For the use of a Registered Medical Practioner or a Hospital or a Laboratory Only

ASTHALIN RESPULES RESPIRATOR SOLUTION 2.5MG/2.5ML

Composition

Each 2.5ml respule contains
Salbutamol Sulphate BP
equivalent to Salbutamol ……..2.5mg
In sodium chloride solution BP…q.s

Description

A clear, colourless to light yellow solution. On visual examination there is no sign of leakage and physical damage

Pharmacology

Pharmacodynamics

Salbutamol stimulates β-adrenergic receptors and has little or no effect on adrenergic receptors. It is believed that β-adrenergic agonists stimulate the production of cyclic adenosine-3',5'-monophosphate (AMP) by activation of the enzyme adenyl cyclase. Cyclic AMP appears to mediate numerous cellular responses. Increased intracellular cyclic AMP enhances the activity of cAMP- dependent protein kinase A, which inhibits the phosphorylation of myosin and lowers intracellular calcium concentrations, resulting in smooth muscle relaxation. Increased intracellular cyclic AMP concentrations are also associated witinhibition of the release of mediators from mast cells in the airways. Salbutamol appears to have a greater stimulating effect on β-adrenergic receptors of the bronchial, uterine, and vascular smooth muscles (β_2-receptors) than on β-adrenergic receptors of the heart (β_2-receptors). The main effect following oral inhalation or oral administration of salbutamol is bronchodilation resulting from relaxation of smooth muscles from the trachea to the terminal bronchial tree; the drug also has some vasodilating effect on peripheral vasculature and may decrease diastolic blood pressure to a small extent. In patients with reversible airway obstruction, salbutamol decreases resistance of the airways as measured by pulmonary function tests such as the forced expiratory volume in I second (FEV_1) and the maximum mid-expiratory flow rate; the drug also increases vital capacity. Although the clinical importance has not been established, tolerance to the bronchodilating effects of salbutamol has been reported in healthy individuals and in patients with asthma. In contrast to isoproterenol, salbutamol does not appear to decrease arterial oxygen tension. Salbutamol may cause reflex tachycardia, especially with higher than usual doses.

β_2-adrenergic stimulation promotes an intracellular shift of potassium from serum, possibly via stimulation of Na^+K^+ATPase, and thereby appears to decrease temporarily both elevated and normal potassium concentrations. Orally inhaled forms of salbutamol have been shown to decrease serum potassium concentrations, which makes the drug potentially useful in the treatment of conditions associated with hyperkalemia (e.g.,hyperkalemia familial periodic paralysis, adjunctively for acute episodes of hyperkalemia in patients with renal failure).

Pharmacokinetics–

Absorption

Although salbutamol appears to be absorbed from the respiratory tract ver several hours following oral inhalation, characterization of this process has not been clearly determined.

In one study in a limited number of patients in whom a solution of radiolabeled salbutamol was instilled directly into the bronchial tree via a bronchoscope, peak plasma radioactivity occurred within 10 minutes; however, following oral inhalation of salbutamol in other studies, peak plasma salbutamol concentrations occurred in 2-5 hours.

It has been suggested that most of an orally inhaled dose of the drug is swallowed and absorbed from the GI tract; studies with isoproterenol indicate that less than 10% of an orally inhaled dose reaches the bronchial tree. Bronchodilation begins within 5-15 minutes after oral inhalation via the metered-dose aerosol with peak effect in 0.5-3 hours, and generally persists 2-5 hours; in some patients, bronchodilation may persist up to 6 hours. Bronchodilation usually begins within 5 minutes following nebulization, with peak effect in approximately 1-2 hours, and generally persists 3-4 hours, but occasionally up to 6 hours or longer. Because of the prompt onset of action and a lack of correlation between plasma salbutamol concentrations and bronchodilation, it has been suggested that the bronchodilating effect of orally inhaled salbutamol results from a local action.

Distribution

Results of animal studies indicate that salbutamol crosses the blood-brain barrier, reaching the brain at concentrations that are approximately 5% of the plasma concentrations. In glands outside the blood -brain barrier (pineal and pituitary glands), the drug achieves concentrations that are 100 times the concentrations achieved in the whole brain. Salbutamol apparently crosses the placenta, but it is not known whether salbutamol is distributed into milk. Studies in pregnant rats given radiolabelled salbutamol indicate that approximately 10% of the maternal dose is transferred to the foetus. Disposition in foetal lungs is comparable to that in maternal lungs, but foetal liver disposition is 1% that of the maternal liver concentrations.

Elimination

Following oral inhalation of radiolabeled salbutamol in patients with asthma in one study, total plasma radioactivity declined with a half-life of 1.7-7.1 hours. After oral inhalation of salbutamol in healthy adults in another study, the elimination half-life of unchanged drug was determined indirectly to be 3.8 hours based on urinary excretion data. Salbutamol is extensively metabolized in the liver, mainly to salbutamol 4'O sulfate which has little or no β-adrenergic stimulating effect and no β-adrenergic blocking effect. Unlike isoproterenol, salbutamol is not metabolized by the enzyme catechol-O-methyltransferase and is not a substrate for catecholamine cellular uptake processes. Salbutamol and its metabolites are rapidly excreted in urine and feces. After oral inhalation of salbutamol in patients with asthma, approximately 70% of a dose is excreted in urine as unchanged drug and metabolites within 24 hours and 80-100% within 72 hours; about 30% of the dose is excreted in urine unchanged in 24 hours. About 10% of an inhaled dose of salbutamol may be excreted in faeces

Indications

Asthalin Respules are indicated for use in the routine management of chronic bronchospasm unresponsive to conventional therapy and in the treatment of acute severe asthma.

Contraindications

Hypersensitivity to the components of the formulation. Inhalation Salbutamol preparations are not appropriate for manging premature labour. Salbutamol preparations should not be used for threatened abortion.

Side effects/Adverse Reactions

A small increase in heart rate may occur in patients who inhale large doses of Asthalin. This is not usually accompanied by any changes in the electrocardiogram. Other side effects which occur with very high doses of Asthalin by inhalation are peripheral vasodilation and fine tremor of skeletal muscle.

As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treatment immediately with an alternative presentation or a different fast acting inhaled bronchodilator. The preparation should be discontinued immediately, the patient assessed, and, if necessary, alternative therapy instituted.

Solutions, which are not of neutral pH, may rarely cause bronchospasm.

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

Tachycardia, with or without peripheral vasodialation, may rarely occur,. Incommon with other beta 2 agonists, cardiac arrhythmias including atrial fibrillation supraventricular tachycardia and extrsystoles) has been reported in association with with the use of salbutamol, usually in susceptible patients.

Headaches have occasionally been reported.

Mouth and throat irritation may occur with inhaled Salbutamol.

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

There have been very rare reports of muscle cramps.

Warnings/Precautions

Asthalin Respules should be used with care with patients known to have received large doses of other sympathomimetic drugs. They should be administered cautiously to patients suffering from thyrotoxicosis.

Patients receiving treatment at home with Asthalin Respules must 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, as adverse effects may be associated with excessive dosing, but should seek medical advice.

Solutions which are not of neutral pH may rarely cause paradoxical bronchospasm in some patients.

Patient Monitoring

Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. If the patient needs more doses of salbutamol than usual, this may be a marker of destabilization of asthma and requires reevaluation of the patient and treatment regimen, giving special consideration to the possible need for anti-inflammatory treatment, (e.g. corticosteroids).

In common with other beta-adrenoreceptor agonist, Asthalin can induce reversible metabolic changes, for example increased blood sugar levels. The diabetic patients may be unable to compensate for this and the development of ketoacidosis has been reported.Concurrent administration of corticosteroid can exaggerate this effects.

Drug Interaction

Salbutamol and non-selective beta-blocking drugs such as propranolol, should not usually be prescribed together. Potentially serious hypokalaemia may result from β_2 –agonist therapy. 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.

Recommended dosage, Dosage Schedule and Route of Administration

Asthalin Respules are to be used with a nebuliser only under the direction of a physician. The solution should not be injected or administered orally.

Adults and children

Start with a dose of 2.5 mg (one Respule) which may be increased upto 5 mg. In infants upto 18 months old the clinical efficacy of nebulised salbutamol is uncertain. Treatment should be repeated upto four times daily by means of a nebuliser. Up to 40 mg/day can be given under strict medical supervision in hospital. Delivery of the aerosol may be by face mask or 'T' piece. Asthalin respules should be used undiluted. However, if delivery time is prolonged (more than 10 minutes), dilution with normal saline (used for injection) may be required.

Symptoms and Treatment of Overdose and antidote(s)

Overdosage of oral or orally inhaled salbutamol produces symptoms that are mainly extensions of common adverse effects. In addition to exaggeration of common adverse effects, angina, hypertension, tachycardia, (with a heart rate of upto 200 beats/minute) and hypokalemia have occurred following overdosage. The oral LD_{50} of the drug in rats and mice is greater than 2g/kg.

In the management of overdosage, the manufacturers suggest that a relatively selective β_1 -adrenergic blocking agent (e.g. metoprolol tartrate) may be used, if necessary, but only with extreme caution in asthmatic patients because an asthmatic attack may be induced. Dialysis is not appropriate therapy for the management of salbutamol overdosage.

Packing/ Pack size

Packing : Carton containing 4 triple laminated pouches each having combitray of 5 FFS respules of 2.5 ml each.
Pack size : Respules of 2.5ml

Storage condition:

Store below 30˚C.Protect from light.

User instructions and pharmaceutical precautions

User Instructions: The product should be used with a respirator or nebuliser only, under the direction of a physician. It is not to be injected or administered orally. Refer to the enclosed leaflet for detail use.

Shelf life:

15 months. Once the foil pouch is opened the respules should be used whin three months.

Cipla

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Verna Industrial Estate,
Verna Goa INDIA

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RESPULES

SAP Code: XXXXXXXX (Ver. 02)
Leaflet size: 160 x 200 mm
Size after folding: 40 x 50 mm
Colours:

Black

Reference / Supersedes: 21058993
Ph_code :
Country : Malaysia
Date: 14-9-2022

Path: PC: F:\Vaibhav\Vinod\Malaysia\
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