PRESCRIBING INFORMATION

Name of Medicine

RESPLIN®

Salbutamol / Ipratropium bromide 2.5mg / 500mcg in 2.5ml

Presentation

RESPLIN 2.5ml nebule contains an isotonic, clear, preservative-free solution for inhalation of:
1.25mg Levosalbutamol and 500 mcg Ipratropium Bromide anhydrous

Uses

Actions

RESPLIN contains two active bronchodilating substances, salbutamol sulphate and ipratropium bromide.

Salbutamol sulphate is a beta$_2$-adrenergic agent which acts on airway smooth muscle resulting in relaxation. Salbutamol relaxes all smooth muscle from the trachea to the terminal bronchioles and protects against all bronchoconstrictor challenges.

Ipratropium bromide is a quaternary ammonium compound with anticholinergic properties. In preclinical studies, it appears to inhibit vagally mediated reflexes by antagonising the action of acetylcholine, the transmitter agent released from the vagus nerve. Anticholinergics prevent the increase of intracellular concentration of cyclic guanosine monophosphate (cyclic GMP) caused by interaction of acetylcholine with muscarinic receptors on bronchial smooth muscle. The bronchodilation following inhalation of ipratropium bromide is primarily local and site specific to the lung and not systemic in nature.

RESPLIN provides the simultaneous release of ipratropium bromide and salbutamol allowing the synergistic efficacy on the muscarinic and beta$_2$-adrenergic receptors in the airways to cause bronchodilation, which is superior to that provided by each single agent and with no potentiation of adverse events.

Pharmacokinetics

Ipratropium bromide is quickly absorbed after oral inhalation. The systemic bioavailability following inhalation is estimated to be less than 10% of the dose. Renal excretion of ipratropium bromide is given as 46% of the dose after intravenous administration. The half-life of the terminal elimination phase is about 1.6 hours as determined after intravenous administration. The half-life elimination of drug and metabolites is 3.6 hours, as determined after radio labelling. Ipratropium bromide does not penetrate the blood brain barrier.

Salbutamol sulphate is rapidly and completely absorbed following administration either by the inhaled or oral route. Peak plasma salbutamol concentrations are seen within three hours of administration and it is excreted unchanged in the urine after 24 hours. The elimination half-life is 4 hours. Salbutamol will cross the blood brain barrier reaching concentrations amounting to about five per cent of the plasma concentrations.

It has been shown that co-nebulisation of ipratropium bromide and salbutamol sulphate does not potentiate the systemic absorption of either component and that therefore the additive activity of RESPLIN is due to the combined local effect on the lung following inhalation.

Indications

RESPLIN is indicated for the treatment of reversible bronchospasm associated with obstructive airway diseases in patients who require more than a single bronchodilator.

Dosage and Administration

RESPLIN inhalation solution in respiratory nebules may be administered from a suitable nebuliser or an intermittent positive pressure ventilator.

Adults (including elderly): One nebule as required for the relief of symptoms or as directed. Up to three to four nebules daily.

Patients should be advised to consult a doctor or the nearest hospital immediately in the case of acute or rapidly worsening dyspnoea if additional inhalations do not produce an adequate improvement.

Contraindications

RESPLIN is contraindicated in patients with hypertrophic obstructive cardiomyopathy and tachyarrhythmia and in patients with a history of hypersensitivity to atropine or its derivatives, or to any other component of the product.

Warnings and Precautions

In the case of acute, rapidly worsening dyspnoea a doctor should be consulted immediately.

Immediate hypersensitivity reactions may occur after administration of RESPLIN as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal oedema.

Ocular complications:
Eye pain or discomfort, blurred vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema may be signs of acute narrow-angle glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately. Patients should be instructed in the correct administration of RESPLIN and care must be taken to prevent RESPLIN from entering the eye. Patients who may be predisposed to glaucoma should be warned specifically to protect their eyes.

In the following situations RESPLIN should only be used after careful risk/benefit assessment, especially when doses higher than recommended are used:
Insufficiently controlled diabetes mellitus, recent myocardial infarction, severe organic heart or vascular disorders, hyperthyroidism, phaeochromocytoma, risk of narrowangle glaucoma, prostatic hypertrophy or bladder-neck obstruction.

Potentially serious hypokalaemia may result from prolonged and / or high dose $beta_2$agonist therapy. Additionally, hypoxia may aggravate the effects of hypokalaemia on cardiac rhythm. It is recommended that serum potassium levels be monitored in such situations.

Patients with cystic fibrosis may be more prone to gastrointestinal motility disturbances.

If higher than recommended doses of RESPLIN are required to control symptoms, the patient's therapy plan should be reviewed by a doctor.

Use in Pregnancy

Although there is little published evidence of the safety of RESPLIN in the early stages of pregnancy, the individual active ingredients, ipratropium bromide and salbutamol have been in widespread use for many years. No suspect teratogenic factors have been observed in general practice or clinical studies. As a general precaution, however, RESPLIN should only be used in pregnancy and during the lactation period if the expected benefit to the mother is greater than any possible risk to the child.

RESPLIN should be used with caution before childbirth in view of salbutamol's inhibitory effects on uterine contractions.

Use in Lactation

Salbutamol sulphate and ipratropium bromide are probably excreted in breast milk and their effects on neonates are not known. Although lipid-insoluble quaternary bases pass into breast milk, it is unlikely that this will happen to any extent especially when taken by inhalation. However, because many drugs are excreted in breast milk, caution should be exercised when RESPLIN is administered to a nursing woman.

Adverse Effects

In common with other beta-agonists containing products, side effects of RESPLIN can include fine tremor of skeletal muscles and nervousness and less frequently, tachycardia, dizziness, palpitations or headache, especially in hypersensitive patients.

Potentially serious hypokalaemia may result from prolonged and / or high dose $beta_2$agonist therapy.

As with use of other inhalation therapy, cough, local irritation and, less commonly, inhalation induced bronchospasm can occur.

As with other beta-mimetics, nausea, vomiting, sweating, weakness and myalgia/muscle cramps may occur. In rare cases decrease in diastolic blood pressure, increase in systolic blood pressure, arrhythmias, particularly after higher doses, may occur.

In individual cases psychological alterations have been reported under inhalation therapy with beta-mimetics.

The most frequent non-respiratory anticholinergic related adverse events are dryness of mouth and dysphonia.

Ocular side effects, gastrointestinal motility disturbances and urinary retention may occur in rare cases and are reversible (see Warning and Precautions). **Interactions**
The concurrent administration of other beta-mimetics, systemically absorbed anticholinergics and xanthine derivatives may increase the side effects.

Beta-agonist induced hypokalaemia may be increased by concomitant treatment with xanthine derivatives, glucocorticosteroids and diuretics. This should be taken into account particularly in patients with severe airway obstruction.

Hypokalaemia may result in an increased susceptibility to arrhythmias in patients receiving digoxin. It is recommended that serum potassium levels be monitored in such situations.

A potentially serious reduction in bronchodilator effect may occur during concurrent administration of beta-blockers.

Beta-adrenergic agonists should be administered with caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of beta-adrenergic agonists may be enhanced.

Inhalation of halogenated hydrocarbon anaesthetics such as halothane, trichloroethylene and enflurane may increase the susceptibility to the cardiovascular effects of beta-agonists.

Overdosage

The effects of overdosage are expected to be primarily related to salbutamol because acute overdosage with ipratropium bromide is unlikely as it is not well absorbed systemically after inhalation or oral administration.

Symptoms

Manifestations of overdosage with salbutamol may include tachycardia, anginal pain, hypertension, hypotension, palpitations, tremor, widening of the pulse pressure, arrhythmia and flushing.

Treatment

Administration of sedatives, tranquillisers and in severe cases, intensive therapy.

Beta-receptor blockers, preferably $beta_1$-selective, are suitable as specific antidotes; however, a possible increase in bronchial obstruction must be taken into account and the dose should be adjusted carefully in patients suffering from bronchial asthma.

Pharmaceutical Precautions

Store below 25ºC.

Medicine Classification

Prescription Medicine

Package Quantities

2.5ml, 7's

Further Information

Excipients

Sodium chloride, disodium edetate, sulphuric acid, purified water

Marketed By

Fides Pharmaceuticals