

AEROVENT®

RESPIRATOR SOLUTION

DRUGS-ABOUT.COM

Composition

Active Ingredient

Each ml (20 drops) contains:

Ipratropium bromide 0.25 mg

Other Ingredients

Sodium chloride, sodium edetate, benzalkonium chloride, hydrochloric acid, purified water.

Mechanism of Action

Ipratropium bromide is an anticholinergic agent with a preferential bronchodilatory action.

Even in extremely low doses, ipratropium bromide has a local effect on the airways, showing a particularly high degree of specificity.

Ipratropium bromide is virtually free from systemic side effects and therefore it is also suitable for use in patients with cardiac and circulatory disorders.

The onset of action occurs 5-10 minutes after inhalation and the effect on the airways lasts for 5-6 hours.

There is evidence that the concurrent administration of ipratropium bromide and β_2 -adrenergic stimulants or xanthines produces a greater relief of bronchospasm than if any of the drugs is given alone.

Ipratropium bromide has been shown to produce effective bronchodilation in patients receiving β -blocking agents.

Preclinical and clinical evidence suggest no deleterious effect of Aerovent on airway mucous secretion, mucociliary clearance or gas exchange.

Indications

For the relief of symptoms of reversible bronchospasm associated with asthma, chronic bronchitis and emphysema. Aerovent Respirator Solution is of particular benefit in relieving acute bronchospasm when used concomitantly with inhaled beta agonists.

Contraindications

Hypersensitivity to the drug, to atropine and its derivatives.

Hypersensitivity to any other ingredient of the preparation.

Warnings

Aerovent is not indicated for the initial treatment of acute episodes of bronchospasm where rapid response is required.

Preclinical Data

Acute toxicity has been investigated with observation periods of 14 days in several rodent and non-rodent species.

When administered by inhalation, the minimum lethal dose in male guinea pigs was 199 mg/kg. In rats, no mortality was observed up to the highest technically feasible dosages (e.g., 0.05 mg/kg after 4 hours of administration or 160 puffs of ipratropium bromide 0.02 mg/puff).

The oral and intravenous LD₅₀, respectively, ranged from 17.5 mg/kg in dogs (I.V.) to 2050 mg/kg in mice (oral).

The rather low oral toxicity compared to the higher intravenous toxicity reflects the poor gastrointestinal absorption.

Animal studies with daily administration have been performed in rats, rabbits, dogs, and rhesus monkeys.

In inhalation studies up to 6 months in rats, dogs, and rhesus monkeys, the no-observed adverse effect level (NOAEL) was 0.38 mg/kg/day, 0.18 mg/kg/day, and 0.8 mg/kg/day, respectively. Histopathologically, no substance-related lesions were observed in the broncho-pulmonary system. In the rat, the oral NOAEL after 18 months administration was 0.5 mg/kg/day.

Repeated dose inhalation toxicity studies in rats lasting up to 6 months, and in dogs lasting up to 3 months, with new development formulations (such as intranasal formulation, lactose powder formulation) revealed no additional information on the general toxicity profile of ipratropium bromide.

Intranasal administration for up to 26 weeks revealed a no effect dose level of greater than 0.20 mg/kg/day in dogs, and confirmed earlier studies with intranasal administration for up to 13 weeks.

An aqueous solution of ipratropium bromide (0.05 mg/kg, duration of administration for 4 hours) was locally well tolerated when administered to rats by inhalation (single administration). In the repeated dose toxicity studies, ipratropium bromide was locally well-tolerated.

Neither active anaphylaxis nor passive cutaneous anaphylactic reactions were demonstrated in guinea pigs.

Mutagenicity

In vitro mutagenicity on bacteria (Ames test) did not indicate a mutagenic potential. The results of *in vivo* assays (micronucleus test, dominant lethal test in mice, cytogenic assay on bone marrow cells of Chinese hamsters), did not demonstrate an increase in rate of chromosomal aberrations.

Carcinogenicity

No tumorigenic or carcinogenic effects were demonstrated in long term studies in mice and rats.

Effect on Fertility and Reproduction

Studies to investigate the possible influence of Aerovent on fertility, embryo-fetotoxicity, and peri/postnatal development have been performed on mice, rats and rabbits.

Even the highest oral dose levels employed (1000 mg/kg/day in the rat and 125 mg/kg/day in the rabbit), which proved to be maternotoxic, and, to some extent embryo/fetotoxic at dosages, far in excess to the human therapeutic dose, did not induce malformations in the offspring.

The highest, technically feasible doses for inhalation of the metered aerosol, 1.5 mg/kg/day in rats and 1.8 mg/kg/day in rabbits, showed no adverse effects on reproduction.

Use in Pregnancy

The safety of ipratropium during human pregnancy has not been established. The benefits of using ipratropium bromide during a confirmed or suspected pregnancy must be weighed against possible hazards to the unborn child. Preclinical studies have shown no embryotoxic or teratogenic effects following inhalation or intranasal application at doses considerably higher than those recommended in man.

Use During Lactation

It is not known whether ipratropium is secreted into breast milk. Although lipid-insoluble quaternary cations pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to an important extent, when administered by inhalation. However, because many drugs are secreted into breast milk, caution should be exercised when ipratropium bromide is administered to nursing mothers.

Use in Pediatrics

Aerovent Respirator Solution is not recommended for use in children under 3 years of age.

Adverse Reactions

Note: Because of the low intestinal absorption of ipratropium bromide, anticholinergic side effects, such as increase in heart rate and palpitation, ocular accommodation disturbances, and urinary retention are rare and reversible, although the risk of urinary retention may be increased in patients with pre-existing outflow tract obstruction.

Some patients may complain of nausea, throat irritation, nervousness, dizziness, cough, tachycardia and palpitations, or allergic reactions. Rarely, Supraventricular tachycardia and atrial fibrillation have been observed. As with other bronchodilators, local irritation, and less commonly, inhalation-induced bronchoconstriction have been observed. Urinary retention, fatigue, insomnia, and hoarseness have only rarely been reported with ipratropium bromide; the risk of urinary retention may be increased in patients with pre-existing outflow tract obstruction.

The most frequent non-respiratory side-effects reported in clinical trials were gastrointestinal disorders (e.g., constipation, diarrhea, and vomiting), dryness of the mouth, headache.

Administration of ipratropium bromide respirator solution has been associated with occasional reports of bronchospasm during early treatment.

Cases of precipitation or worsening of narrow-angle glaucoma, acute eye pain and hypotension have been reported.

Allergic-type reactions such as skin rash, angioedema of tongue, lips and face, urticaria (including giant urticaria), laryngospasm and anaphylactic reaction have been reported, with positive rechallenge in some cases.

Precautions

Note: Immediate hypersensitivity reactions may occur after administration of Aerovent, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal edema, and anaphylaxis..

Aerovent should be used with caution in patients predisposed to narrow-angle glaucoma, with prostatic hyperplasia, or bladder-neck obstruction.

Patients should be reminded that Aerovent is not intended for occasional use, but rather, in order to be maximally effective, must be used consistently as prescribed throughout the course of therapy.

Ocular complications

There have been isolated reports of ocular complications (i.e. mydriasis, increased intraocular pressure, angle-closure glaucoma, eye pain) when aerosolized ipratropium bromide either alone or in combination with an adrenergic β_2 -agonist, has escaped into the eyes. Thus patients must be instructed in the correct administration of Aerovent.

Eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema may be signs of acute angle-closure glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately.

Patients must be instructed in the correct administration of Aerovent inhalation solution. Care must be taken not to allow the solution or mist into the eyes. It is recommended that the nebulized solution be administered via a mouth piece. If this is not available and a nebulizer mask is used, it must fit properly. Patients who may be predisposed to glaucoma should be warned specifically to protect their eyes.

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

The patient should be instructed to seek medical advice should a reduced response become apparent.

Because of occasional reports of bronchospasm associated with the use of Aerovent Respirator Solution, due to the preservative (benzalkonium chloride) and the stabilizer (sodium edetate), it is recommended that the patient be subject to medical supervision during the first week of treatment.

Drug Interactions

Additive effect has been reported when ipratropium bromide is used in patients treated with β_2 -adrenergic stimulants and xanthine preparations.

Anticholinergic effects of other drugs can be enhanced.

The risk of acute glaucoma in patients with a history of narrow-angle glaucoma may be increased when nebulized ipratropium bromide and beta sympathomimetics are administered simultaneously.

Dosage and Administration

The dosage should be adapted to the individual requirements of the patient; patients should also be kept under medical supervision during treatment. It is advisable not to greatly exceed the recommended daily dose during both acute and maintenance treatment.

If therapy does not produce a significant improvement or if the patient's condition worsens, medical advice must be sought in order to determine a new regimen of therapy. In the case of acute or rapidly worsening dyspnea, a doctor should be consulted immediately.

Aerovent Respirator Solution is not recommended for use in children under 3 years of age.

Note: Aerovent and disodium cromoglycate inhalation solutions should not be simultaneously administered in the same nebulizer as precipitation may occur.

Aerovent Respirator Solution may be administered from an intermittent positive pressure ventilator or from suitable nebulizers..

The recommended dosage is as follows:

Adults

0.1 - 0.5 mg (0.4 - 2.0 ml = 8-40 drops) up to 4 times daily.

Children

6-12 Years: 0.25 mg (20 drops, i.e., 1 ml) 3 to 4 times daily.

3-6 Years: 0.1-0.25 mg (8-20 drops, i.e.: 0.4-1.0 ml) 3 to 4 times daily.

N.B. For ease of administration, the dose may need to be diluted in order to obtain a final volume suitable for the nebulizer being used. If dilution is necessary, only normal saline should be used.

Overdosage

No symptoms specific to overdosage have been encountered. . In view of the wide therapeutic range and topical administration of ipratropium bromide, no serious anticholinergic symptoms are to be expected. Minor systemic manifestations of anticholinergic action, including dry mouth, visual accommodation disturbances and tachycardia may occur.

Inhaled doses of 5.0 mg produced an increase in heart rate and palpitation but single doses of 2.0 mg in adults and 1.0 mg in children caused no untoward effects.

Single doses of ipratropium bromide 30 mg by mouth caused anticholinergic side-effects but these were not severe and did not require specific reversal.

Pharmaceutical Precautions

Store in a cool dark place.

Once the bottle has been opened, the contents should not be kept for longer than one month.

Following dilution, any unused portion should be discarded after 24 hours.

Presentation

Bottle of 20 ml with dropper.

Manufacturer

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