

PACKAGE INSERT TEMPLATE FOR SALBUTAMOL INJECTION & SALBUTAMOL SOLUTION FOR INTRAVENOUS INFUSION

Brand or Product Name

[Product name] Injection 0.5mg/ml

[Product name] Solution for IV Infusion 1mg/ml

Name and Strength of Active Substance(s)

[Injection]

Salbutamol sulphatemg equivalent to salbutamol 0.5mg/ml

[Solution for IV Infusion]

Salbutamol sulphatemg equivalent to salbutamol 1mg/ml

Product Description

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

eg A sterile, clear colourless solution

Pharmacodynamics

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.

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%.

Indication

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.

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Recommended Dosage

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

The contents of the ampoules of Salbutamol Solution For IV Infusion must not be injected undiluted. The concentration should be reduced by 50% before administration. Salbutamol 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 micrograms (8 micrograms /kg bodyweight) and repeated every four hours as required.

Intramuscular Route

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

Intravenous Route

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

Intravenous Infusion

In status asthmaticus, infusion rates of 3 to 20 micrograms per minute are generally adequate but in patients with respiratory failure, higher dosage has been used with success. A starting dose of 5 micrograms 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 Salbutamol Solution for Intravenous Infusion in 500ml of an infusion solution such as sodium chloride and dextrose injection BP to provide a salbutamol dose of 10 micrograms /ml of solution.

In the management of premature labour

For this indication Salbutamol Solution for Intravenous Infusion is recommended using a solution prepared as above. Infusion rates of 10-45 micrograms per minute are generally

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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 10 micrograms 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. Careful attention should be given to cardio-respiratory function and fluid balance monitoring. The maternal pulse rate should be monitored and the infusion rate adjusted to avoid excessive maternal heart rates (above 140 beats per minute). Treatment discontinuation should be considered should signs of pulmonary oedema or myocardial ischaemia develop.

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 Salbutamol Tablets 4 milligram given three or four times daily.

As an alternative procedure or to counteract inadvertent overdosage with oxytocic drugs, Salbutamol Injection may be administered as a single injection by the intravenous or intramuscular routes. The usual recommended dose is 100 to 250 micrograms 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.

Mode of Administration

[Injection]

Subcutaneous, intramuscular and slow intravenous injection

[Solution for IV Infusion]

Intravenous infusion

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, salbutamol preparations should not be used for threatened abortion.

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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.

The use of salbutamol 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 salbutamol is recommended, particularly when it is given by intravenous infusion to hypoxic patients.

In common with other β -adrenoceptor agonists, salbutamol 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 salbutamol so that remedial steps (e.g. an increase in insulin dosage) can be taken to counter any metabolic change occurring. For these patients Salbutamol 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 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.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

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Tocolysis: Serious adverse reactions including death have been reported of salbutamol to women in labor. In the mother, these include increased heart rate, transient hyperglycaemia, hypokalaemia, cardiac arrhythmias, pulmonary oedema and myocardial ischaemia. Increased fetal heart rate and neonatal hypoglycaemia may occur as a result of maternal administration.

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.

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 salbutamol 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.

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 contra-indicated 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.

Updated October 2011

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.

Adverse Effects / Undesirable Effects

Immune system disorders

Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse

Metabolism and nutrition disorders

Hypokalaemia, Lactic acidosis

Nervous system disorders

Tremor, headache, hyperactivity

Cardiac disorders

Tachycardia, palpitations, myocardial ischaemia (in the management of pre-term labour with salbutamol injection/solution for infusion), cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles.

Vascular disorders

Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders

Pulmonary oedema.

Gastrointestinal disorders

Nausea, vomiting

Musculoskeletal and connective tissue disorders

Muscle cramps

Injury, poisoning and procedural complications

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

Updated October 2011

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.

Incompatibilities

[To add appropriate information based on formulation]

Instructions for Use

[To add appropriate information and graphic]

Storage Conditions

[eg Store below °C]

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]

Updated October 2011