonged delivery time is desirable (more than 10 minutes) dilution using sterile normal saline as a diluent may be required. Salbutamol (*Ventolin*® *Nebules*®) are to be used with a nebuliser, under the direction of a physician.

The solution must not be injected, or swallowed.

Increasing use of beta2 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.

Delivery of the aerosol may be by facemask, 'T' piece or via an endotracheal tube. Intermittent positive pressure ventilation 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 there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

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

• Adults and Children

A suitable starting dose of salbutamol by wet inhalation is 2.5 milligrams.

This may be increased to 5 milligrams. Treatment may be repeated four times daily. In adults higher dosing, up to 40 milligrams per day, can be given under strict medical supervision in hospital for the treatment of severe airways obstruction.

Clinical efficacy of nebulised Salbutamol (*Ventolin*®) in infants under 18 months is uncertain. As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

CONTRAINDICATIONS

Salbutamol (*Ventolin*® *Nebules*®) are contraindicated in patients with a history of hypersensitivity to any of their components.

Non-i.v. formulations of Salbutamol (*Ventolin*®) must not be used to arrest uncomplicated premature labour or threatened abortion.

WARNINGS AND PRECAUTIONS

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

Increasing use of short-acting inhaled beta2 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.

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

Patients receiving treatment at home with Salbutamol (*Ventolin*® *Nebules*®) must be warned that if either the usual relief is diminished or the usual duration of action reduced, they should not increase the dose or its frequency of administration, but should seek medical advice.

Salbutamol (*Ventolin*® *Nebules*®) should be used with caution in patients known to have received large doses of other sympathomimetic drugs.

Salbutamol (*Ventolin*®) should be administered cautiously to patients with thyrotoxicosis.

A small number of cases of acute angle closure glaucoma have been reported in patients treated with a combination of nebulised Salbutamol (*Ventolin*®) and ipratropium bromide. A combination of nebulised Salbutamol (*Ventolin*®) 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.

Potentially serious hypokalaemia may result from beta2 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, 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. Salbutamol (*Ventolin® Nebules®*) should be discontinued, and if necessary a different fast-acting bronchodilator instituted for ongoing use.

In common with other beta-adrenoceptor agonists, Salbutamol (*Ventolin®*) can induce reversible metabolic changes, for example increased blood sugar levels.

The diabetic patient may be unable to compensate for this and the development of ketacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Lactic acidosis has been reported very rarely 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 Adverse Reaction section*). 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.

Effects on Ability to Drive and Use Machines

None reported.

DRUG INTERACTIONS

Salbutamol (*Ventolin®*) and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together.

Salbutamol (*Ventolin®*) is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

PREGNANCY AND LACTATION

Fertility

There is no information on the effects of Salbutamol (*Ventolin®*) on human fertility. There were no adverse effects on fertility in animals (*see Pre-clinical Safety Data*).

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.

As 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.

Lactation

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.

ADVERSE 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 ($< 1/10,000$) 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, urticaria, bronchospasm, hypotension and collapse.

Metabolism and nutrition disorders

Rare: Hypokalaemia.

Potentially serious hypokalaemia may result from beta2 agonist therapy.

Very rare: Lactic acidosis

Lactic acidosis has been reported very rarely in patients receiving intravenous and nebulised salbutamol therapy for the treatment of acute asthma exacerbation.

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

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

Overdosage and treatment

The most common signs and symptoms of overdose with Salbutamol (*Ventolin*®) are transient beta agonist pharmacologically mediated events (see *Warnings and Precautions and Adverse Reactions*). Hypokalaemia may occur following overdose with Salbutamol (*Ventolin*®). 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.

Storage condition

Store below 30°C and protected from light.

Instructions for Use and Handling

Dilution:

Salbutamol (*Ventolin*® *Nebules*®) may be diluted with sterile normal saline.

Any unused solution in the chamber of the nebuliser must be discarded.

Availability

Salbutamol (*Ventolin*® *Nebules*®) 1mg/mL Solution for Inhalation:

Plastic ampoule x 2.5 mL packaged in an aluminium foil flowwrap pack x 5's (Box of 20's)

Caution

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Keep all medicines out of reach of children.

VENTOLIN and NEBULES are registered trademarks of the GSK group of companies.

©2014, GSK. All rights reserved.

Version number: GDS25/IPI09

Revision date: 14 April 2014

Imported by:

GlaxoSmithKline Philippines Inc

2266 Chino Roces Avenue, City of Makati

Tel. 892-0761

Manufactured by:

GlaxoSmithKline Australia Pty Ltd

Boronia, Australia