

PACKAGE INSERT TEMPLATE FOR SALBUTAMOL RESPIRATOR SOLUTION & SALBUTAMOL SOLUTION FOR INHALATION

Brand or Product Name

[Product name] Respirator Solution 0.5% w/v

[Product name] Solution for Inhalation 0.1% w/v

Name and Strength of Active Substance(s)

Salbutamol sulphate ...mg equivalent to salbutamol 0.5% w/v (5mg/ml)

Salbutamol sulphate ...mg equivalent to salbutamol 0.1% w/v (1mg/ml)

Product Description

[Visual description of the appearance of the product (eg colour, markings etc)]

eg Respirator Solution - An aqueous colourless solution adjusted with acid to pH 3.5 in amber glass bottle

Solution for Inhalation – An aqueous, colourless solution adjusted to pH 4.0 in plastic ampoule (nebules)

Pharmacodynamics

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. It is suitable for the management and prevention of attack in asthma.

Pharmacokinetics

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%.

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 sulphate. The swallowed portion of an inhaled dose is absorbed from the

Updated October 2011

gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulphate. Both unchanged drug and conjugate are excreted primarily in the urine.

Indication

Salbutamol Respirator Solution is indicated for the treatment of acute severe asthma (status asthmaticus) and for routine management of chronic bronchospasm-unresponsive to conventional therapy.

Recommended Dosage

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

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

Salbutamol Respirator Solution

Salbutamol Respirator Solution is to be used with a respirator or nebuliser, only under the direction of a physician. The solution must not be injected.

i) By intermittent administration

Intermittent treatment may be repeated four times daily.

Adults

Salbutamol Respirator Solution 0.5 - 1.0ml (2.5 - 5.0 milligrams of salbutamol) should be diluted to a final volume of 2.0 or 2.5ml using normal saline for injection as a diluent. The resulting solution is inhaled from a suitably driven nebuliser until aerosol generation ceases. Using a correctly matched nebuliser and driving source this should take about ten minutes.

Salbutamol Respirator Solution may be used undiluted for intermittent administration. For this, 2.0ml of Salbutamol Respirator Solution (10.0 milligrams salbutamol) is placed in the nebuliser and the patient allowed to inhale the nebulised solution until bronchodilatation is achieved. This usually takes 3 – 5 minutes.

Some adult patients may require higher doses of salbutamol, up to 10 milligrams, in which case nebulisation of the undiluted solution may continue until aerosol generation ceases.

Updated October 2011

Children

The same mode of administration for intermittent administration is also applicable to children. The usual dosage for children under the age of twelve years is 0.5ml (2.5 milligrams salbutamol) diluted to 2.0 or 2.5ml using normal saline for injection as diluent. Some children may however require higher doses of salbutamol up to 5.0 milligrams.

Clinical efficacy of nebulised salbutamol in infants under 18 months is uncertain. As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

ii) By continuous administration

Salbutamol Respirator Solution is diluted using normal saline for injection to contain 50 - 100 micrograms of salbutamol per ml, (1 - 2ml solution made up to 100ml with diluent). The diluted solution is administered as an aerosol by a suitable driven nebuliser. The usual rate of administration is 1 - 2 milligrams per hour.

Salbutamol Solution for Inhalation

Salbutamol Solution for Inhalation is to be used with a nebuliser, under the direction of a physician. The solution must not be injected.

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

If a previously effective dose fails to give adequate relief which lasts for at least three hours, seek medical advice immediately.

Adults and Children

A suitable starting dose of salbutamol by wet inhalation is 2.5mg. This may be increased to 5mg. Treatment may be repeated four times daily. In adults higher dosing, up to 40mg per day, can be given under strict medical supervision in hospital for the treatment of severe airways obstruction. Clinical efficacy of nebulised salbutamol in infants under 18 months is uncertain. As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

Updated October 2011

Mode of Administration

Inhalation

Contraindications

Salbutamol preparations are contraindicated 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, inhaled salbutamol preparations are not appropriate for managing premature labour. Salbutamol preparations should not be used for 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 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.

Patients should 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 Respirator Solution and Salbutamol Solution for Inhalation should be used with care in patients known to have received large doses of other sympathomimetic drugs.

Salbutamol 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 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.

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

Updated October 2011

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

In common with other β -adrenoceptor agonists, salbutamol 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.

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 oral corticosteroid therapy and/or the maximum recommended dose of inhaled corticosteroid in those patients.

Effect on ability to drive and use machines – none known

Interactions with Other Medicaments

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

Concomitant use of salbutamol and tricyclic antidepressants or monoamine oxidase inhibitors may cause a potentiation of the vascular effects of Salbutamol. Salbutamol is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

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

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 / Undesirable Effects

Salbutamol Respirator Solution and Salbutamol Solution for Inhalation may cause a fine tremor of skeletal muscle, usually the hands are obviously affected. This effect is common to all beta-adrenergic stimulants.

Updated October 2011

Occasionally headaches have been reported.

Peripheral vasodilatation and a compensatory small increase in heart rate may occur in some patients.

Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse have been reported very rarely.

There have been very rare reports of muscle cramps.

As the 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. Salbutamol Respirator Solution and Salbutamol Solution for Inhalation should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

Potentially serious hypokalaemia may result from β_2 agonists therapy.

As with other beta-2 agonists hyperactivity has been reported rarely in children.

Mouth and throat irritation may occur with inhaled salbutamol.

Tachycardia may occur in some patients.

Overdose and Treatment

Overdosage symptoms are those of excessive β -stimulation, e.g. seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, fatigue and insomnia. Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

Treatment consists of discontinuation of salbutamol together with appropriate symptomatic therapy. Administer a cardioselective β -adrenergic blocker (e.g. acebutalol, atenolol, metoprolol), if necessary for cardiac arrhythmias. However, β -adrenergic blocker should be used with caution because it could induce severe bronchospasm.

Instructions for Use

[To add appropriate information and graphic]

Storage Conditions

[eg Store below °C]

Updated October 2011

Dosage Forms and Packaging Available

[Packaging type & pack size]

Name and Address of Manufacturer

[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder

[Name & full address of marketing authorization holder]

Date of Revision of Package Insert

[day/month/year]