Brand Names

Cuvposa, Dartisla, Glycate, GLYRX-PF, Lonhala Magnair, Robinul, Robinul Forte, Seebri Neohaler

Indication Specific Dosing

For use as a preoperative antimuscarinic to reduce salivary, tracheobronchial, and pharyngeal secretions; reduce gastric acid production and acidity (aspiration prophylaxis); and to block vagal inhibitory reflexes during intubation and induction of anesthesia

Intramuscular dosage

Adults

4 mcg/kg IM 30 to 60 minutes prior to induction or at the same time preanesthetic narcotics and/or sedation are given.

Children and Adolescents 2 to 17 years

4 mcg/kg IM 30 to 60 minutes prior to induction or at the same time preanesthetic narcotics and/or sedation are given.

Infants and Children 1 month to 1 year

4 to 9 mcg/kg IM 30 to 60 minutes prior to induction or at the same time preanesthetic narcotics and/or sedation are given.

For the treatment of sialorrhea

For the treatment of severe chronic sialorrhea associated with neurologic conditions such as cerebral palsy in pediatric patients

Oral dosage (solution)

Children and Adolescents 3 to 16 years

Initially, 0.02 mg/kg/dose PO 3 times daily; titrate in 0.02 mg/kg/dose increments every 5 to 7 days based on therapeutic response and adverse effects. Do not exceed 0.1 mg/kg/dose PO 3 times daily or the following maximum doses by weight: weight 13 to 17 kg: Max: 1.5 mg/dose; weight 18 to 22 kg: Max: 2 mg/dose; weight 23 to 27 kg: Max: 2.5 mg/dose; weight 28 kg or more: Max: 3 mg/dose.

Oral dosage (tablet)†

Children and Adolescents weighing 30 kg or more

Glycopyrrolate has been used for the treatment of drooling in children and adolescents with neuropsychiatric disorders for many years. A variety of weight-based dose regimens have been employed. One double-blind, placebo-controlled, prospective trial of glycopyrrolate in children ages 4 to 19 years (n = 39) with neurodevelopmental conditions and severe sialorrhea used the following dose in children weighing 30 kg or more: initially, 1.2 mg/dose PO, and titrated weekly to 1.8 mg/dose, 2.4 mg/dose, and 3 mg/dose or the highest tolerated dose in this range. Doses were given 2 or 3 times per day. The mean highest tolerated dose was 0.11 mg/kg PO (range: 0.04 to 0.2 mg/kg PO). Caregivers scored drooling with a modified Teacher's Drooling Scale (mTDS) score of 1 (never drools) to 9 (clothing, hands, and objects frequently become wet). Titration could be halted for side effects; 27 children completed the study. Mean baseline drooling scores significantly improved with glycopyrrolate vs. placebo ($p < 0.001$). Twenty-five children improved their mean drooling score, defined as a reduction of 4 points or more. Adverse effects increased with dose, and 81% of children experienced side effects at highest titration. Adverse effects were seen more frequently in younger children than in older children (difference not statistically significant). Eight patients (21%) withdrew from the study due to side effects such as behavioral changes (irritability and hyperactivity), constipation, diarrhea, excessive oral dryness, thick secretions, urinary retention, dehydration, drowsiness, dizziness, dilated pupils, blurred vision, headache, nasal congestion, facial flushing, rash, urinary tract infection, and fever. Another study of pediatric patients with cerebral palsy and other developmental disabilities (n = 40) reported glycopyrrolate was effective in 90% of patients; the final effective dose range was 0.01 to 0.82 mg/kg/day PO. Side effects resulted in discontinuation of treatment in 28% of patients.

Children weighing less than 30 kg

Glycopyrrolate has been used for the treatment of drooling in children and

adolescents with neuropsychiatric disorders for many years. A variety of weight-based dose regimens have been employed. One double-blind, placebo-controlled, prospective trial of glycopyrrolate in children ages 4 to 19 years (n = 39) with neurodevelopmental conditions and severe sialorrhea used the following dose in children weighing less than 30 kg: initially, 0.6 mg/dose PO, and titrated weekly to 1.2 mg/dose, 1.8 mg/dose, and 2.4 mg/dose or the highest tolerated dose in this range. Doses were given 2 or 3 times per day. The mean highest tolerated dose was 0.11 mg/kg PO (range: 0.04 to 0.2 mg/kg PO). Caregivers scored drooling with a modified Teacher's Drooling Scale (mTDS) score of 1 (never drools) to 9 (clothing, hands, and objects frequently become wet). Titration could be halted for side effects; 27 children completed the study. Mean baseline drooling scores significantly improved with glycopyrrolate vs. placebo ($p < 0.001$). Twenty-five children improved their mean drooling score, defined as a reduction of 4 points or more. Adverse effects increased with dose, and 81% of children experienced side effects at highest titration. Adverse effects were seen more frequently in younger children than in older children (difference not statistically significant). Eight patients (21%) withdrew from the study due to side effects such as behavioral changes (irritability and hyperactivity), constipation, diarrhea, excessive oral dryness, thick secretions, urinary retention, dehydration, drowsiness, dizziness, dilated pupils, blurred vision, headache, nasal congestion, facial flushing, rash, urinary tract infection, and fever. Another study of pediatric patients with cerebral palsy and other developmental disabilities (n = 40) reported glycopyrrolate was effective in 90% of patients; the final effective dose range was 0.01 to 0.82 mg/kg/day PO. Side effects resulted in discontinuation of treatment in 28% of patients.

For the treatment of clozapine-induced sialorrhea†

Oral dosage

Adults

1 mg PO twice daily was found effective based on changes from baseline in the Drooling Rating Scale scores in 1 small, randomized, double-blind crossover trial. Glycopyrrolate was superior to biperiden, the comparator drug, in both efficacy and impact on cognition as assessed by changes in the Mini Mental State Examination (MMSE) scores. A dose of 1 mg PO twice daily was effective in improving the Drooling Severity Frequency Scale (DSFS) scores in 3 case reports. In a fourth case in the series, the dose was initiated at 1 mg PO twice daily and titrated up to 1 mg PO 4 times daily with minimal response; a final dose of 2 mg PO 3 times daily was prescribed.

For the treatment of sialorrhea† associated with amyotrophic lateral sclerosis (ALS)

Oral dosage

Adults

1 to 2 mg PO 3 times daily.

For the treatment of cardiac arrhythmias (e.g., bradycardia) that occur intraoperatively and are drug-induced or are associated with visceral traction stimulation of vagal reflexes

Intravenous dosage

Adults

100 mcg IV, repeated at 2 to 3 minute intervals as necessary.

Infants, Children, and Adolescents 1 month and older

4 mcg/kg IV (maximum single dose is 100 mcg), repeated at 2 to 3 minute intervals. If glycopyrrolate is given pre-operatively, intraoperative doses are rarely needed.

For cholinesterase inhibitor-induced muscarinic effects prophylaxis when anticholinesterase agents (i.e., neostigmine, physostigmine, pyridostigmine) are used to reverse neuromuscular blockade produced by curariform agents

Intravenous dosage

Adults

200 mcg IV for every 1 mg of neostigmine or every 5 mg of pyridostigmine administered. Administer glycopyrrolate simultaneously with the cholinesterase inhibitor.

Infants, Children, and Adolescents 1 month to 17 years

200 mcg IV for every 1 mg of neostigmine or every 5 mg of pyridostigmine administered. Administer glycopyrrolate simultaneously with the cholinesterase inhibitor.

For use to reduce symptoms of a peptic ulcer as adjunctive therapy in the treatment of peptic ulcer disease

Oral dosage (oral tablet)

Adults

Initially, 1 mg PO 3 times daily (in the morning, early afternoon, and at bedtime). Some patients may require 2 mg at bedtime dose to assure overnight control of symptoms. For maintenance, a dosage of 1 mg PO twice daily is frequently adequate. Usual Range: 1 to 2 mg PO given 2 to 3 times daily. Max: 8 mg/day PO. Use the lowest effective dose to attain clinical goals. LIMITATION OF USE: Glycopyrrolate is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

Children and Adolescents 12 years and older

1 to 2 mg PO 2 to 3 times per day. Use the lowest effective dose to attain clinical goals. Max: 8 mg/day PO. LIMITATION OF USE: Glycopyrrolate is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

Oral dosage (orally disintegrating tablet; i.e., Dartisla ODT)

Adults

1.7 mg PO 2 to 3 times daily. Max: 6.8 mg/day. Use the lowest effective dosage to control symptoms. The ODT is not recommended for patients who can take or are taking a lower dosage strength of glycopyrrolate (e.g., 1 mg tablet). Patients receiving a 2 mg oral tablet may be switched to the 1.7 mg glycopyrrolate ODT. LIMITATION OF USE: Glycopyrrolate ODT is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

Intramuscular and Intravenous dosage

Adults

100 to 200 mcg IM or IV, may repeat at 4 hour intervals if needed. LIMITATION OF USE: Glycopyrrolate is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

Adolescents 16 years and older

100 to 200 mcg IM or IV, may repeat at 4 hour intervals if needed. LIMITATION OF USE: Glycopyrrolate is not indicated as monotherapy for treatment of peptic ulcer because effectiveness in peptic ulcer healing has not been established.

For the treatment of irritable bowel syndrome† and/or diarrhea†

Oral dosage

Adults

1—2 mg PO 2—3 times per day.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components. Individuals with benzyl alcohol hypersensitivity should avoid parenteral glycopyrrolate.

glaucoma

Oral glycopyrrolate is contraindicated in people with glaucoma due to its ability to cause mydriasis and possibly increase intraocular pressure. Parenteral glycopyrrolate is contraindicated when used chronically as an adjunct for peptic ulcer treatment in people with glaucoma, but is not contraindicated when used during anesthesia. In anesthesia cases use with caution in people with glaucoma. Be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., ocular pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema) and instruct treated individuals to seek immediate medical attention if such symptoms occur.

colitis, constipation, GI bleeding, GI obstruction, hemorrhagic shock, hiatal hernia, toxic megacolon

Glycopyrrolate decreases gastrointestinal (GI) motility and is contraindicated in mechanical or functional GI obstruction disorders (e.g., pyloroduodenal stenosis,

strictures, and GI motility disorders such as achalasia, paralytic ileus, intestinal atony), GI bleeding due to peptic ulcer, if there is unstable cardiovascular status in acute hemorrhage (hemorrhagic shock), active inflammatory colitis or infectious colitis which can lead to toxic megacolon, or a history of or current toxic megacolon. Glycopyrrolate may aggravate and worsen these conditions. Glycopyrrolate is not recommended in patients with other conditions exacerbated by anticholinergic adverse reactions such as hiatal hernia associated with reflux esophagitis. An incomplete mechanical intestinal obstruction due to glycopyrrolate may present as diarrhea; if this occurs during treatment, stop glycopyrrolate and evaluate. Glycopyrrolate may worsen or cause constipation. During chronic use, assess patients for constipation, particularly within 4 to 5 days of initial dosing or after a dose increase.
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prostatic hypertrophy, urinary tract obstruction

The anticholinergic properties of glycopyrrolate can aggravate urinary retention. Glycopyrrolate oral tablets are contraindicated in individuals with obstructive uropathies (urinary tract obstruction), including prostatic hypertrophy. Parenteral glycopyrrolate is contraindicated when used chronically as an adjunct for peptic ulcer treatment in people with obstructive uropathies, including prostatic hypertrophy, but is not contraindicated when used during anesthesia. In anesthesia cases use with caution in people with obstructive uropathy or prostatic hypertrophy.

cardiac disease, hypertension, hyperthyroidism

Glycopyrrolate is not recommended in people with cardiac conditions that may be exacerbated by anticholinergic adverse reactions (e.g., cardiac disease). Investigate any tachycardia before giving glycopyrrolate because an increase in the heart rate may occur. Use with caution in patients with coronary artery disease, congestive heart failure, cardiac arrhythmias, hypertension, or hyperthyroidism.

autonomic neuropathy, myasthenia gravis

Glycopyrrolate should be used cautiously in individuals with autonomic neuropathy as these conditions can be exacerbated by the anticholinergic actions of the drug. Parenteral glycopyrrolate is contraindicated in people with myasthenia gravis.

conditions contributing to an elevated core body temperature

In the presence of conditions contributing to an elevated core body temperature, people being treated with glycopyrrolate may experience heat prostration due to decreased

sweating. Individuals receiving glycopyrrolate should be cautioned about fever, exposure to hot or humid environments, or heat prostration due to vigorous physical exercise because of the risk of heat stroke. Older adults may be particularly susceptible to these effects.

activities requiring coordination and concentration, driving or operating machinery

Glycopyrrolate may cause blurred vision. Drowsiness may also occur, particularly if combined with other CNS depressants. If blurred vision or drowsiness occurs, individuals should be warned to avoid driving or operating machinery or other activities requiring coordination and concentration until the full effects of the medication have dissipated.

brain injury, Down syndrome, infants, neonates, spastic paralysis

Infants, people with Down syndrome, and pediatric patients with spastic paralysis or brain injury/damage may experience an increased response to anticholinergics, thus increasing the potential for side effects from glycopyrrolate injection. Due to its benzyl alcohol content, glycopyrrolate injection should not be used in neonates (infants less than 1 month of age) due to a risk for "gasping syndrome" (characterized by central nervous system depression, metabolic acidosis, gasping respirations, gradual neurologic deterioration, potential for seizures, and high levels of benzyl alcohol and its metabolites found in the blood and urine). This syndrome has been associated with benzyl alcohol dosages above 99 mg/kg/day in neonates and low-birth-weight neonates. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

renal failure, renal impairment

Renal elimination of glycopyrrolate may be severely impaired in people with severe renal impairment or renal failure. Dosage adjustments may be necessary in this population.

hepatic disease

Although glycopyrrolate is mostly eliminated renally, the parenteral product labels state that glycopyrrolate injections should be used with caution in people with hepatic disease since anticholinergic drugs may aggravate this condition.

geriatric

The Beers Criteria recommend avoiding systemic anticholinergic medications in geriatric adults with the following conditions due to the potential for symptom exacerbation or adverse effects: dementia/cognitive impairment (adverse CNS effects), delirium/high risk of delirium (possible new-onset or worsening delirium), or lower urinary tract symptoms/benign prostatic hyperplasia in men (possible urinary retention or hesitancy). Monitor older adults carefully due to an increased susceptibility to anticholinergic effects of the drug versus younger adults. The effects of other anticholinergic medications are additive to the effects of glycopyrrolate, especially older adults.

pregnancy

Although a drug-associated risk of birth defects and miscarriage has not been identified, the limited available data on glycopyrrolate use during pregnancy are insufficient and most recorded exposures occurred after the first trimester. Published literature suggest the following regarding the use of glycopyrrolate during pregnancy. Unlike atropine, glycopyrrolate in normal doses (0.004 mg/kg) does not appear to affect fetal heart rate or fetal heart rate variability to a significant degree. Concentrations of glycopyrrolate in umbilical venous and arterial blood and in the amniotic fluid are low after intramuscular administration to parturients. Therefore, glycopyrrolate does not appear to penetrate through the placental barrier in significant amounts. No adverse effects on maternal outcomes or infant Apgar scores have been identified with glycopyrrolate exposures at the time of Cesarean-section delivery. In animal reproduction studies in pregnant rats and rabbits administered glycopyrrolate orally (rats) and intramuscularly (rabbits) during the period of organogenesis, no teratogenic effects were seen at 640-times and 10-times the maximum recommended human dose (MRHD) of 1 mg (on a mg/m2 basis), respectively.

breast-feeding

Use glycopyrrolate with caution during breast-feeding. There are no data on the presence of glycopyrrolate or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Glycopyrrolate and its metabolites were detected in the milk of lactating rats. As with other anticholinergics, glycopyrrolate may cause suppression of lactation, particularly when lactation is starting to be established. However, single doses may be unlikely to cause concern; the quaternary ammonium structure of glycopyrrolate makes it unlikely to be absorbed and reach the bloodstream of the infant after single doses. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated maternal condition.

Pregnancy And Lactation

Although a drug-associated risk of birth defects and miscarriage has not been identified, the limited available data on glycopyrrolate use during pregnancy are insufficient and most recorded exposures occurred after the first trimester. Published literature suggest the following regarding the use of glycopyrrolate during pregnancy. Unlike atropine, glycopyrrolate in normal doses (0.004 mg/kg) does not appear to affect fetal heart rate or fetal heart rate variability to a significant degree. Concentrations of glycopyrrolate in umbilical venous and arterial blood and in the amniotic fluid are low after intramuscular administration to parturients. Therefore, glycopyrrolate does not appear to penetrate through the placental barrier in significant amounts. No adverse effects on maternal outcomes or infant Apgar scores have been identified with glycopyrrolate exposures at the time of Cesarean-section delivery. In animal reproduction studies in pregnant rats and rabbits administered glycopyrrolate orally (rats) and intramuscularly (rabbits) during the period of organogenesis, no teratogenic effects were seen at 640-times and 10-times the maximum recommended human dose (MRHD) of 1 mg (on a mg/m2 basis), respectively.

Interactions

AbobotulinumtoxinA: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Acetaminophen; Aspirin; diphenhydrAMINE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when dihydrocodeine is used concomitantly with an anticholinergic drug. The concomitant use of dihydrocodeine and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Acetaminophen; Caffeine; Pyrilamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Chlorpheniramine: (Moderate) Monitor for signs or symptoms of

anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Chlorpheniramine; Phenylephrine : (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Acetaminophen; Dextromethorphan; Doxylamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; diphenhydrAMINE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Acetaminophen; HYDROcodone: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant hydrocodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Acetaminophen; oxyCODONE: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant oxycodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Acetaminophen; Pamabrom; Pyrilamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

Acetylcholine Chloride: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Aclidinium: (Moderate) Although aclidinium is minimally absorbed into the systemic circulation after inhalation, there is the potential for aclidinium to have additive anticholinergic effects when administered with other anticholinergics or antimuscarinics. Per the manufacturer, avoid concomitant administration of aclidinium with other anticholinergic medications, when possible.
Aclidinium; Formoterol: (Moderate) Although aclidinium is minimally absorbed into the systemic circulation after inhalation, there is the potential for aclidinium to have additive anticholinergic effects when administered with other anticholinergics or antimuscarinics. Per the manufacturer, avoid concomitant administration of aclidinium with other anticholinergic medications, when possible.
ALFentanil: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when alfentanil is used concomitantly with an anticholinergic drug. The concomitant use of alfentanil and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Aliskiren; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Alogliptin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Alosetron: (Major) Concomitant use of alosetron and anticholinergics, which can decrease GI motility, may seriously worsen constipation, leading to events such as GI obstuction, impaction, or paralytic ileus. Although specific recommendations are not available from the manufacturer, it would be prudent to avoid anticholinergics in patients taking alosetron.
Aluminum Hydroxide: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Aluminum Hydroxide; Magnesium Carbonate: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided

when feasible; separate dosing by at least 2 hours to limit an interaction.
Aluminum Hydroxide; Magnesium Hydroxide: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Aluminum Hydroxide; Magnesium Hydroxide; Simethicone: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Aluminum Hydroxide; Magnesium Trisilicate: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Amantadine: (Major) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with other drugs that possess antimuscarinic properties, such as amantadine.
aMILoride; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Amitriptyline: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
amLODIPine; Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Amoxapine: (Moderate) Depending on the specific agent, additive anticholinergic effects may be seen when amoxapine is used concomitantly with other anticholinergic agents. Clinicians should note that anticholinergic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive CNS effects are also possible when these drugs are combined with amoxapine.
Antacids: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Aspirin, ASA; Caffeine; Orphenadrine: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with other drugs with moderate to significant anticholinergic effects including orphenadrine.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation,

which may lead to paralytic ileus.
Aspirin, ASA; oxyCODONE: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant oxycodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Atenolol: (Moderate) Atenolol bioavailability may increase with coadministration of glycopyrrolate. A reduction in the atenolol dose may be necessary.
Atenolol; Chlorthalidone: (Moderate) Atenolol bioavailability may increase with coadministration of glycopyrrolate. A reduction in the atenolol dose may be necessary. (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Atropine; Difenoxin: (Moderate) Diphenoxylate is a synthetic opiate derivative that appears to exert its effect locally and centrally on the smooth mucle cells of the GI tract to inhibit GI motility and slow excess GI propulsion. The effects can be additive to antimuscarinic agents, such as glycopyrrolate. In some cases, constipation might occur, and effects on the CNS or bladder function may also be additive.
Azilsartan; Chlorthalidone: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Belladonna; Opium: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when opium is used concomitantly with an anticholinergic drug. The concomitant use of opium and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Benazepril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Benzgalantamine: (Moderate) The therapeutic benefits of galantamine, a cholinesterase inhibitor, may be diminished during chronic co-administration with antimuscarinics or medications with potent anticholinergic activity. When concurrent use is not avoidable, the patient should be monitored for cognitive decline and anticholinergic side effects.

Clinicians should generally avoid multiple medications with anticholinergic activity in the patient with dementia. Some of the common selective antimuscarinic drugs for bladder problems, (such as oxybutynin, darifenacin, trospium, fesoterodine, tolerodine, or solifenacin), do not routinely cause problems with medications used for dementia, but may cause anticholinergic side effects in some patients. Atropine may be used to offset bradycardia in cholinesterase inhibitor overdose.
Benzhydrocodone; Acetaminophen: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when benzhydrocodone is used concomitantly with an anticholinergic drug. The concomitant use of benzhydrocodone and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Bethanechol: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Bisoprolol; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Botulinum Toxins: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Brompheniramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Brompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Brompheniramine; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Brompheniramine; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Brompheniramine; Pseudoephedrine; Dextromethorphan: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and

glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Buprenorphine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant buprenorphine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Buprenorphine; Naloxone: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant buprenorphine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
buPROPion: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with bupropion. Additive drowsiness may occur. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
buPROPion; Naltrexone: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with bupropion. Additive drowsiness may occur. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Butorphanol: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when butorphanol is used concomitantly with an anticholinergic drug. The concomitant use of butorphanol and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Calcium Carbonate: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of anticholinergics.
Calcium Carbonate; Famotidine; Magnesium Hydroxide: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of anticholinergics.
Calcium Carbonate; Magnesium Hydroxide: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of

anticholinergics.
Calcium Carbonate; Magnesium Hydroxide; Simethicone: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of anticholinergics.
Calcium Carbonate; Simethicone: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of anticholinergics.
Calcium; Vitamin D: (Major) Avoid concomitant use of calcium carbonate and anticholinergics. Antacids may interfere with the absorption of anticholinergics.
Canagliflozin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Candesartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Captopril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Carbidopa; Levodopa: (Moderate) Monitor for a decrease in levodopa efficacy during concomitant use of levodopa and oral glycopyrrolate; a levodopa dosage adjustment may be required based on response. Concomitant use may reduce levodopa exposure.
Carbidopa; Levodopa; Entacapone: (Moderate) Monitor for a decrease in levodopa efficacy during concomitant use of levodopa and oral glycopyrrolate; a levodopa dosage adjustment may be required based on response. Concomitant use may reduce levodopa exposure.
Carbinoxamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Celecoxib; Tramadol: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant tramadol and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Cetirizine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Cetirizine; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of

anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Cevimeline: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Chlophedianol; Dexbrompheniramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlophedianol; Dexchlorpheniramine; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorcyclizine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
chlordiazePOXIDE; Amitriptyline: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorothiazide: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Chlorpheniramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Dextromethorphan: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for signs

or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; HYDROcodone: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant hydrocodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Ibuprofen; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Chlorpheniramine; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
chlorproMAZINE: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including chlorpromazine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur.
Chlorthalidone: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Cholinergic agonists: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Cisapride: (Moderate) The use of drugs that decrease GI motility, such as glycopyrrolate, may pharmacodynamically oppose the effects of cisapride.
Clemastine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
clomiPRAMINE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use

may result in additive anticholinergic adverse effects.
cloZAPine: (Major) Avoid co-prescribing clozapine with other anticholinergic medicines that can cause gastrointestinal hypomotility, due to a potential to increase serious constipation, ileus, and other potentially serious bowel conditions that may result in hospitalization. Clozapine exhibits potent anticholinergic effects. Additive anticholinergic effects may be seen when clozapine is used concomitantly with anticholinergic agents. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur, depending on the anticholinergic agent used.
Codeine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Codeine; Dexbrompheniramine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Codeine; guaiFENesin: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Codeine; Phenylephrine; Promethazine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant promethazine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Codeine; Promethazine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant codeine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant promethazine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Crofelemer: (Moderate) Pharmacodynamic interactions between crofelemer and

antimuscarinics are theoretically possible. Crofelemer does not affect GI motility mechanisms, but does have antidiarrheal effects. Patients taking medications that decrease GI motility, such as antimuscarinics, may be at greater risk for serious complications from crofelemer, such as constipation with chronic use. Use caution and monitor GI symptoms during coadministration.
Cyclobenzaprine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cyclobenzaprine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Cyproheptadine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dapagliflozin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Dasiglucagon: (Major) The concomitant use of intravenous glucagon and anticholinergics increases the risk of gastrointestinal adverse reactions due to additive effects on inhibition of gastrointestinal motility. Concomitant use is not recommended.
DaxibotulinumtoxinA: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Desipramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dexbrompheniramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dexbrompheniramine; Dextromethorphan; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dexbrompheniramine; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dexchlorpheniramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dexchlorpheniramine; Dextromethorphan; Pseudoephedrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker

and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dextromethorphan; buPROPion: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with bupropion. Additive drowsiness may occur. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
Dextromethorphan; diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Dextromethorphan; quiNIDine: (Moderate) The anticholinergic effects of quinidine may be significant and may be enhanced when combined with antimuscarinics.
Digoxin: (Moderate) Anticholinergics, because of their ability to cause tachycardia, can antagonize the beneficial actions of digoxin in atrial fibrillation/flutter. Routine therapeutic monitoring should be continued when an antimuscarinic agent is prescribed with digoxin until the effects of combined use are known.
dimenhyDRINATE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
diphenhydrAMINE: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
diphenhydrAMINE; Ibuprofen: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
diphenhydrAMINE; Naproxen: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
diphenhydrAMINE; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Diphenoxylate; Atropine: (Moderate) Diphenoxylate is a synthetic opiate derivative that appears to exert its effect locally and centrally on the smooth mucle cells of the GI tract to inhibit GI motility and slow excess GI propulsion. The effects can be additive to antimuscarinic agents, such as glycopyrrolate. In some cases, constipation might occur, and effects on the CNS or bladder function may also be additive.
Disopyramide: (Moderate) In addition to its electrophysiologic effects, disopyramide exhibits clinically significant anticholinergic properties. These can be additive with other anticholinergics. Clinicians should be aware that urinary retention, particularly in males, and aggravation of glaucoma are realistic possibilities of using disopyramide with other

anticholinergic agents.
Donepezil: (Moderate) The therapeutic benefits of donepezil, a cholinesterase inhibitor, may be diminished during chronic co-administration with antimuscarinics or medications with potent anticholinergic activity. When concurrent use is not avoidable, the patient should be monitored for cognitive decline and anticholinergic side effects. Clinicians should generally avoid multiple medications with anticholinergic activity in the patient with dementia. Some of the common selective antimuscarinic drugs for bladder problems, (such as oxybutynin, darifenacin, trospium, fesoterodine, tolerodine, or solifenacin), do not routinely cause problems with medications used for dementia, but may cause anticholinergic side effects in some patients. Atropine may be used to offset bradycardia in cholinesterase inhibitor overdose.
Donepezil; Memantine: (Moderate) The adverse effects of anticholinergics, such as dry mouth, urinary hesitancy or blurred vision may be enhanced with use of memantine; dosage adjustments of the anticholinergic drug may be required when memantine is coadministered. In addition, preliminary evidence indicates that chronic anticholinergic use in patients with Alzheimer's Disease may possibly have an adverse effect on cognitive function. Therefore, the effectiveness of drugs used in the treatment of Alzheimer's such as memantine, may be adversely affected by chronic antimuscarinic therapy. (Moderate) The therapeutic benefits of donepezil, a cholinesterase inhibitor, may be diminished during chronic co-administration with antimuscarinics or medications with potent anticholinergic activity. When concurrent use is not avoidable, the patient should be monitored for cognitive decline and anticholinergic side effects. Clinicians should generally avoid multiple medications with anticholinergic activity in the patient with dementia. Some of the common selective antimuscarinic drugs for bladder problems, (such as oxybutynin, darifenacin, trospium, fesoterodine, tolerodine, or solifenacin), do not routinely cause problems with medications used for dementia, but may cause anticholinergic side effects in some patients. Atropine may be used to offset bradycardia in cholinesterase inhibitor overdose.
Doxepin: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Doxylamine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Doxylamine; Pyridoxine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
droNABinol: (Moderate) Use caution if coadministration of dronabinol with anticholinergics is necessary. Concurrent use of dronabinol, THC with anticholinergics may result in additive drowsiness, hypertension, tachycardia, and possibly cardiotoxicity.

Eluxadoline: (Major) Avoid use of eluxadoline with medications that may cause constipation, such as anticholinergics. Discontinue use of eluxadoline in patients who develop severe constipation lasting more than 4 days.
Empagliflozin; Linagliptin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Empagliflozin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Enalapril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Ertugliflozin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
fentaNYL: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant fentanyl and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
fluPHENAZine: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including fluphenazine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur.
Fluticasone; Umeclidinium; Vilanterol: (Moderate) There is the potential for umeclidinium to have additive anticholinergic effects when administered with other anticholinergics or antimuscarinics. Per the manufaturer, avoid concomitant administration of umeclidinium with other anticholinergic medications when possible.
Foscarbidopa; Foslevodopa: (Moderate) Monitor for a decrease in levodopa efficacy during concomitant use of levodopa and oral glycopyrrolate; a levodopa dosage adjustment may be required based on response. Concomitant use may reduce levodopa exposure.
Fosinopril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate

of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Galantamine: (Moderate) The therapeutic benefits of galantamine, a cholinesterase inhibitor, may be diminished during chronic co-administration with antimuscarinics or medications with potent anticholinergic activity. When concurrent use is not avoidable, the patient should be monitored for cognitive decline and anticholinergic side effects. Clinicians should generally avoid multiple medications with anticholinergic activity in the patient with dementia. Some of the common selective antimuscarinic drugs for bladder problems, (such as oxybutynin, darifenacin, trospium, fesoterodine, tolerodine, or solifenacin), do not routinely cause problems with medications used for dementia, but may cause anticholinergic side effects in some patients. Atropine may be used to offset bradycardia in cholinesterase inhibitor overdose.
Gepotidacin: (Moderate) Monitor for reduced efficacy of both medications during concomitant use. Gepotidacin is a cholinesterase inhibitor. Anticholinergic medications and cholinesterase inhibitors antagonize each other.
glipiZIDE; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Glucagon: (Major) The concomitant use of intravenous glucagon and anticholinergics increases the risk of gastrointestinal adverse reactions due to additive effects on inhibition of gastrointestinal motility. Concomitant use is not recommended.
glyBURIDE; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Glycopyrronium: (Moderate) Although glycopyrronium is minimally absorbed into the systemic circulation after topical application, there is the potential for glycopyrronium to have additive anticholinergic effects when administered with other antimuscarinics. Per the manufaturer, avoid concomitant administration of glycopyrronium with other anticholinergic medications.
Guanidine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Haloperidol: (Moderate) Coadministration of glycopyrrolate with haloperidol may decrease haloperidol serum concentrations, which may lead to worsening of psychiatric symptoms and the development of tardive dyskinesia. If coadministration is necessary, closely monitor patient.
Homatropine; HYDROcodone: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant hydrocodone and glycopyrrolate use.

Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
hydroCHLOROthiazide, HCTZ; Moexipril: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
HYDROcodone: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant hydrocodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
HYDROcodone; Ibuprofen: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant hydrocodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
HYDROmorphone: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when hydromorphone is used concomitantly with an anticholinergic drug. The concomitant use of hydromorphone and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
hydrOXYzine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Ibritumomab Tiuxetan: (Major) Glycopyrrolate oral solution is contraindicated with concomitant solid oral dosage forms of potassium chloride due to risk for gastrointestinal mucosal injury. Glycopyrrolate orally disintegrating tablets are not recommended for use with solid oral dosage forms of potassium chloride. Use other glycopyrrolate dosage forms with solid oral dosage forms of potassium chloride with caution. Anticholinergics may decrease gastric motility and increase the transit time of solid oral dosage forms of potassium chloride leading to prolonged contact with the gastrointestinal mucosa.
Imipramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may

result in additive anticholinergic adverse effects.
IncobotulinumtoxinA: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Ipratropium: (Moderate) Although ipratropium is minimally absorbed into the systemic circulation after inhalation, there is the potential for additive anticholinergic effects when administered with other antimuscarinic or anticholinergic medications. Per the manufacturer, avoid coadministration.
Ipratropium; Albuterol: (Moderate) Although ipratropium is minimally absorbed into the systemic circulation after inhalation, there is the potential for additive anticholinergic effects when administered with other antimuscarinic or anticholinergic medications. Per the manufacturer, avoid coadministration.
Irbesartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Itraconazole: (Moderate) Antimuscarinics can raise intragastric pH. This effect may decrease the oral bioavailability of itraconazole; antimuscarinics should be used cautiously in patients receiving itraconazole.
Levocetirizine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant cetirizine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Levodopa: (Moderate) Monitor for a decrease in levodopa efficacy during concomitant use of levodopa and oral glycopyrrolate; a levodopa dosage adjustment may be required based on response. Concomitant use may reduce levodopa exposure.
Levorphanol: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when levorphanol is used concomitantly with an anticholinergic drug. The concomitant use of levorphanol and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Linaclotide: (Moderate) Anticholinergics can promote constipation and pharmacodynamically oppose the action of drugs used for the treatment of constipation or constipation-associated irritable bowel syndrome, such as linaclotide.
Linagliptin; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical

response to metformin and adjust metformin dose accordingly.
Lisinopril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Losartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Loxapine: (Moderate) Loxapine has anticholinergic activity. The concomitant use of loxapine and other anticholinergic drugs can increase the risk of anticholinergic adverse reactions including exacerbation of glaucoma, constipation, and urinary retention. Depending on the agent used, additive drowsiness/dizziness may also occur.
Lubiprostone: (Moderate) Antimuscarinic drugs can promote constipation and pharmacodynamically oppose the action of drugs used for the treatment of constipation, such as lubiprostone. The clinical significance of these potential interactions is uncertain.
Lurasidone: (Moderate) Antipsychotic agents may disrupt core temperature regulation; therefore, caution is recommended during concurrent use of lurasidone and medications with anticholinergic activity such as antimuscarinics. Concurrent use of lurasidone and medications with anticholinergic activity may contribute to heat-related disorders. Monitor patients for heat intolerance, decreased sweating, or increased body temperature if lurasidone is used with antimuscarinics.
Macimorelin: (Major) Avoid use of macimorelin with drugs that may blunt the growth hormone response to macimorelin, such as antimuscarinic anticholinergic agents. Healthcare providers are advised to discontinue anticholinergics at least 1 week before administering macimorelin. Use of these medications together may impact the accuracy of the macimorelin growth hormone test.
Magnesium Hydroxide: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Magnesium Salts: (Moderate) Antacids may inhibit the oral absorption of anticholinergics. Simultaneous oral administration should be avoided when feasible; separate dosing by at least 2 hours to limit an interaction.
Maprotiline: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with other commonly used drugs with moderate to significant anticholinergic effects including maprotiline.
Meclizine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during

concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Memantine: (Moderate) The adverse effects of anticholinergics, such as dry mouth, urinary hesitancy or blurred vision may be enhanced with use of memantine; dosage adjustments of the anticholinergic drug may be required when memantine is coadministered. In addition, preliminary evidence indicates that chronic anticholinergic use in patients with Alzheimer's Disease may possibly have an adverse effect on cognitive function. Therefore, the effectiveness of drugs used in the treatment of Alzheimer's such as memantine, may be adversely affected by chronic antimuscarinic therapy.
Meperidine: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when meperidine is used concomitantly with an anticholinergic drug. The concomitant use of meperidine and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
metFORMIN; sAXagliptin: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
metFORMIN; SITagliptin: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Methadone: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when methadone is used concomitantly with an anticholinergic drug. The concomitant use of methadone and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Metoclopramide: (Moderate) Drugs with significant antimuscarinic activity, such as anticholinergics and antimuscarinics, may slow GI motility and thus may reduce the prokinetic actions of metoclopramide. Monitor patients for an increase in gastrointestinal complaints, such as reflux or constipation. Additive drowsiness may

occur as well. The clinical significance is uncertain.
metOLazone: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Metoprolol; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Molindone: (Moderate) Antipsychotics are associated with anticholinergic effects; therefore, additive effects may be seen during concurrent use of molindone and other drugs having anticholinergic activity such as antimuscarinics. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other CNS effects may also occur.
Morphine: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant morphine and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Nalbuphine: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when nalbuphine is used concomitantly with an anticholinergic drug. The concomitant use of nalbuphine and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Neostigmine: (Minor) The muscarinic actions of neostigmine can antagonize the antimuscarinic actions of glycopyrrolate.
Neostigmine; Glycopyrrolate: (Minor) The muscarinic actions of neostigmine can antagonize the antimuscarinic actions of glycopyrrolate.
Nortriptyline: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
OLANZapine: (Moderate) Additive anticholinergic effects may be seen when olanzapine and anticholinergics are used concomitantly; use with caution. Use of olanzapine and other drugs with anticholinergic activity can increase the risk for severe gastrointestinal adverse reactions related to hypomotility. Olanzapine exhibits anticholinergic activity. Adverse effects may be seen not only on GI smooth muscle, but also on bladder

function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur, depending on the anticholinergic agent used.
OLANZapine; FLUoxetine: (Moderate) Additive anticholinergic effects may be seen when olanzapine and anticholinergics are used concomitantly; use with caution. Use of olanzapine and other drugs with anticholinergic activity can increase the risk for severe gastrointestinal adverse reactions related to hypomotility. Olanzapine exhibits anticholinergic activity. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur, depending on the anticholinergic agent used.
OLANZapine; Samidorphan: (Moderate) Additive anticholinergic effects may be seen when olanzapine and anticholinergics are used concomitantly; use with caution. Use of olanzapine and other drugs with anticholinergic activity can increase the risk for severe gastrointestinal adverse reactions related to hypomotility. Olanzapine exhibits anticholinergic activity. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur, depending on the anticholinergic agent used.
Oliceridine: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when oliceridine is used with glycopyrrolate. Use of anticholinergics may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Olmesartan; amLODIPine; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Olmesartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
OnabotulinumtoxinA: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Orphenadrine: (Moderate) Additive anticholinergic effects may be seen when glycopyrrolate is used concomitantly with other drugs with moderate to significant anticholinergic effects including orphenadrine.
oxyCODONE: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant oxycodone and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to

paralytic ileus.
oxyMORphone: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when oxymorphone is used concomitantly with an anticholinergic drug. The concomitant use of oxymorphone and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
PARoxetine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant anticholinergic medication and paroxetine use. Concomitant use may result in additive anticholinergic adverse effects.
Pentazocine; Naloxone: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when pentazocine is used concomitantly with an anticholinergic drug. The concomitant use of pentazocine and anticholinergic medications may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Perphenazine: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including perphenazine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur.
Perphenazine; Amitriptyline: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including perphenazine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur. (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Phentermine; Topiramate: (Moderate) Monitor for decreased sweating and increased body temperature, especially in hot weather, during concomitant use of topiramate and other drugs that predispose persons to heat-related disorders, such as anticholinergic medications. Concomitant use increases the risk for oligohidrosis and hyperthermia.
PHYSostigmine: (Minor) The muscarinic actions of physostigmine can antagonize the antimuscarinic actions of glycopyrrolate.
Pilocarpine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.

Pioglitazone; metFORMIN: (Moderate) Coadministration of glycopyrrolate with metformin my increase metformin plasma concentrations, which may lead to increased metformin effects and possible adverse events. If coadministration is necessary, monitor clinical response to metformin and adjust metformin dose accordingly.
Potassium Bicarbonate: (Major) Glycopyrrolate oral solution is contraindicated with concomitant solid oral dosage forms of potassium chloride due to risk for gastrointestinal mucosal injury. Glycopyrrolate orally disintegrating tablets are not recommended for use with solid oral dosage forms of potassium chloride. Use other glycopyrrolate dosage forms with solid oral dosage forms of potassium chloride with caution. Anticholinergics may decrease gastric motility and increase the transit time of solid oral dosage forms of potassium chloride leading to prolonged contact with the gastrointestinal mucosa.
Potassium Chloride: (Major) Glycopyrrolate oral solution is contraindicated with concomitant solid oral dosage forms of potassium chloride due to risk for gastrointestinal mucosal injury. Glycopyrrolate orally disintegrating tablets are not recommended for use with solid oral dosage forms of potassium chloride. Use other glycopyrrolate dosage forms with solid oral dosage forms of potassium chloride with caution. Anticholinergics may decrease gastric motility and increase the transit time of solid oral dosage forms of potassium chloride leading to prolonged contact with the gastrointestinal mucosa.
Pralidoxime: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Pramlintide: (Major) Pramlintide therapy should not be considered in patients taking medications that alter gastric motility, such as anticholinergics. Pramlintide slows gastric emptying and the rate of nutrient delivery to the small intestine. Medications that have depressive effects on GI could potentiate the actions of pramlintide.
Procainamide: (Moderate) The anticholinergic effects of procainamide may be significant and may be enhanced when combined with anticholinergics. Anticholinergic agents administered concurrently with procainamide may produce additive antivagal effects on AV nodal conduction, although this is not as well documented for procainamide as for quinidine.
Prochlorperazine: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including prochlorperazine. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur.
Promethazine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant promethazine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.

Promethazine; Dextromethorphan: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant promethazine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Promethazine; Phenylephrine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant promethazine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Protriptyline: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Pseudoephedrine; Triprolidine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
pyRIDostigmine: (Minor) The muscarinic actions of pyridostigmine can antagonize the antimuscarinic actions of glycopyrrolate.
QUEtiapine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant quetiapine and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Quinapril; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
quiNIDine: (Moderate) The anticholinergic effects of quinidine may be significant and may be enhanced when combined with antimuscarinics.
Rasagiline: (Moderate) MAOIs exhibit secondary anticholinergic actions. Additive anticholinergic effects may be seen when MAOIs are used concomitantly with antimuscarinics. Clinicians should note that antimuscarinic effects might be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive CNS effects are also possible when many of these drugs are combined with MAOIs.
Remifentanil: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when remifentanil is used concomitantly with an anticholinergic drug. The concomitant use of remifentanil and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Revefenacin: (Moderate) Although revefenacin is minimally absorbed into the systemic circulation after inhalation, there is the potential for additive anticholinergic effects when administered with other antimuscarinics. Avoid concomitant administration with

other anticholinergic and antimucarinic medications.
RimabotulinumtoxinB: (Moderate) The use of systemic antimuscarinic/anticholinergic agents following the administration of botulinum toxins may result in a potentiation of systemic anticholinergic effects (e.g., blurred vision, dry mouth, constipation, or urinary retention).
Rivastigmine: (Moderate) The therapeutic benefits of rivastigmine, a cholinesterase inhibitor, may be diminished during chronic co-administration with antimuscarinics or medications with potent anticholinergic activity. When concurrent use is not avoidable, the patient should be monitored for cognitive decline and anticholinergic side effects. Clinicians should generally avoid multiple medications with anticholinergic activity in the patient with dementia. Some of the common selective antimuscarinic drugs for bladder problems, (such as oxybutynin, darifenacin, trospium, fesoterodine, tolerodine, or solifenacin), do not routinely cause problems with medications used for dementia, but may cause anticholinergic side effects in some patients. Atropine may be used to offset bradycardia in cholinesterase inhibitor overdose.
Secretin: (Major) Discontinue anticholinergic medications at least 5 half-lives before performing a secretin stimulation test. Anticholinergics may cause a hyporesponse to secretin stimulation testing and interfere with the test's diagnostic accuracy.
Sedating H1-blockers: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Sincalide: (Moderate) Sincalide-induced gallbladder ejection fraction may be affected by anticholinergics. False study results are possible in patients with drug-induced hyper- or hypo-responsiveness; thorough patient history is important in the interpretation of procedure results.
Sodium Sulfate; Magnesium Sulfate; Potassium Chloride: (Major) Glycopyrrolate oral solution is contraindicated with concomitant solid oral dosage forms of potassium chloride due to risk for gastrointestinal mucosal injury. Glycopyrrolate orally disintegrating tablets are not recommended for use with solid oral dosage forms of potassium chloride. Use other glycopyrrolate dosage forms with solid oral dosage forms of potassium chloride with caution. Anticholinergics may decrease gastric motility and increase the transit time of solid oral dosage forms of potassium chloride leading to prolonged contact with the gastrointestinal mucosa.
Solifenacin: (Moderate) Additive anticholinergic effects may be seen when drugs with antimuscarinic properties like solifenacin are used concomitantly with other antimuscarinics. Blurred vision and dry mouth would be common effects. Clinicians should note that additive antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur.
Spironolactone; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and

antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
SUFentanil: (Moderate) Monitor patients for signs of urinary retention or reduced gastric motility when sufentanil is used concomitantly with an anticholinergic drug. The concomitant use of sufentanil and anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect.
Tapentadol: (Moderate) Tapentadol should be used cautiously with anticholinergic medications since additive depressive effects on GI motility or bladder function may occur. Monitor patients for signs of urinary retention or reduced gastric motility. Opiates increase the tone and decrease the propulsive contractions of the smooth muscle of the gastrointestinal tract. Prolongation of the gastrointestinal transit time may be the mechanism of the constipating effect. Opiate analgesics combined with antimuscarinics can cause severe constipation or paralytic ileus, especially with chronic use. Additive CNS effects like drowsiness or dizziness may also occur.
Tegaserod: (Major) Drugs that exert significant anticholinergic properties such as antimuscarinics may pharmacodynamically oppose the effects of prokinetic agents such as tegaserod. Avoid administering antimuscarinics along with tegaserod under most circumstances. Inhaled respiratory antimuscarinics, such as ipratropium, are unlikely to interact with tegaserod. Ophthalmic anticholinergics may interact if sufficient systemic absorption of the eye medication occurs.
Telmisartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Tenapanor: (Moderate) Anticholinergics can promote constipation and pharmacodynamically oppose the action of drugs used for the treatment of constipation or constipation-associated irritable bowel syndrome, such as tenapanor.
Thiazide diuretics: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Thioridazine: (Moderate) Additive anticholinergic effects may be seen when drugs with anticholinergic properties like thioridazine are used concomitantly with anticholinergic

agents. Adverse effects may be seen not only on GI smooth muscle, but also on bladder function, the CNS, the eye, and temperature regulation. Additive drowsiness may also occur, depending on the interacting agent.
Thiothixene: (Moderate) Anticholinergics may have additive effects with thiothixene, an antipsychotic with the potential for anticholinergic activity. Monitor for anticholinergic-related adverse effects such as xerostomia, blurred vision, constipation, and urinary retention during concurrent use.
Tiotropium: (Major) Avoid concomitant use of anticholinergic medications and tiotropium due to increased risk for anticholinergic adverse effects.
Tiotropium; Olodaterol: (Major) Avoid concomitant use of anticholinergic medications and tiotropium due to increased risk for anticholinergic adverse effects.
Tolterodine: (Moderate) Additive anticholinergic effects may be seen when tolterodine is used concomitantly with other antimuscarinics. When possible, avoid concurrent use, especially in the elderly, who are more susceptible to the anticholinergic effects. Consider alternatives to these other medications, if available. Clinicians should note that antimuscarinic effects might be seen not only on bladder smooth muscle, but also on GI function, the eye, and temperature regulation. Blurred vision, constipation, and dry mouth may be more prominent additive effects. With many of the listed agents, additive drowsiness may also occur when combined.
Topiramate: (Moderate) Monitor for decreased sweating and increased body temperature, especially in hot weather, during concomitant use of topiramate and other drugs that predispose persons to heat-related disorders, such as anticholinergic medications. Concomitant use increases the risk for oligohidrosis and hyperthermia.
traMADol: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant tramadol and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Tramadol; Acetaminophen: (Moderate) Monitor for signs of urinary retention or reduced gastric motility during concomitant tramadol and glycopyrrolate use. Concomitant use may increase the risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Triamterene; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Tricyclic antidepressants: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Trifluoperazine: (Moderate) Additive anticholinergic effects may be seen when anticholinergics are used concomitantly with phenothiazines, including trifluoperazine.

Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation. Additive drowsiness or other additive CNS effects may also occur.
Trimethobenzamide: (Moderate) Trimethobenzamide has CNS depressant effects and may cause drowsiness. The concurrent use of trimethobenzamide with other medications that cause CNS depression, like the anticholinergics, may potentiate the effects of either trimethobenzamide or the anticholinergic.
Trimipramine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant tricyclic antidepressant and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Triprolidine: (Moderate) Monitor for signs or symptoms of anticholinergic toxicity during concomitant sedating H1-blocker and glycopyrrolate use. Concomitant use may result in additive anticholinergic adverse effects.
Trospium: (Moderate) Additive anticholinergic effects may be seen when trospium is used concomitantly with other antimuscarinics. When possible, avoid concurrent use, especially in the elderly, who are more susceptible to the anticholinergic effects. Consider alternatives to these other medications, if available. Clinicians should note that antimuscarinic effects might be seen not only on bladder smooth muscle, but also on GI function, the eye, and temperature regulation. Blurred vision, constipation, and dry mouth may be more prominent additive effects. With many of the listed agents, additive drowsiness may also occur when combined with trospium.
Umeclidinium: (Moderate) There is the potential for umeclidinium to have additive anticholinergic effects when administered with other anticholinergics or antimuscarinics. Per the manufaturer, avoid concomitant administration of umeclidinium with other anticholinergic medications when possible.
Umeclidinium; Vilanterol: (Moderate) There is the potential for umeclidinium to have additive anticholinergic effects when administered with other anticholinergics or antimuscarinics. Per the manufaturer, avoid concomitant administration of umeclidinium with other anticholinergic medications when possible.
Valsartan; hydroCHLOROthiazide, HCTZ: (Minor) Coadministration of thiazides and antimuscarinics (e.g., atropine and biperiden) may result in increased bioavailability of the thiazide. This is apparently a result of a decrease in gastrointestinal motility and rate of stomach emptying by the antimuscarinic agent. In addition, diuretics can increase urinary frequency, which may aggravate bladder symptoms.
Vibegron: (Moderate) Vibegron should be administered with caution in patients taking anticholinergics because of potential for an increased risk of urinary retention. Monitor for symptoms of urinary difficulties or urinary retention. Patients may note constipation or dry mouth with use of these drugs together.
Xanomeline; Trospium: (Moderate) Additive anticholinergic effects may be seen when trospium is used concomitantly with other antimuscarinics. When possible, avoid

concurrent use, especially in the elderly, who are more susceptible to the anticholinergic effects. Consider alternatives to these other medications, if available. Clinicians should note that antimuscarinic effects might be seen not only on bladder smooth muscle, but also on GI function, the eye, and temperature regulation. Blurred vision, constipation, and dry mouth may be more prominent additive effects. With many of the listed agents, additive drowsiness may also occur when combined with trospium.
Zonisamide: (Moderate) Zonisamide use is associated with case reports of decreased sweating, hyperthermia, heat intolerance, or heat stroke and should be used with caution in combination with other drugs that may also predispose patients to heat-related disorders like anticholinergics.

Adverse Reaction

anaphylactoid reactions, angioedema, bronchospasm, injection site reaction, pruritus, rash, urticaria, xerosis

Hypersensitivity and dermal reactions have included reports of urticaria, pruritus, hypersensitivity reactions, and anaphylactoid reactions with oral and parenteral glycopyrrolate. Dry skin (xerosis), pruritus, and rash are reported in less than 2% of patients. An injection site reaction including pruritus, edema, erythema, and pain has been reported with parenteral administration. Immediate hypersensitivity reactions have been reported after administration of inhaled glycopyrrolate as well. Rash (unspecified), pruritus, and hypersensitivity have been reported in less than 1% of patients during clinical trials with inhaled glycopyrrolate. Angioedema and paradoxical bronchospasm were reported during postmarketing experience with inhaled glycopyrrolate. If signs suggesting allergic reactions occur, particularly angioedema, urticaria, or skin rash, therapy should be discontinued immediately and alternative therapy instituted.

agitation, anhidrosis, confusion, dizziness, drowsiness, emotional lability, fatigue, flushing, headache, impotence (erectile dysfunction), insomnia, lactation suppression, nystagmus, restlessness, seizures, weakness

The majority of the adverse effects associated with glycopyrrolate therapy are usually related to the pharmacological actions common to all anticholinergic agents. These effects include flushing (greater than 10%), headache (15%), nervousness, drowsiness, weakness, dizziness, insomnia, impotence (erectile dysfunction). Anhidrosis may occur, and, in hot or humid environments, there is a risk of patients experiencing dehydration along with hyperthermia due to the suppression of sweat gland activity and anticholinergic effects that lead to heat prostration. Instruct patients and caregivers to

avoid patient exposure to very warm environmental conditions. Fatigue (1% and up to 2%) and headache (2% or more) were reported in patients receiving glycopyrrolate nebulizer solution. Insomnia was reported in less than 1% of patients during clinical trials with inhaled glycopyrrolate. Lactation suppression has been reported postmarketing with oral products. Insomnia was reported in less than 1% of patients during clinical trials with inhaled glycopyrrolate. Other neurologic side effects reported in less than 2% of patients may include seizures, nystagmus, and dysgeusia or other taste disturbances. Psychiatric effects reported in less than 2% of patients include agitation, restlessness, abnormal behavior, aggression, crying, impulse control disorder, moaning, or emotional lability. Glycopyrrolate does not cross the blood-brain barrier as extensively as other systemic anticholinergic medications, such as atropine or scopolamine. However, mental confusion, psychiatric effects, and/or paradoxical excitement may occur, especially in the elderly or in young pediatric patients, who may be more sensitive to anticholinergic effects.

abdominal pain, constipation, diarrhea, dysgeusia, flatulence, GI obstruction, nausea, vomiting, xerostomia

Gastrointestinal and related adverse effects associated with glycopyrrolate therapy are usually due to the pharmacological actions common to all anticholinergic agents. Xerostomia is probably the most common adverse effect (10 to 40%). Constipation is a common dose-limiting adverse effect that can sometimes lead to discontinuation. Assess patients for constipation, particularly within 4 to 5 days of initial dosing or after a dose escalation. GI obstruction, specifically intestinal pseudo-obstruction, has been reported and may present as abdominal distention, abdominal pain, nausea, or vomiting. In addition, diarrhea may present as an early symptom of incomplete mechanical intestinal obstruction, especially in patients with ileostomy or colostomy. If incomplete mechanical intestinal obstruction is suspected, discontinue glycopyrrolate and evaluate the patient for intestinal obstruction. Nausea and vomiting occur infrequently. Dysgeusia, stomach discomfort, chapped lips, flatulence, retching, and dry tongue are other GI effects reported to occur in less than 2% of patients with chronic use. During clinical trials with glycopyrrolate inhaler, gastroenteritis and vomiting were reported in less than 1% of patients. In clinical trials, diarrhea was reported in 2% or more of patients receiving glycopyrrolate nebulizer solution.

arrhythmia exacerbation, atrial fibrillation, bradycardia, cardiac arrest, chest pain (unspecified), hypertension, hypotension, pallor, palpitations, QT prolongation, sinus tachycardia, ventricular tachycardia

Cardiovascular effects of anticholinergic drugs like glycopyrrolate may infrequently

result in palpitations or sinus tachycardia. Pallor was reported in less than 2% of patients in clinical trials where glycopyrrolate was given chronically. The following adverse events have been reported from postmarketing experience with glycopyrrolate: malignant hyperthermia; cardiac arrhythmia exacerbation (including sinus bradycardia, ventricular tachycardia, ventricular fibrillation); cardiac arrest; hypertension; hypotension; chest pain (unspecified); and respiratory arrest. Atrial fibrillation was reported in less than 1% of patients during clinical trials with inhaled glycopyrrolate. Postmarketing reports have included cases of heart block and QT prolongation associated with the combined use of glycopyrrolate and a cholinesterase inhibitor; causality and incidence rates are not known. The effect of inhaled glycopyrrolate was evaluated in a Phase 1 randomized placebo and positive controlled double-blind, single-dose, crossover through QTc study in 73 healthy subjects. At the dose 16-fold the therapeutic daily dose, inhaled glycopyrrolate did not prolong QTc to any clinically relevant extent. In clinical trials, hypertension was reported in 2% or more of patients receiving glycopyrrolate nebulizer solution.

dysuria, urinary retention

In clinical trials during chronic use of systemic glycopyrrolate, urinary retention occurred in 15% of patients or less, and is due to anticholinergic activity; systemic glycopyrrolate should be avoided in patients with known urinary tract obstruction (e.g., bladder-neck obstruction). Urinary tract infections (1.4% vs. 1.3% placebo) and dysuria (less than 1%) were reported during clinical trials with glycopyrrolate inhaler; urinary retention is possible with inhaled use. In clinical trials, urinary tract infection was reported in 2% or more of patients receiving glycopyrrolate nebulizer solution. Prescribers and patients should be alert for signs and symptoms of urinary retention (e.g., difficulty passing urine, painful urination or dysuria), especially in male patients with prostatic hypertrophy or other risk for urinary obstruction.

blurred vision, cycloplegia, mydriasis, ocular hypertension, photophobia

The majority of the adverse effects associated with glycopyrrolate therapy are usually related to the pharmacological actions common to all anticholinergic agents. Ocular anticholinergic effects include blurred vision, and patients should use care when driving or operating machinery until drug effects are known. Also, dilatation of the pupil (mydriasis), cycloplegia, and ocular hypertension or aggravation of closed-angle glaucoma can occur. Patients should use care to avoid inadvertent ocular exposure to glycopyrrolate inhalational powder. Prescribers and patients should be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival

congestion and corneal edema). Instruct patients to consult a physician immediately should any of these signs or symptoms develop. Patients should use care to avoid inadvertent ocular exposure to glycopyrrolate inhalational powder. Patients may experience photophobia; advise patients to protect their eyes from light.

back pain, cough, dyspnea, edema, hyperglycemia, infection, nasal congestion, nasal dryness, peripheral edema, pharyngitis, sinusitis, wheezing

Upper respiratory infection and sinusitis have been reported as common side effects during chronic use of systemic glycopyrrolate; an increased viscosity (thickening) of bronchial secretions, nasal congestion, and nasal dryness have been reported as infrequent (less than 2%). Respiratory depression and throat irritation have also been reported during postmarketing use with glycopyrrolate or other anticholinergic drugs. The most common respiratory adverse reactions during clinical trials with glycopyrrolate inhaler, and occurring at an incidence higher than placebo, were upper respiratory tract infection (3.4%), sinusitis (1.4%), oropharyngeal pain or pharyngitis (1.8% to 2.1%), and productive cough (less than 1%). Additionally, pain in extremity (less than 1%) and diabetes mellitus and/or hyperglycemia (1%) were also reported with use of the glycopyrrolate inhaler. In clinical trials with glycopyrrolate nebulizer solution, the following adverse events were reported in 1% or more, but less than 2% of patients: wheezing, upper respiratory tract infection, peripheral edema, and nasopharyngitis. In clinical trials with glycopyrrolate nebulizer solution, the following adverse events were reported in 2% of patients or more: bronchitis, nasopharyngitis, pneumonia, sinusitis, upper respiratory tract infection, cough, dyspnea, edema, back pain, and oropharyngeal pain. Dyspnea was reported in 2% to 4.9% of patients receiving glycopyrrolate nebulizer solution.

Description

Glycopyrrolate is an antimuscarinic anticholinergic agent. Parenterally, glycopyrrolate is used as a preanesthetic and intraoperative antimuscarinic agent, where it helps block cardiac vagal inhibitory reflexes and helps reduce excessive salivary, tracheobronchial, and pharyngeal secretions. Since glycopyrrolate is a quaternary (i.e., charged) compound, it is less likely to penetrate the CNS and cause CNS side effects when compared to atropine or scopolamine. Historically, oral and parenteral glycopyrrolate products are indicated in the adjunctive treatment of symptoms due to peptic ulcers; however, due to the availability of more effective alternatives for healing and treatment, antimuscarinics have limited utility for this purpose. Oral products are commonly used to reduce severe chronic drooling (sialorrhea) in patients 3 years and older with certain neurologic conditions. Glycopyrrolate inhalation powder and nebulizer solution are

beneficial for the long-term maintenance treatment of airflow obstruction in adults with chronic obstructive pulmonary disease (COPD). According to guidelines, inhaled long-acting antimuscarinic agents (LAMAs), like glycopyrrolate, may be used as initial monotherapy in COPD patients in group A. A long-acting bronchodilator is the preferred choice except in patients with very occasional breathlessness. In patients with stable disease, LAMAs have a greater effect on exacerbation reduction compared to long-acting beta-agonists (LABAs) and decrease hospitalizations. In patients in Group B and Group E, LAMAs are used as initial therapy in combination with LABAs. At follow-up, if the patient is still experiencing dyspnea, consider switching inhaler device, implement or escalate non-pharmacologic treatment(s), and investigate for other causes of dyspnea. If the patient has exacerbations, consider triple therapy with a LAMA, a LABA, and an inhaled corticosteroid (ICS).

Mechanism Of Action

Antimuscarinic anticholinergic agents inhibit the action of acetylcholine at autonomic effectors innervated by postganglionic cholinergic nerves and on smooth muscles that respond to acetylcholine, but lack cholinergic innervation. The peripheral cholinergic receptors are present in the autonomic effector cells of smooth muscle, cardiac muscle, the sinoatrial node, the atrioventricular node, exocrine glands, and to a lesser degree, in the autonomic ganglia. Therefore, parenteral glycopyrrolate diminishes the volume and free acidity of gastric secretions and controls excessive pharyngeal, tracheal, and bronchial secretions.

Clinically, parenteral glycopyrrolate is used mostly prior to general anesthesia to reduce GI and pulmonary secretions and lessen the chance of acid aspiration during surgery. Glycopyrrolate has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airway, inhalational glycopyrrolate exhibits pharmacological effects through inhibition of M3 receptor at the smooth muscle leading to bronchodilation. Oral glycopyrrolate inhibits the action of acetylcholine on salivary glands thereby reducing the extent of salivation.

Glycopyrrolate has a polar quaternary ammonium group that reduces its ability to cross membranes such as the blood-brain barrier. This group differentiates the drug from other anticholinergic agents, such as scopolamine hydrobromide and atropine sulfate, which are nonpolar amines and readily cross the blood-brain barrier.

Pharmacokinetics

Glycopyrrolate is administered orally, via oral respiratory inhalation, or parenterally by intramuscular or intravenous routes. The drug distributes rapidly, but the exact metabolic fate of a dose is unknown. Mean volume of distribution is estimated to be 0.42 + 0.22 L/kg. Glycopyrrolate is primarily renally eliminated. In both urine and bile, greater than 80% of a radiolabeled dose corresponds to unchanged parent drug, suggesting that only a small proportion of the dose is excreted as 1 or more metabolites.

Affected Cytochrome P450 (CYP450) isoenzymes and drug transporters: None

Route-Specific Pharmacokinetics

- **Oral Route**

Glycopyrrolate is not well absorbed after oral administration.
Oral tablet: In a study of pediatric patients (7 to 14 years) receiving either intravenous or the oral tablet formulation of glycopyrrolate, the mean absolute bioavailability of the tablet formulation was approximately 3% (range 1.3% to 13.3%); similar bioavailability is seen in adults.
Orally disintegrating tablet (ODT): After administration of 1.7 mg ODT, the Cmax and AUC of glycopyrrolate were comparable to an oral 2 mg glycopyrrolate tablet. When the ODT was placed in the mouth and immediately swallowed with 240 mL water, the mean Cmax and AUC of glycopyrrolate decreased by 24% and 20%, respectively, compared to administration without water. In healthy adults, a high-fat, high-calorie meal (939 calories, 60% fat) significantly reduced the absorption of glycopyrrolate following administration of 1.7 mg ODT. The mean Cmax and AUC were approximately 83% and 77% lower, respectively, than those observed under fasted conditions.
Oral solution: When compared to the oral tablet, the Cmax and AUC of glycopyrrolate oral solution in fasting patients is 23% and 28% (respectively) lower than the oral tablet. The mean time to maximum plasma concentration (mean Tmax) for the oral solution is 3.1 hours. The mean plasma half-life is 3 hours. Administering the oral solution with a high fat meal significantly lowers Cmax and AUC by 74% and 78% respectively, compared to administration while fasting.

- **Intravenous Route**

The onset of action is within 1 minute following intravenous (IV) administration. Anticholinergic effects last up to 7 hours after parenteral administration, and vagal inhibition lasts 2 to 3 hours. The mean clearance and half-life values were reported to be 0.54 + 0.14 L/kg/hour and 0.83 + 0.13 hour, respectively post IV administration. After IV administration of a 0.2 mg radiolabeled glycopyrrolate, 85% of dose was recovered in urine 48 hours postdose and some of radioactivity was also recovered in bile.

- **Intramuscular Route**

The onset of action is 15 to 30 minutes following intramuscular (IM) injection. Anticholinergic effects last up to 7 hours after parenteral administration, and vagal inhibition lasts 2 to 3 hours. After IM administration of glycopyrrolate to adults, the mean half-life value is reported to be 0.55 to 1.25 hours. Over 80% of IM dose administered was recovered in urine and the bile as unchanged drug and 50% of the IM dose is excreted within 3 hours.

- **Inhalation Route**

Glycopyrrolate oral inhalation powder (i.e., Seebri Neohaler): Linear pharmacokinetics of glycopyrrolate were observed following inhalation of 31.2 mcg to 249.6 mcg per day via oral inhalation powder administration. Following oral inhalation, glycopyrrolate is rapidly absorbed and reaches peak plasma concentrations at 5 minutes post dose. The absolute bioavailability of inhaled glycopyrrolate is estimated to be about 40%; about 90% of systemic exposure is due to lung absorption and 10% is due to gastrointestinal absorption. Glycopyrrolate steady-state is reached within 1 week of treatment and there is no indication that the pharmacokinetics change over time. Glucuronide and/or sulfate conjugates of glycopyrrolate are found in urine of humans after repeated inhalation, accounting for about 3% of the dose. Following inhalation of single and repeated once-daily doses between 62.4 mcg and 249.6 mcg glycopyrrolate by healthy volunteers and patients with COPD, mean renal clearance of glycopyrrolate is in the range of 17.4 L/hour and 24.4 L/hour indicating active tubular secretion contributes to the renal elimination of glycopyrrolate. Glycopyrrolate plasma concentrations decline in a multi-phasic manner. The mean terminal elimination t1/2 is much longer after inhalation (33 to 53 hours) than after intravenous (6.2 hours) and oral (2.8 hours) administration. Glycopyrrolate oral inhalation solution (i.e., Lonhala Magnair): Following oral inhalation, glycopyrrolate was rapidly absorbed and reached peak plasma levels less than 20 minutes post dose. The steady-state plasma levels of glycopyrrolate were reached within 1 week of the start of treatment. A twice daily dose regimen leads to approximately 2 to 3 fold accumulation of systemic glycopyrrolate exposure at steady-state. The in vitro human plasma protein binding of glycopyrrolate was 38% to 41% at concentrations of 1 to 10 ng/mL. In vitro metabolism studies show glycopyrrolate hydroxylation resulting in a variety of mono- and bishydroxylated metabolites and direct hydrolysis resulting in the formation of a carboxylic acid derivative (M9). Further in vitro investigations showed that multiple CYP isoenzymes contribute to the oxidative biotransformation of glycopyrrolate and the hydrolysis to M9 is likely to be catalyzed by members from the cholinesterase family pre-systemically and/or via first pass metabolism from the swallowed dose fraction of orally inhaled glycopyrrolate.

- **Hepatic Impairment**

Glycopyrrolate pharmacokinetic data in patients with hepatic impairment are not available.

- **Renal Impairment**

The elimination of glycopyrrolate is impaired in patients with severe renal impairment (estimated GFR 30 mL/minute/1.73 m2 or greater) or in end-stage renal disease patients on dialysis. Approximately 85% of a systemically-absorbed glycopyrrolate dose is excreted in the urine as the parent drug. Glycopyrrolate was administered IV in uremic patients undergoing renal transplantation. The mean elimination half-life was significantly longer (46.8 minutes) than in patients with normal renal function (18.6 minutes). The mean AUC (10.6 hour x mcg/L), mean plasma clearance (0.43 L/hour/kg), and mean 3-hour urine excretion (0.7%) for glycopyrrolate were also significantly different than those of controls.

- **Pediatrics**

After IV administration (5 mcg/kg glycopyrrolate) to infants and children, the mean half-life values of glycopyrrolate were reported to be 22 to 130 minutes and 19 to 99 minutes, respectively.

- **Geriatric**

Glycopyrrolate pharmacokinetics have not been established in the elderly.

- **Gender Differences**

Pharmacokinetic evaluation of adults and children administered glycopyrrolate parenteral, oral products, or inhalational powder identified no effect of gender on glycopyrrolate clearance or systemic exposure.

- **Ethnic Differences**

The pharmacokinetics of glycopyrrolate do not appear to be influenced by ethnicity. Changes in pharmacokinetic parameters of oral glycopyrrolate by race have not been established. There is no evidence of a clinically significant ethnic/race effect (across Caucasian, Chinese, Hispanic/Latino, Japanese subjects) after oral inhalation of the glycopyrrolate powder.

- **Other**

Smoking

Smoking status and baseline FEV1 have no apparent effect on maximal or average glycopyrrolate systemic exposure after oral inhalation of the glycopyrrolate powder.

Administration

For storage information, see the specific product information within the How Supplied section.

Oral Administration

Oral Solid Formulations

Oral tablet
Administer on an empty stomach, 1 hour before or 2 hours after meals to maximize absorption.
Do not administer within 1 hour of antacids or antidiarrheal medications.

Orally disintegrating tablet (e.g., Dartisla ODT)
Administer at least 1 hour before or 2 hours after food.
Use dry hands when opening the blister card and do not open the blister until ready to administer.
Open the package and peel back the foil on the blister to expose the tablet and gently remove from the blister. Do not push the tablet through the foil.
Do not break or cut the tablet.
Immediately place the tablet on the tongue, allow it to disintegrate, and swallow without water.

Oral Liquid Formulations

Oral solution (e.g., Cuvposa)
Administer at least 1 hour before or 2 hours after meals.
To ensure accurate dosage, measure the dose using a calibrated oral dosing device.

Injectable Administration

Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.

Intravenous Administration

Direct IV Injection
May be given IV with or without dilution with a compatible fluid.
Inject via Y-site or through a 3-way stopcock at a rate of 0.2 mg over 1 to 2 minutes.
Glycopyrrolate injection may be administered via the tubing of a running infusion of Sodium Chloride 0.9% injection.
Compatible with Dextrose 5% and 10% in Water injection or with Dextrose 5% with Sodium Chloride 0.9% injection, Dextrose 5% with Sodium Chloride 0.45% injection, Sodium Chloride 0.9% injection, and Ringer's injection.
Not compatible with Lactated Ringer's injection. There are many other incompatibilities; screen for compatibility before injection with other fluids or medications. The stability of glycopyrrolate injection is questionable above a pH of 6.0.

Single-dose, Prefilled Syringe
Push plunger rod slightly in to break the stopper loose while tip cap is still on. Do not remove the tamper evident seal.

Remove tip cap and tamper evident seal by twisting off. Discard the tip cap.
Expel air bubble and adjust dose into sterile material (if applicable).
Connect the syringe to an appropriate IV connection. Ensure that the syringe is securely attached to the needle or needless luer access device (NLAD) before injecting. Do not introduce any other fluid into the syringe at any time.
Depress plunger rod to deliver medication. Ensure that pressure is maintained on the plunger rod during the entire administration.
Remove syringe from NLAD (if applicable) and discard into appropriate receptacle. Do not recap needle when needle is connected to syringe.
Discard unused portions.

Intramuscular Administration

No dilution necessary.
Inject into a large muscle mass.

Maximum Dosage Limits

- **Adults**
  0.004 mg/kg IM preanesthesia; 0.2 mg/dose IV; 8 mg/day PO for oral tablets and 6.8 mg/day PO for orally disintegrating tablets; 2 capsules/day (total of 31.2 mcg) via oral inhalation (Seebri Neohaler) or 2 vials/day (total of 50 mcg) via oral inhalation (Longhala Magnair).
- **Geriatric**
  0.004 mg/kg IM preanesthesia; 0.2 mg/dose IV; 8 mg/day PO for oral tablets and 6.8 mg/day PO for orally disintegrating tablets; 2 capsules/day (total of 31.2 mcg) via oral inhalation (Seebri Neohaler) or 2 vials/day (total of 50 mcg) via oral inhalation (Longhala Magnair).
- **Adolescents**
  17 years and older: Safety and efficacy of inhaled glycopyrrolate not established; maximum dosage is dependent on indication for parenteral therapy; 8 mg/day PO for oral tablets.
  16 years: Safety and efficacy of inhaled glycopyrrolate not established; maximum dosage is dependent on indication for parenteral therapy; 0.1 mg/kg/dose PO 3 times daily, not to exceed 1.5 to 3 mg/dose PO (depending on weight) for oral solution or 8 mg/day PO for oral tablets.
  13 to 15 years: Safety and efficacy of parenteral and inhaled glycopyrrolate have not been established; 0.1 mg/kg/dose PO 3 times daily, not to exceed 1.5 to 3 mg/dose PO (depending on weight) for oral solution or 8 mg/day PO for oral tablets.

- **Children**
  12 years: Safety and efficacy of parenteral and inhaled glycopyrrolate have not been established; 0.1 mg/kg/dose PO 3 times daily, not to exceed 1.5 to 3 mg/dose PO (depending on weight) for oral solution or 8 mg/day PO for oral tablets.
  3 to 11 years: Safety and efficacy of parenteral and inhaled glycopyrrolate have not been established; 0.1 mg/kg/dose PO 3 times daily, not to exceed 1.5 to 3 mg/dose PO (depending on weight) for oral solution.
  Less than 3 years: Safety and efficacy have not been established.
- **Infants**
  Safety and efficacy have not been established.
- **Neonates**
  Safety and efficacy have not been established.

Dosage Forms

- Bevespi Aerosphere 9mcg-4.8mcg/actuation Inhalation Aerosol
- Cuvposa 1mg/5ml Solution
- Dartisla ODT 1.7mg Orally Disintegrating Tablet
- Glycate 1.5mg Tablet
- Glycopyrrolate 0.2mg/1mL Solution for injection
- Glycopyrrolate 1.5mg Oral tablet
- Glycopyrrolate 1mg Oral tablet
- Glycopyrrolate 1mg/5mL Oral solution
- Glycopyrrolate 2mg Oral tablet
- Glycopyrrolate Bulk powder
- GLYRX-PF 0.2mg/mL Solution for Injection
- GLYRX-PF 0.4mg/2mL Solution for Injection
- GLYRX-PF 0.6mg/3mL Solution for Injection
- GLYRX-PF 1mg/5mL Solution for Injection
- Robinul 1mg Tablet
- Robinul Forte 2mg Tablet

Dosage Adjustment Guidelines

Hepatic Impairment

Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

Renal Impairment

Mild to moderate renal impairment (estimated GFR 30 mL/minute/1.73 m2 or more): No dosage adjustments are required.
Severe renal impairment (estimated GFR less than 30 mL/minute/1.73 m2) or end stage renal disease (ESRD) requiring dialysis: Dose adjustments may be needed for systemic therapy; however, no specific recommendations are available. Use parenteral glycopyrrolate with caution. Use inhaled glycopyrrolate only if the expected benefits outweigh the potential risks; systemic exposure to glycopyrrolate may be increased in this population.