

Salbutamol Sulphate respirator solution

## **ASTHALIN RESPIRATOR SOLUTION**

### **COMPOSITION**

#### **ASTHALIN RESPIRATOR SOLUTION**

Each 1 ml contains:

Salbutamol Sulphate IP equivalent to Salbutamol IP..... 5 mg

### **DOSAGE FORM**

Solution for inhalation via a nebulizer

### **PHARMACOLOGY**

#### **Pharmacodynamics**

Salbutamol is a selective beta<sub>2</sub>-agonist providing short-acting (4-6 hours) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction. At therapeutic doses, it acts on the beta<sub>2</sub>-adrenoceptors of bronchial muscle. With its fast onset of action, it is particularly suitable for the management and prevention of attack in asthma.

#### **Pharmacokinetics**

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.

### **INDICATIONS**

**ASTHALIN RESPIRATOR SOLUTION** is 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**

**ASTHALIN RESPIRATOR SOLUTION** is 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. **ASTHALIN RESPIRATOR SOLUTION** may be administered intermittently or continuously. Salbutamol's duration of action is 4-6 hours in most patients.

### **Intermittent Administration**

#### ***Adults***

**ASTHALIN RESPIRATOR SOLUTION** 0.5 ml (2.5 mg of salbutamol) should be diluted to a final volume of 2 ml with sterile normal saline. This may be increased to 1 ml (5 mg of salbutamol), diluted to a final volume of 2.5 ml. The resulting solution is inhaled from a suitably driven nebulizer until aerosol generation ceases. When using a correctly matched nebulizer and driving source, this should take about 10 minutes.

**ASTHALIN RESPIRATOR SOLUTION** may be used undiluted for intermittent administration. For this, 2 ml of **ASTHALIN RESPIRATOR SOLUTION** (10 mg of salbutamol) is placed in the nebulizer and the patient is allowed to inhale the nebulized solution until bronchodilation is achieved. This usually takes 3-5 minutes. Some adult patients may require higher doses of salbutamol up to 10 mg, in which case, nebulization of the undiluted solution may continue until aerosol generation ceases.

#### ***Children***

The same mode of administration for intermittent administration is also applicable to children. The minimum starting dosage for children below the age of 12 years is 0.5 ml (2.5 mg of salbutamol), diluted to 2-2.5 ml with sterile normal saline. Some children may, however, require higher doses of salbutamol up to 5 mg. Intermittent treatment may be repeated up to four times daily.

### **Continuous Administration**

**ASTHALIN RESPIRATOR SOLUTION** is diluted with sterile normal saline to contain 50-100 mcg of salbutamol per ml (1-2 ml solution made up to 100 ml with diluents). The diluted solution is administered as an aerosol by a suitably driven nebulizer. The usual rate of administration is 1-2 mg per hour.

In infants below 18 months of age, the clinical efficacy of nebulized salbutamol is uncertain. As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

## **CONTRAINDICATIONS**

**ASTHALIN RESPIRATOR SOLUTION** is contraindicated in patients with a history of hypersensitivity to any of the components.

## **WARNINGS AND PRECAUTIONS**

**ASTHALIN RESPIRATOR SOLUTION** 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 receiving treatment at home should be warned to seek medical advice if treatment with **ASTHALIN RESPIRATOR SOLUTION** becomes less effective. As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

### **Deterioration of Asthma**

Patients being treated with **ASTHALIN RESPIRATOR SOLUTION** may also be receiving other dosage forms of short-acting inhaled bronchodilators to relieve symptoms. Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. If the patient needs more doses of **ASTHALIN** than usual, this may be a marker of destabilization of asthma and requires re-evaluation of the patient and treatment regimen, with special consideration to the possible need for anti-inflammatory treatment, e.g., corticosteroids.

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

**ASTHALIN RESPIRATOR SOLUTION** 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<sub>2</sub>-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.

In common with 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.

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 mist enter the eyes.

Salbutamol should be administered cautiously to patients suffering from thyrotoxicosis.

### **Cardiovascular Effects**

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.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic 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. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

### **Immediate Hypersensitivity Reactions**

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

### **Do Not Exceed Recommended Dose**

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma. The exact cause of death is unknown, but cardiac arrest following an unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

### **Drug Interactions**

**ASTHALIN RESPIRATOR SOLUTION** should not normally be prescribed with non-selective beta-blocking drugs, such as propranolol.

### **Pregnancy**

Administration of **ASTHALIN RESPIRATOR SOLUTION** during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

### **Lactation**

Caution should be exercised when **ASTHALIN RESPIRATOR SOLUTION** is administered to a nursing woman.

### **UNDESIRABLE EFFECTS**

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (1/10), common ( 1/100 and <1/10), uncommon ( 1/1000 and <1/100), rare ( 1/10,000 and <1/1000) and very rare (<1/10,000). Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown 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.

Unknown: Lactic acidosis

#### 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

Unknown: Myocardial ischaemia\*

#### Vascular disorders

Rare: Peripheral vasodilatation.

Respiratory, thoracic and mediastinal 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.

#### Gastrointestinal disorders

Uncommon: Mouth and throat irritation.  
Musculoskeletal and connective tissue disorders  
Uncommon: Muscle cramps

\* reported spontaneously in post-marketing data therefore frequency regarded as unknown

### **OVERDOSAGE**

The expected symptoms of overdose 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) and fatigue. Cardiac arrest and, even, death is associated with the abuse of **ASTHALIN**.

The preferred antidote to overdose with salbutamol is a cardioselective betablocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

### **PACKAGING INFORMATION**

**ASTHALIN RESPIRATOR SOLUTION** .....Bottle of 15 ml

*Last updated: June 2010*