Acetylcholinesterase Inhibitors; Gastrointestinal Agents; Bronchodilators

Generic Availability (US) May be product dependent

Usage

Nebulization: Treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema alone or in combination with bronchodilators (FDA approved in ages ≥12 years and adults); has also been used to treat bronchospasm associated with asthma and as a rescue medication in adult bronchopulmonary dysplasia and neonatal respiratory distress syndrome.

Oral inhalation: Atrovent HFA: Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema (FDA approved in adults); has also been used to treat bronchospasm associated with asthma and as a bronchodilating agent in bronchopulmonary dysplasia and neonatal respiratory distress syndrome.

Pregnancy Risk Factor B

Pregnancy Considerations

Adverse events have not been specifically evaluated in animal reproduction studies.

Breastfeeding Considerations

It is not known if ipratropium is present in breast milk. The manufacturer recommends caution when administering ipratropium to breastfeeding women.

Contraindications

Hypersensitivity to ipratropium, atropine (and its derivatives), or any component of the formulation.

Warnings/Precautions

Hypersensitivity reactions (urticaria, angioedema, rash, bronchospasm, oropharyngeal edema), including anaphylaxis, have been reported. Discontinue therapy immediately if patient develops an allergic reaction. Paradoxical bronchospasm that may be life-threatening and may occur with use of inhaled bronchodilating agents; this should be distinguished from inad- equate treatment response. Paradoxical bronchospasm may occur in neonates with immature lung function and is characterized by increased airway resistance. Do not puncture inhaler, throw into a fire or incinerator, or use or store near heat or open flame.

Nebulization solution: Store at 15°C to 30°C (59°F to 86°F). Protect from light. Store unused vials in foil pouch. Nebulizer: Store at 25°C (77°F); excursions to 15°C to 30°C (59°F to 86°F). Exposure to temperatures >48°C (120°F) may cause bursts. Do not puncture inhaler, throw into a fire or incinerator, or use or store near heat or open flame.

Neonatal Bronchopulmonary dysplasia/Respiratory distress syndrome (RDS), ventilated patients: Very limited data available; optimal dose not established.

Nebulization: Weight-based dosing: 25 mcg/kg dose 3 times daily. Dosing based on a placebo controlled, comparative trial in 17 preterm infants (ipratropium group, n=5; EGA 25 to 29 weeks; PNA 19 to 103 days) with BPD and reported a significant decrease in respiratory resistance (Wilkie 1987).

Fixed-dose dosing: Some centers have used 175 mcg/dose 3 times daily administered through the ventilator circuit; dosing based on a dose range study of 10 premature infants with BPD (EGA 24 to 28 weeks; PNA 18 to 34 days) which showed significant reduction in respiratory resistance; additional benefit observed when administered albuterol (Brundage 1990). Intravenous infusion: MDI: 4 puff dose every 6 to 8 hours delivered either as either a single dose or 2 puffs every 20 minutes for 2 inhalations. In a randomized, placebo-controlled trial in preterm neonates (n=10, PNA 1 week; EGA 26 to 34 weeks) with BPD which evaluated a single 72 mcg dose (4 puffs [18 mcg/puff product used; not currently available in the US]) and reported beneficial effects on blood gases and ventilator efficiency. In another trial, which was a cross-over, randomized, controlled, double-blind trial of preterm neonates (n=21, PNA 20 ± 9 days; EGA: 27 weeks ± 4 weeks) with BPD, significant reduction in respiratory resistance was reported in 38% of patients after a total dose of 80 mcg (40 mcg every 20 minutes for 2 doses [20 mcg/puff product used; not currently available in the US]); higher doses (120 mcg [6 puffs]) were not shown to have additional benefit (Fayon 2007, Lee 1994).

Pediatric

Acute Asthma, severe exacerbation: Limited data available (GINA 2018; NAEPP 2007): Note: For moderate to severe exacerbations, ipratropium may be considered if poor response to initial short-acting beta-2 agonist (SABA) therapy during management of acute care setting (eg, emergency department). Ipratropium has not been shown to provide further benefit (eg, after first SABA dose) once the patient is hospitalized (GINA 2018; Vézina 2014).

Children

Nebulization: 0.25 to 0.5 mg (250 to 500 mcg) every 20 minutes for 1 hour (ie, 3 doses), then as needed;
in trials, the usual reported dose is 0.25 mg (250 mcg) and reported interval range is every 1 to 4 hours typically with an increasing dosing interval as patient improves; some trials continued combination SABA/ipratropium therapy for duration of hospitalization (up to 49 hours) although trials have not demonstrated additional benefit with extended use (Vézina 2014)

Metered-dose inhaler: 4 to 8 puffs every 20 minutes as needed for up to 3 hours

Adolescents:
Nebulization: 0.5 mg (500 mcg) every 20 minutes for 3 doses, then as needed
Metered-dose inhaler: 8 puffs every 20 minutes as needed for up to 2 hours

Asthma, maintenance (nonacute): Limited data available; Note: Evidence is lacking that ipratropium provides added benefit to beta-2 agonists in long-term control asthma therapy (GINA 2018; NAEPP 2007)

Children <12 years:
Nebulization: 0.25 to 0.5 mg (250 to 500 mcg) every 6 to 8 hours
Metered-dose inhaler: 1 to 2 inhalations every 6 hours; not to exceed 12 inhalations/day

Children ≥12 years and Adolescents:
Nebulization: 0.25 to 0.5 mg (250 to 500 mcg) every 6 hours

Metered-dose inhaler: 2 to 3 inhalations every 6 hours; maximum daily dose: 12 inhalations/day

Bronchospasm associated with chronic pulmonary conditions: Children ≥12 years and Adolescents: Nebulization: 0.25 to 0.5 mg (500 mcg, one unit-dose vial) 3 to 4 times daily with doses 6 to 8 hours apart

Bronchospasm, wheezing: Limited data available; efficacy results variable: Infants: Nebulization: 0.125 to 0.25 mg (125 to 250 mcg) every 4 hours has been found helpful in some infants with chronic or recurrent wheezing, and some patients with bronchiolitis; however, most bronchiolitis data suggests ipratropium is not effective (Hodges 1981; Prendiville 1987; Schuh 1992; Stokes 1993; Wang 1992).

Renal Impairment: Pediatric There are no dosage adjustments provided in the manufacturer's labeling (not studied); however, dosage adjustment unlikely necessary due to low systemic absorption.

Hepatic Impairment: Pediatric There are no dosage adjustments provided in the manufacturer's labeling (not studied); however, dosage adjustment unlikely necessary due to low systemic absorption.

Administration: Pediatric Inhalation: Nebulization: May be administered with or without dilution soya lecithin or any soy ingredients like the previous Solution, Inhalation, as bromide: when available (limited, particularly for generics); consult specific product labeling.

Central nervous system: Dizziness, fatigue, headache, insomnia, nervousness, pain, voice disorder

Cardiovascular: Angina pectoris, cardiac arrhythmia, chest discomfort, edema, hypertension, palpitations, tachycardia

Gastrointestinal: Constipation, diarrhea, dysgeusia, dyspepsia, nausea, vomiting, xerostomia

Genitourinary: Dysuria, urinary tract infection

Neuromuscular & skeletal: Myalgia, asthenia, muscle spasm, myalgia, tremor

Ophthalmic: Eye pain

Respiratory: Bronchitis, bronchospasm, cough, dry throat, dyspnea, flu-like symptoms, increased bronchial secretions, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, respiratory insufficiency, sinusitis, upper respiratory tract infection, wheezing

Other: Ataxia, dizziness, fever, fever, hearing loss, hypokalemia, confusion, decreased appetite, decreased weight, diarrhea, flatulence, headache, nervousness, migraine, nervousness, pain, paresthesia, pruritus, rhinitis, stomatitis, status asthmaticus, syncope, tachycardia, toothache, tongue pain, respiratory insufficiency, sinusitis, upper respiratory tract infection, wheezing

Rare but important or life-threatening: Accommodation disturbance, anaphylaxis, angioedema, blurred vision, central nervous system stimulation, conjunctival hyperemia, corneal edema, decreased diastolic blood pressure, dry secretions, eye irritation, gastrointestinal motility disorder, glaucoma, hyperhidrosis, hypersensitivity reaction, increased systolic blood pressure, ischemic heart disease, mouth edema, myasthenia, mydriasis, nasal congestion, paradoxical bronchospasm, pharyngeal edema, psychiatric disturbance, stomatitis, throat irritation, urinary retention, visual halos around lights

Drug Interactions Metabolism/Transport Effects None known.
Avoid Concomitant Use Avoid concomitant use of Ipratropium and Albuterol with any of the following: Acidinium; Anticholinergic Agents; Beta-Blockers (Nonselective); Cimetropium; Clonidine; Cyclophosphamide; Cytostatics; Diazepam (Oral Inhalation); Glycopyrronium (Topical); Levoephedrine; Loxapine; Oxatomide; Potassium Chloride; Potassium Sulfate; Raloxifene; Ticlopidine; Uremidum
Increased Effect/Toxicity See individual agents.
Decreased Effect See individual agents.

Sound- alike/look- alike issues:
DuoNeb may be confused with DuoTrav, Duovent UDV.

Brand Names: Canada Apo-Salvelen-Ipratrop Sterules; Combivent Resipmat
Brand Names: US Combivent Respimat

Therapeutic Category Bronchodilator

Generic Availability (US) Yes: Solution for nebulization
Use Treatment of chronic obstructive pulmonary disease (COPD) in those patients who are currently on a regular bronchodilator who continue to have bronchospasms and require a second bronchodilator (FDA approved in adults); has also been used in the treatment of asthma exacerbations

Pregnancy Risk Factor C
Pregnancy Considerations Animal reproduction studies have not been conducted with this combination. See individual agents.
Breastfeeding Considerations It is not known if ipratropium or albuterol are present in breast milk. According to the manufacturer, the decision to continue or discontinue breastfeeding during therapy should take into account the benefit to the infant vs. the benefit to the mother. See individual agents.

Contraindications Hypersensitivity to ipratropium, albuterol, atropine (and its derivatives) or any component of the formulation Documentation of allergic cross-reactivity for anticholinergic systems is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty

Canadian labeling: Additions to contraindications (not in US labeling): Cardiac tachyarrhythmias, hypertrophic obstructive cardiomyopathy

Warnings/Precautions See individual agents.

Adverse Reactions Also see individual agents.

Cardiovascular: Angina pectoris, cardiac arrhythmia, chest discomfort, edema, hypertension, palpitations, tachycardia

Central nervous system: Dizziness, fatigue, headache, insomnia, nervousness, pain, voice disorder

Dermatologic: Pruritus, skin rash

Endocrine & metabolic: Hypokalemia

Gastrointestinal: Constipation, diarrhea, dysgeusia, dyspepsia, nausea, vomiting, xerostomia

Genitourinary: Dysuria, urinary tract infection

Neuromuscular & skeletal: Myalgia, asthenia, muscle spasm, myalgia, tremor

Ophthalmic: Eye pain

Respiratory: Bronchitis, bronchospasm, cough, dry throat, dyspnea, flu-like symptoms, increased bronchial secretions, nasopharyngitis, pharyngitis, pharyngolaryngeal pain, respiratory insufficiency, sinusitis, upper respiratory tract infection, wheezing

Other: Ataxia, dizziness, fever, fever, hearing loss, hypokalemia, confusion, decreased appetite, decreased weight, diarrhea, flatulence, headache, nervousness, migraine, nervousness, pain, paresthesia, pruritus, rhinitis, stomatitis, status asthmaticus, syncope, tachycardia, toothache, tongue pain, respiratory insufficiency, sinusitis, upper respiratory tract infection, wheezing

Rare but important or life-threatening: Accommodation disturbance, anaphylaxis, angioedema, blurred vision, central nervous system stimulation, conjunctival hyperemia, corneal edema, decreased diastolic blood pressure, dry secretions, eye irritation, gastrointestinal motility disorder, glaucoma, hyperhidrosis, hypersensitivity reaction, increased systolic blood pressure, ischemic heart disease, mouth edema, myasthenia, mydriasis, nasal congestion, paradoxical bronchospasm, pharyngeal edema, psychiatric disturbance, stomatitis, throat irritation, urinary retention, visual halos around lights