

DATA SHEET

Ventolin™ Injection

Ventolin™ Solution for Intravenous Infusion

Salbutamol injection and salbutamol solution for intravenous injection 500µg/mL, 1mg/mL.

Qualitative and quantitative composition

VENTOLIN INJECTION 500µg (0.5mg) in 1mL (500µg/ml) is presented in ampoules of 1mL each containing 0.5mg Salbutamol BP as Salbutamol Sulphate BP, in a sterile isotonic solution adjusted to pH 3.5 with sulphuric acid.

VENTOLIN SOLUTION FOR INTRAVENOUS INFUSION 5mg in 5mL (1mg/mL) is presented as ampoules of 5mL each containing 5mg Salbutamol BP as Salbutamol Sulphate BP, in a sterile isotonic solution adjusted to pH 3.5 with sulphuric acid.

The ampoules are of clear, neutral glass and the solution is colourless or faintly straw coloured.

Clinical particulars

Therapeutic indications

Salbutamol is a selective β_2 adrenoceptor agonist. At therapeutic doses it acts on the β_2 adrenoceptors in the bronchi and uterus, with little or no action on the β_1 adrenoceptors of the heart. It is suitable for the management of an asthmatic attack, and for uncomplicated premature labour, under the direction of a physician.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment as death may occur. 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 (e.g >1mg/day beclomethasone dipropionate) or oral corticosteroid therapy. Sudden worsening of symptoms may require increased corticosteroid dosage which should be administered under urgent medical supervision.

Relief of severe bronchospasm associated with asthma or bronchitis and for the treatment of status asthmaticus.

Management of uncomplicated premature labour in the last trimester of pregnancy.

Posology and method of administration

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

Ventolin parenteral preparations are to be used under the direction of a physician.

Increasing use of β_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.

Note : The contents of the ampoules of Ventolin Solution For Intravenous Infusion must not be injected undiluted. The concentration should be reduced by 50% before administration.

Ventolin parenteral preparations should not be administered in the same syringe or infusion as any other medication.

Adults:-

In severe bronchospasm and status asthmaticus:

Subcutaneous Route:-

500 μ g (8 μ g/kg bodyweight) and repeated every four hours as required.

Intramuscular Route:-

500 μ g (8 μ g/kg bodyweight) and repeated every four hours as required.

Intravenous Route:-

250 μ g (4 μ g/kg bodyweight) injected slowly. If necessary the dose may be repeated.

Ventolin Injection 250 μ g in 5mL (50 μ g/mL) is a suitably dilute preparation for slow intravenous injection but if Ventolin Injection 500 μ g in 1mL (500 μ g/mL) is used the injection may be facilitated by dilution with water for injections.

Infusion:-

In status asthmaticus, infusion rates of 3 to 20 μ g per minute are generally adequate but in patients with respiratory failure, higher dosage has been used with success. A starting dose of 5 μ g per minute is recommended with appropriate adjustment in dosage according to patient response.

A suitable solution for infusion may be prepared by diluting 5mL of Ventolin Solution for Intravenous Infusion in 500mL of an infusion solution such as sodium chloride and dextrose injection BP to provide a salbutamol dose of 10µg/mL of solution.

In the management of premature labour:-

For this indication Ventolin Solution for Intravenous Infusion is recommended using a solution prepared as above. Infusion rates of 10-45µg per minute are generally adequate to control uterine contractions but greater or lesser infusion rates may be required according to the strength and frequency of contractions. A starting rate of 10µg per minute is recommended, increasing the rate at 10-minute intervals until there is evidence of patient response shown by diminution in strength, frequency or duration of contractions. Thereafter the infusion rate may be increased slowly until contractions cease. The maternal pulse rate should be monitored and the infusion rate adjusted to avoid excessive maternal heart rates (above 140 beats per minute).

Once uterine contractions have ceased the infusion rate should be maintained at the same level for one hour and then reduced by 50% decrements at 6-hourly intervals. Treatment may be continued orally with Ventolin Tablets 4 milligram given three or four times daily.

As an alternative procedure or to counteract inadvertent overdosage with oxytocic drugs, Ventolin Injection may be administered as a single injection by the intravenous or intramuscular routes. The usual recommended dose is 100 to 250µg of salbutamol. The dose may be repeated according to the response of the patient.

Children:-

At present there is insufficient evidence to recommend a dosage regimen for routine use in children.

Contra-indications

Ventolin parenteral preparations are contra-indicated in patients with a history of hypersensitivity to any of their components.

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 toxemia of pregnancy, salbutamol presentations should not be used for threatened abortion.

Special warnings and special precautions for use

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 β_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.

The use of Ventolin parenteral preparations in the treatment of severe bronchospasm or status asthmaticus does not obviate the requirement for glucocorticoid steroid therapy as appropriate.

When practicable, administration of oxygen concurrently with parenteral Ventolin is recommended, particularly when it is given by intravenous infusion to hypoxic patients.

In common with other β -adrenoceptor agonists, Ventolin can induce reversible metabolic changes such as reversible hypokalaemia and increased blood glucose levels. The diabetic patient may be unable to compensate for this and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

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

Diabetic patients and those concurrently receiving corticosteroids should be monitored frequently during intravenous infusion of Ventolin so that remedial steps (e.g. an increase in insulin dosage) can be taken to counter any metabolic change occurring. For these patients Ventolin Solution for Intravenous Infusion should be diluted with Sodium Chloride Injection BP, rather than Sodium Chloride and Dextrose Injection BP.

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 Undesirable Effects 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. The population at risk primarily includes patients with an acute exacerbation of the underlying respiratory disease undergoing high dose treatment regimens, particularly with intravenous and nebulised salbutamol. It is therefore recommended that patients are monitored for the development of elevated serum lactate and consequent metabolic acidosis in this setting.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

As maternal pulmonary oedema and myocardial ischaemia have been reported during or following treatment of premature labour with β_2 agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG, should be monitored. If signs of pulmonary oedema or myocardial ischaemia develop, discontinuation of treatment should be considered (see Undesirable Effects).

In the treatment of premature labour by intravenous infusion of salbutamol increases in maternal heart rate of the order 20 to 50 beats per minute usually accompany the infusion. The maternal pulse rate should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.

Maternal blood pressure may fall slightly during the infusion; the effect being greater on diastolic than on systolic pressure. Falls in diastolic pressure are usually within the range of 10 to 20mmHg. The effect of infusion on foetal rate is less marked but increases of up to 20 beats per minute may occur.

In the treatment of premature labour, before Ventolin parenteral preparations are given to any patient with known heart disease, an adequate assessment of the patient's cardiovascular status should be made by a physician experienced in cardiology.

Interaction with other medicaments and other forms of interaction

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

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

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 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.

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.

Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1000$ and $< 1/100$), rare ($\geq 1/10,000$ 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, 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

Very common: Tremor.

Common: Headache.

Very rare: Hyperactivity.

Cardiac disorders

Very common: Tachycardia, palpitations.

Uncommon: Myocardial ischaemia.

In the management of pre-term labour.

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

Vascular disorders

Rare: Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders

Uncommon: Pulmonary oedema.

In the management of pre-term labour, salbutamol injection/solution for infusion have uncommonly been associated with pulmonary oedema. Patients with predisposing factors including multiple pregnancies, fluid overload, maternal infection and pre-eclampsia may have an increased risk of developing pulmonary oedema.

Gastrointestinal disorders

Very rare: Nausea, vomiting.

In the management of premature labour, intravenous infusion of Ventolin has very rarely been associated with nausea and vomiting.

Musculoskeletal and connective tissue disorders

Common: Muscle cramps.

Injury, poisoning and procedural complications

Very rare: Slight pain or stinging on i.m. use of undiluted injection.

Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events (see Special Warnings and Special Precautions for Use and Undesirable Effects).

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

Consideration should be given to discontinuation of treatment and appropriate symptomatic treatment such as a cardio-selective β -blocking agent, in patients presenting with cardiac symptoms (e.g. tachycardia, palpitations). Beta-

blocking agents should be used with caution in patients with a history of bronchospasm.

Pharmacological properties

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_1 adrenoceptors of cardiac muscle.

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

Pre-clinical safety data

In common with other potent selective β_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 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.

Pharmaceutical particulars

Shelf Life

36 months

Special Precautions for Storage:-

Ventolin parenteral preparations should be protected from light and stored at a temperature below 30°C.

All unused admixtures of Ventolin Parenteral Preparations with infusion fluids should be discarded twenty-four hours after preparation.

Dilution:-

Ventolin parenteral preparations may be diluted with Water for Injections BP, Sodium Chloride Injection BP, Sodium Chloride and Dextrose Injection BP or Dextrose Injection BP. These are the only recommended diluents.

Package Quantities

Ventolin Injection 0.5mg in 1mL (500micrograms/mL) is available in boxes of 5 ampoules.

Ventolin Solution for Intravenous Infusion 5mg in 5mL (1mg/mL) is available in boxes of 10 ampoules.

Medicines classification

Prescription Only Medicine

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