airsal respules(salbutamol salphate)

It is a inhalation solution which is used via a nebulizer in airway disese.

Composition

Each 2.5 ml respule contains:

Salbutamol Sulphate IP equivalent to Salbutamol IP …. 2.5 mg

Normal saline solution …….q.s.

DESCRIPTION

AIRSAL RESPULEs solution contain a racemic mixture of Salbutamol sulphate in equal amounts (50:50) of (R) and (S)-isomers. A white or almost white, crystalline powder. Clear solution in methanol. Sparingly soluble in water; soluble in ethanol (96%); slightly soluble in ether

PHARMACOLOGY

PHARMACODYNEMICS

AIRSAL RESPULES (Salbutamol) is a selective beta$_2$-agonist providing short-acting (4-6 hours) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction. At therapeutic doses, it acts on the beta$_2$-adrenoceptors of bronchial muscle. With its fast onset of action, it is particularly suitable for the management and prevention of attack in asthma.

PHARMACOKINETICS

AIRSAL RESPULES (Salbutamol) administered intravenously has a half-life of 4-6 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. 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 metabolized by the lungs. On reaching the systemic circulation,

it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged drug and as phenolic sulphate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to phenolic sulphate. Both unchanged drug and conjugate are excreted primarily in the urine.

INDICATION

AIRSAL RESPULES (SALBUTAMOL SOLUTION) are indicated for use in the routine management of chronic bronchospasm unresponsive to conventional therapy, and in the treatment of acute severe asthma.

DOSAGE AND ADMINISTRATION

AIRSAL RESPULES are for inhalation use only, to be inhaled in through the mouth via a suitable nebulizer, as instructed by a physician.
The solution should not be injected or swallowed.

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

Children (4 years and above)
2.5mg to 5mg up to four times a day.

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.

CONTRAINDICATION

AIRSAL RESPULES is contraindicated in patients with a history of hypersensitivity to any of the components.

Rare cases of hypersensitivity reactions including urticaria, angioedema and rash have been reported after the use of salbutamol.

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 toxaemia of pregnancy, inhaled salbutamol preparations are not appropriate for managing premature labour. Salbutamol preparations should not be used for threatened abortion.

WARNING AND PRECAUTIONS

AIRSAL RESPULES must only be used for inhalation, to be inhaled in through the mouth via a suitable nebulizer, 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 being treated with AIRSAL RESPULES may also be receiving other dosage forms of short-acting inhaled bronchodilators to relieve symptoms. Increasing use of bronchodilators, particular short-acting inhaled $beta_2$-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 corticosteroids).

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

Salbutamol should be administered cautiously to patients suffering from thyrotoxicosis.

Salbutamol, like all other beta-adrenergic agonists, can produce clinically significant cardiovascular effects in some patients as measured by pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon after administration of salbutamol at recommended doses, if they occur, the drug may need to be discontinued. In addition, beta-agonists have been reported to produce electrocardiogram (ECG) changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, salbutamol, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Immediate hypersensitivity reactions may occur after administration of salbutamol, as demonstrated by cases of urticaria, angio-oedema, rash, bronchospasm, anaphylaxis, and oropharyngeal oedema.

AIRSAL RESPULES should be used with care in patients who are known to have received large doses of other sympathomimetic drugs. Potentially serious hypokalaemia may result from $beta_2$-agonist therapy, mainly from parenteral and nebulized 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.
Like other beta-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. 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.

In the following cases, salbutamol should only be used with caution and if strictly indicated: serious cardiac disorders, in particular recent myocardial infarction, coronary heart disease, hypertrophic obstructive cardiomyopathy and tachyarrhythmia (due to the positive ionotropic effect of β2 – agonists) severe and untreated hypertension, aneurysm, hyperthyroidism, diabetes which is difficult to control, pheochromocytoma. The administration of salbutamol in patients with acute asthma may cause a further reduction of the O_2 saturation. Exceeding the prescribed dose can be dangerous with resultant cardiac effects, hypokalaemia, taste alteration, nausea, restlessness, sweating, headache, or tremor.

There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischemic 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.

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

DRUG INTERATIONS

Salbutamol preparations should be used with caution in patients suffering from thyrotoxicosis. AIRSAL RESPULES and non-selective beta-blocking drugs such as propranolol should generally not be prescribed together. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to use beta-adrenergic blocking agents in patients with asthma. In this setting, cardio selective beta-blockers should be considered, although they should be administered with caution.

Tricyclic antidepressants may increase the risk of cardiovascular side effects. Corticosteroids may increase the risk of hyperglycaemia.

The ECG changes and/or hypokalemia that may result from the administration of non-potassium-sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical

relevance of these effects is not known, caution is advised in the co-administration of beta-agonists with non-potassium-sparing diuretics. Consider monitoring potassium levels.

Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, digoxin, diuretics, and by hypoxia. It is recommended that serum potassium levels be monitored in such situations.

Exceeding the prescribed dose can be dangerous with resultant cardiac effects, hypokalaemia, taste alteration, nausea, restlessness, sweating, headache, or tremor.

AIRSAL RESPULES should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants or within 2 weeks discontinuation of such agents, because the action of salbutamol on the vascular system may be potentiated.

PREGNANCY

Administration of AIRSAL RESPULES 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 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.

LACTATION

As AIRSAL RESPULE (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.

IMMUNE SYSTEM DISORDER

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

METABOLISM AND NUTRITION

Rare: Hypokalaemia, Hyperglycaemia

Potentially serious hypokalaemia may result from $beta_2$-agonist therapy.
Unknown: Lactic acidosis

PSYCHIATRIC DISORDERS

Common: Restlessness

NERVOUS SYSTEM DISORDERS

Common: Tremor, headache

Very rare: Hyperactivity, Hyperexcitability, sleeping disturbances, hallucinations.

CARDIAC DISORDERS

Common: Tachycardia

Uncommon: Palpitations, Angina pectoris, blood pressure effects (lowering/increase)

Very rare: Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles

Unknown: Myocardial ischaemia*

VASCULAR DISORDERS

Rare: Peripheral vasodilatation, collapse

RESPIRATORY, THORACIC DISORDERS

Very rare: Paradoxical bronchospasm

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.

AIRSAL RESPULES should be discontinued immediately, the patient assessed, and, if necessary, alternative therapy instituted.

GASTROINTESTINAL DISORDERS

Uncommon: Mouth and throat irritation, Nausea, taste alteration

MUSCULOSKELETAL AND CONNECTIVE TISSUES DISCORDERS

Uncommon: Muscle cramps

SKIN AND SUBCUTANIOUS TISSUE DISORDERS

Pruritis, rash, erythema, urticaria, angioedema

GENERAL DISORDERS

Headache, application site reaction (mouth and throat irritation, burning sensation of the tongue)

OVERDOSE

The expected symptoms of overdosage are those of excessive beta-adrenergic stimulation, viz., seizures, angina, hypertension or hypotension, tachycardia (with rates up to 200 beats/min), arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, malaise, sleeplessness hypokalemia (serum potassium levels should be monitored), lactic acidosis and fatigue. Cardiac arrest and, even, death is associated with the abuse of AIRSAL RESPULE.
Typical symptoms are: tachycardia, palpitations, arrhythmia, restlessness, sleep disturbances, chest pain and vigorous tremor, especially on hands but also on the whole body. Nausea, dizziness, increased systolic blood pressure and decreased diastolic blood pressure may also be observed.

Occasionally, psychotic reactions were observed after excessive doses of salbutamol. In the case of a salbutamol overdose there can increasingly be a shift of potassium into the intracellular space resulting in hypokalaemia, as well as hyperglycaemia, hyperlipidaemia, and hyperketonaemia.

Increased serum lactate levels and rarely, lactic acidosis, have been reported following therapy with salbutamol, particularly after high dose administration. Symptoms include deep, rapid breathing, cold and blue coloured fingers and toes, inability to concentrate and general malaise. If hypokalemia occurs, potassium replacement via the oral route should be given. In patients with severe hypokalemia, intravenous replacement may be necessary. The preferred antidote for overdosage with salbutamol is a cardio selective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

PACKING INFORMATION

AIRSAL RESPULES 2.5mg……Pack of 50 Respules with 2.5ml solution in each unit.