HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GLYCOPYRROLATE INJECTION safely and effectively. See full prescribing information for GLYCOPYRROLATE INJECTION.

GLYCOPYRROLATE injection, for intramuscular or intravenous use
Initial U.S. Approval: 2022

INDICATIONS AND USAGE

- ***In Anesthesia:*** Glycopyrrolate Injection, USP is indicated for use as a preoperative antimuscarinic to reduce salivary, tracheobronchial, and pharyngeal secretions; to reduce the volume and free acidity of gastric secretions; and to block cardiac vagal inhibitory reflexes during induction of anesthesia and intubation. When indicated, Glycopyrrolate Injection, USP may be used intraoperatively to counteract surgically or drug- induced or vagal reflexes associated arrhythmias. Glycopyrrolate protects against the peripheral muscarinic effects (e.g., bradycardia and excessive secretions) of cholinergic agents such as neostigmine and pyridostigmine given to reverse the neuromuscular blockade due to non-depolarizing muscle relaxants. (1)
- ***In Peptic Ulcer:*** For use in adults as adjunctive therapy for the treatment of peptic ulcer when rapid anticholinergic effect is desired or when oral medication is not tolerated. (1)

DOSAGE AND ADMINISTRATION

- Glycopyrrolate injection may be administered intramuscularly, or intravenously, without dilution, in Adults and Pediatric Patients.
- Do not use this prefilled syringe to administer a dose of less than 0.1 mg (0.5 mL). (2)

DOSAGE FORMS AND STRENGTHS

- Glycopyrrolate Injection, USP is available in 0.6 mg/3 mL (0.2 mg/mL) prefilled disposable syringes. (3)

CONTRAINDICATIONS

- Known hypersensitivity to glycopyrrolate or any of its inactive ingredients. (4)
- In addition, in the management of *peptic ulcer* patients, because of the longer duration of therapy, glycopyrrolate injection may be contraindicated in patients with the following concurrent conditions: glaucoma; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis, etc.); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. (4)

WARNINGS AND PRECAUTIONS

- This drug should be used with great caution, if at all, in patients with glaucoma. (5)
- Investigate any tachycardia before giving glycopyrrolate injection since an increase in the heart rate may occur. (5)
- Use with caution in patients with: coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension; hyperthyroidism. (5)
- Use with caution in patients with renal disease since the renal elimination of glycopyrrolate may be severely impaired in patients with renal failure. Dosage adjustments may be necessary. (5, 12.3)
- Use glycopyrrolate with caution in the elderly and in all patients with autonomic neuropathy, hepatic disease, ulcerative colitis, prostic hypertrophy, or hiatal hernia, since anticholinergic drugs may aggravate these conditions. (5)
- The use of anticholinergetic drugs in the treatment of gastric ulcer may produce a delay in gastric emptying due to antral statis. (5)

ADVERSE REACTIONS

- Anticholinergics, including glycopyrrolate injection, can produce certain effects, most of which are extensions of their pharmacologic actions. Adverse reactions may include xerostomia (dry mouth); urinary hesitancy and retention; blurred vision and photophobia due to mydriasis (dilation of the pupil); cycloplegia; increased ocular tension; tachycardia; palpitation; decreased sweating; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reactions including anaphylactic/anaphylactoid reactions; hypersensitivity; urticaria, pruritus, dry skin, and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons. (6)
- In addition, the following adverse events have been reported from post-marketing experience with glycopyrrolate: malignant hyperthermia; cardiac arrhythmias (including bradycardia, ventricular tachycardia, ventricular fibrillation); cardiac arrest; hypertension; hypotension; seizures; and respiratory arrest. Post-marketing reports have included cases of heart block and QTc interval prolongation associated with the combined use of glycopyrrolate and an anticholinesterase. Injection site reactions including pruritus, edema, erythema, and pain have also been reported. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- The concurrent use of glycopyrrolate injection with other anticholinergics or medications with anticholinergic activity, such as phenothiazines, antiparkinson drugs, or tricyclic antidepressants, may intensify the antimuscarinic effects and may result in an increase in anticholinergic side effects. (7)
- Concomitant administration of glycopyrrolate injection and potassium chloride in a wax matrix may increase the severity of potassium chloride-induced gastrointestinal lesions as a result of a slower gastrointestinal transit time. (7)

USE IN SPECIFIC POPULATIONS

- Pediatric Use: Infants, patients with Down's Syndrome, and pediatric patients with spastic paralysis or brain damage may experience an increased response to anticholinergics, thus increasing the potential for side effects. Large doses may cause hyperexcitability. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 1/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

In Anesthesia

Glycopyrrolate Injection, USP is indicated for use as a preoperative antimuscarinic to reduce salivary, tracheobronchial, and pharyngeal secretions; to reduce the volume and free acidity of gastric secretions; and to block cardiac vagal inhibitory reflexes during induction of anesthesia and intubation. When indicated, Glycopyrrolate Injection, USP may be used intraoperatively to counteract surgically or drug- induced or vagal reflexes associated arrhythmias. Glycopyrrolate protects against the peripheral muscarinic effects (e.g., bradycardia and excessive secretions) of cholinergic agents such as neostigmine and pyridostigmine given to reverse the neuromuscular blockade due to non-depolarizing muscle relaxants.

In Peptic Ulcer

For use in adults as adjunctive therapy for the treatment of peptic ulcer when rapid anticholinergic effect is desired or when oral medication is not tolerated.

2 DOSAGE AND ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Glycopyrrolate injection may be administered intramuscularly, or intravenously, without dilution, in the following indications.

Adults

Preanesthetic Medication

The recommended dose of glycopyrrolate injection is 0.004 mg/kg by intramuscular injection, given 30 to 60 minutes prior to the anticipated time of induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered.

Do not use this prefilled syringe to administer a dose of less than 0.1 mg (0.5 mL).

Intraoperative Medication

Glycopyrrolate injection may be used during surgery to counteract drug-induced or vagal reflexes and their associated arrhythmias (e.g., bradycardia). It should be administered intravenously as single doses of 0.1 mg and repeated, as needed, at intervals of 2 to 3 minutes. The usual attempts should be made to determine the etiology of the arrhythmia, and the surgical or anesthetic manipulations necessary to correct parasympathetic imbalance should be performed.

Reversal of Neuromuscular Blockade

The recommended dose of glycopyrrolate injection is 0.2 mg for each 1.0 mg of neostigmine or 5.0 mg of pyridostigmine.

Peptic Ulcer

The usual recommended dose of glycopyrrolate injection is 0.1 mg administered at 4-hour intervals, 3 or 4 times daily intravenously or intramuscularly. Where more profound effect is required, 0.2 mg may be given. Some patients may need only a single dose, and frequency of administration should be dictated by patient response up to a maximum of four times daily.

Glycopyrrolate injection is not recommended for the treatment of peptic ulcer in pediatric patients [see *Pediatric Use (8.4)*]

Pediatric Patients

[see *Pediatric Use (8.4)*]

Preanesthetic Medication

The recommended dose of glycopyrrolate injection in pediatric patients is 0.004 mg/kg intramuscularly, given 30 to 60 minutes prior to the anticipated time of induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered.

Do not use this prefilled syringe to administer a dose of less than 0.1 mg (0.5 mL).

Infants

1 month to 2 years of age may require up to 0.009 mg/kg.

Intraoperative Medication

Because of the long duration of action of glycopyrrolate injection if used as preanesthetic medication, additional glycopyrrolate injection for anticholinergic effect intraoperatively is rarely needed; in the event it is required the recommended pediatric dose is 0.004 mg/kg intravenously, not to exceed 0.1 mg in a single dose which may be repeated, as needed, at intervals of 2 to 3 minutes. The usual attempts should be made to determine the etiology of the arrhythmia, and the surgical or anesthetic manipulations necessary to correct parasympathetic imbalance should be performed.

Do not use this prefilled syringe to administer a dose of less than 0.1 mg (0.5 mL).

Reversal of Neuromuscular Blockade

The recommended pediatric dose of glycopyrrolate injection is 0.2 mg for each 1.0 mg of neostigmine or 5.0 mg of pyridostigmine.

Peptic Ulcer

Glycopyrrolate injection is not recommended for the treatment of peptic ulcer in pediatric patients [see *Pediatric Use (8.4)*].

Diluent Incompatibilities

Lactated Ringer's solution.

Admixture Compatibilities

Physical Compatibility

This list does not constitute an endorsement of the clinical utility or safety of co-administration of glycopyrrolate with these drugs. Glycopyrrolate injection is compatible for mixing and injection with the following injectable dosage forms: atropine sulfate, USP; Antilirium® (physostigmine salicylate); Benadryl® (diphenhydramine HCl); codeine phosphate, USP; Emete-Con® (benz-quinamide HCl); hydromorphone HCl, USP; Inapsine® (droperidol); Levo-Dromoran® (levorphanol tartrate); lidocaine, USP; meperidine HCl, USP; Mestinon®/Regonol® (pyridostigmine bromide); morphine sulfate, USP; Nubain® (nalbuphine HCl); Numorphan® (oxymorphone HCl); procaine HCl, USP; promethazine HCl, USP; Prostigmin® (neostigmine methylsulfate, USP); scopolamine HBr, USP; Stadol® (butorphanol tartrate); Sublimaze® (fentanyl citrate); Tigan® (trimethobenzamide HCl); and Vistaril® (hydroxyzine HCl). Glycopyrrolate injection may be administered via the tubing of a running infusion of normal saline.

Admixture Incompatibilities

Physical Incompatibility

Since the stability of glycopyrrolate is questionable above a pH of 6.0 do not combine glycopyrrolate injection in the same syringe with Brevital® (methohexital Na); Chloromycetin® (chloramphenicol Na succinate); Dramamine® (dimenhydrinate); Nembutal® (pentobarbital Na); Pentothal® (thiopental Na); Seconal® (secobarbital Na); Solu-Cortef® (hydrocortisone sodium succinate); Valium® (diazepam); Decadron® (dexamethasone Na phosphate); or Talwin® (pentazocine lactate). These mixtures will result in a pH higher than 6.0 and may result in gas production or precipitation.

3 DOSAGE FORMS AND STRENGTHS

Glycopyrrolate Injection, USP is available in 0.6 mg/3 mL (0.2 mg/mL) prefilled disposable syringes.

4 CONTRAINDICATIONS

Known hypersensitivity to glycopyrrolate or any of its inactive ingredients.

In addition, in the management of *peptic ulcer* patients, because of the longer duration of therapy, glycopyrrolate injection may be contraindicated in patients with the following concurrent conditions: glaucoma; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis, etc.); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis.

5 WARNINGS AND PRECAUTIONS

This drug should be used with great caution, if at all, in patients with glaucoma.

Glycopyrrolate injection may produce drowsiness or blurred vision. The patient should be cautioned regarding activities requiring mental alertness such as operating a motor vehicle or other machinery or performing hazardous work while taking this drug.

In addition, in the presence of fever, high environmental temperature and/or during physical exercise, heat prostration can occur with use of anticholinergic agents including glycopyrrolate (due to decreased sweating), particularly in children and the elderly.

Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with glycopyrrolate injection would be inappropriate and possibly harmful.

General

Investigate any tachycardia before giving glycopyrrolate injection since an increase in the heart rate may occur.

Use with caution in patients with: coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension; hyperthyroidism.

Use with caution in patients with renal disease since the renal elimination of glycopyrrolate may be severely impaired in patients with renal failure. Dosage adjustments may be necessary [see *Pharmacokinetics (12.3)*]

Use glycopyrrolate with caution in the elderly and in all patients with autonomic neuropathy, hepatic disease, ulcerative colitis, prostic hypertrophy, or hiatal hernia, since anticholinergic drugs may aggravate these conditions.

The use of anticholinergetic drugs in the treatment of gastric ulcer may produce a delay in gastric emptying due to antral statis.

6 ADVERSE REACTIONS

Anticholinergics, including glycopyrrolate injection, can produce certain effects, most of which are extensions of their pharmacologic actions. Adverse reactions may include xerostomia (dry mouth); urinary hesitancy and retention; blurred vision and photophobia due to mydriasis (dilation of the pupil); cycloplegia; increased ocular tension; tachycardia; palpitation; decreased sweating; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reactions including anaphylactic/anaphylactoid reactions; hypersensitivity; urticaria, pruritus, dry skin, and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons.

In addition, the following adverse events have been reported from post-marketing experience with glycopyrrolate: malignant hyperthermia; cardiac arrhythmias (including bradycardia, ventricular tachycardia, ventricular fibrillation); cardiac arrest; hypertension; hypotension; seizures; and respiratory arrest. Post-marketing reports have included cases of heart block and QTc interval prolongation associated with the combined use of glycopyrrolate and an anticholinesterase. Injection site reactions including pruritus, edema, erythema, and pain have also been reported.

Glycopyrrolate is chemically a quaternary ammonium compound; hence, its passage across lipid membranes, such as the blood-brain barrier is limited in contrast to atropine sulfate and scopolamine hydrobromide. For this reason the occurrence of CNS-related side effects is lower, in comparison to their incidence following administration of anticholinergics which are chemically tertiary amines that can cross this barrier readily.

7 DRUG INTERACTIONS

The concurrent use of glycopyrrolate injection with other anticholinergics or medications with anticholinergic activity, such as phenothiazines, antiparkinson drugs, or tricyclic antidepressants, may intensify the antimuscarinic effects and may result in an increase in anticholinergic side effects.

Concomitant administration of glycopyrrolate injection and potassium chloride in a wax matrix may increase the severity of potassium chloride-induced gastrointestinal lesions as a result of a slower gastrointestinal transit time.

8 USE IN SPECIFIC POPULATIONS

Gender

Gender differences in pharmacokinetics of glycopyrrolate have not been investigated.

Renal Impairment

In one study glycopyrrolate was administered IV in uremic patients undergoing renal transplantation. The mean elimination half-life was significantly longer (46.8 minutes) than in healthy patients (18.6 minutes). The mean area-under-the-concentration-time curve (10.6 hr· mcg /L), mean plasma clearance (0.43 L/hr/kg), and mean 3-hour urine excretion (0.7%) for glycopyrrolate were also significantly different than those of controls (3.73 hr·mcg/L, 1.14 L/hr/kg, and 50%, respectively). These results suggest that the elimination of glycopyrrolate is severely impaired in patients with renal failure.

Hepatic Impairment

Pharmacokinetic information in patients with hepatic impairment is unavailable.

8.1 Pregnancy

Risk summary

Limited data available with glycopyrrolate use during pregnancy have not identified a drug-associated risk of birth defects and miscarriage, however, most of the reported exposures occurred after the first trimester. Most of the available data are based on studies with exposures that occurred at the time of Cesarean-section delivery, and these studies have not identified an adverse effect on maternal outcomes or infant Apgar.

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/m^2 basis), respectively.

The estimated background risk for major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in the clinically recognized pregnancies is 2-4% and 15–20%, respectively.

Data

Human Data

Published, randomized, controlled trials over several decades, which compared the use of glycopyrrolate to another antimuscarinic agent in pregnant women during Cesarean section, have not identified adverse maternal or infant outcomes. In normal doses (0.004 mg/kg), glycopyrrolate 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.

There are no studies on the safety of glycopyrrolate exposure during the period of organogenesis, and therefore, it is not possible to draw any conclusions on the risk of birth defects following exposure to glycopyrrolate during pregnancy. In addition, there are no data on the risk of miscarriage following fetal exposure to glycopyrrolate.

Animal Data

Reproduction studies with glycopyrrolate were performed in rats at a dietary dose of approximately 65 mg/kg/day (exposure was approximately 640 times the maximum recommended daily human dose of 1 mg on a mg/m^2 basis) and rabbits at intramuscular doses of up to 0.5 mg/kg/day (exposure was approximately 10 times the maximum recommended daily human dose on a mg/m^2 basis). These studies produced no teratogenic effects to the fetus. A preclinical study on reproductive performance of rats given glycopyrrolate resulted in a decreased rate of conception and survival at weaning.

8.2 Lactation

Risk summary

There are no data on the presence of glycopyrrolate in either human milk or animal milk, the effects on the breastfed infant, or the effects on milk production. As with other anticholinergics, glycopyrrolate may cause suppression of lactation. The developmental and health benefits of breast feeding should be considered along with the mother's clinical need for Glycopyrrolate Injection and any potential adverse effects on the breastfed child from Glycopyrrolate Injection or from the underlying maternal condition.

8.4 Pediatric Use

Following IV administration (5 mcg/kg glycopyrrolate) to infants and children, the mean $t_{1/2}$ values were reported to be between 21.6 and 130.0 minutes and between 19.2 and 99.2 minutes, respectively.

Safety and effectiveness in pediatric patients have not been established for the management of peptic ulcer.

Dysrhythmias associated with the use of glycopyrrolate intravenously as a premedicant or during anesthesia have been observed in pediatric patients.

Infants, patients with Down's syndrome, and pediatric patients with spastic paralysis or brain damage may experience an increased response to anticholinergics, thus increasing the potential for side effects.

A paradoxical reaction characterized by hyperexcitability may occur in pediatric patients taking large doses of anticholinergics including glycopyrrolate injection. Infants and young children are especially susceptible to the toxic effects of anticholinergics.

8.5 Geriatric Use

Clinical Studies of glycopyrrolate injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other therapy.

10 OVERDOSAGE

To combat peripheral anticholinergic effects, a quaternary ammonium anticholinesterase such as neostigmine methylsulfate (which does not cross the blood-brain barrier) may be given intravenously in increments of 0.25 mg in adults. This dosage may be repeated every five to ten minutes until anticholinergic overactivity is reversed or up to a maximum of 2.5 mg. Proportionately smaller doses should be used in pediatric patients. Indication for repetitive doses of neostigmine should be based on close monitoring of the decrease in heart rate and the return of bowel sounds.

If CNS symptoms (e.g., excitement, restlessness, convulsions, psychotic behavior) occur, physostigmine (which does cross the blood–brain barrier) may be used. Physostigmine 0.5 to 2 mg should be slowly administered intravenously and repeated as necessary up to a total of 5 mg in adults. Proportionately smaller doses should be used in pediatric patients.

To combat hypotension, administer IV fluids and/or pressor agents along with supportive care.

Fever should be treated symptomatically.

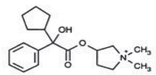
Following overdosage, a curare-like action may occur, i.e., neuromuscular blockade leading to muscular weakness and possible paralysis. In the event of a curare-like effect on respiratory muscles, artificial respiration should be instituted and maintained until effective respiratory action returns.

11 DESCRIPTION

Glycopyrrolate Injection, USP is a synthetic anticholinergic agent. Each 1 mL contains:
Glycopyrrolate, USP 0.2 mg, Water for Injection, USP q.s., pH adjusted, when necessary, with hydrochloric acid and/or sodium hydroxide. Solution does not contain preservatives.

Glycopyrrolate is a quaternary ammonium salt with the following chemical name:
3[(Cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethyl pyrrolidinium bromide.

Its structural formula is as follows:



$C_{19}H_{28}BrNO_3$ MW 398.33

Glycopyrrolate occurs as a white, odorless crystalline powder. It is soluble in water and alcohol, and practically insoluble in chloroform and ether.

Unlike atropine, glycopyrrolate is completely ionized at physiological pH values. Glycopyrrolate Injection, USP is a clear, colorless, sterile liquid; pH 2.0 to 3.0. The partition coefficient of glycopyrrolate in a *n*-octanol/water system is 0.304 ($\log_{10}$ P= -1.52) at ambient room temperature (24°C).

12 CLINICAL PHARMACOLOGY

Glycopyrrolate, like other anticholinergic (antimuscarinic) agents, inhibits the action of acetylcholine on structures innervated by postganglionic cholinergic nerves and on smooth muscles that respond to acetylcholine but lack cholinergic innervation. These 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 limited degree, in the autonomic ganglia. Thus, it diminishes the volume and free acidity of gastric secretions and controls excessive pharyngeal, tracheal, and bronchial secretions.

Glycopyrrolate antagonizes muscarinic symptoms (e.g., bronchorrhea, bronchospasm, bradycardia, and intestinal hypermotility) induced by cholinergic drugs such as the anticholinesterases.

The highly polar quaternary ammonium group of glycopyrrolate limits its passage across lipid membranes, such as the blood-brain barrier, in contrast to atropine sulfate and scopolamine hydrobromide, which are highly non-polar tertiary amines which penetrate lipid barriers easily.

With intravenous injection, the onset of action is generally evident within one minute. Following intramuscular administration, the onset of action is noted in 15 to 30 minutes, with peak effects occurring within approximately 30 to 45 minutes. The vagal blocking effects persist for 2 to 3 hours and the antisialagogue effects persist up to 7 hours, periods longer than for atropine.

12.3 Pharmacokinetics

The following pharmacokinetic information and conclusions were obtained from published studies that used nonspecific assay methods.

Distribution

The mean volume of distribution of glycopyrrolate was estimated to be 0.42 ± 0.22 L/kg.

Metabolism

The *in vivo* metabolism of glycopyrrolate in humans has not been studied.

Excretion

The mean clearance and mean $t_{1/2}$ values were reported to be 0.54 ± 0.14 L/kg/hr and 0.83 ± 0.13 hr, respectively post IV administration. After IV administration of a 0.2 mg radiolabeled glycopyrrolate, 85% of dose recovered was recovered in urine 48 hours postdose and some of the radioactivity was also recovered in bile. After IM administration of glycopyrrolate to adults, the mean $t_{1/2}$ value is reported to be between 0.55 to 1.25 hrs. Over 80% of IM dose administered was recovered in urine and the bile as unchanged drug and half the IM dose is excreted within 3 hrs. The following table summarizes the mean and standard deviation of pharmacokinetic parameters from a study.

Group	$t_{1/2}$ (hr)	V_z (L/kg)	CL (L/kg/hr)	T_{max} (min)	C_{max}(mcg /L)	AUC (mcg/L•hr)
(6 mcg/kg IV)	0.83 ± 0.27	0.42 ± 0.22	0.54 ± 0.14	-	-	8.64 ± 1.49*
(8 mcg/kg IM)	-	-	-	27.48 ± 6.12	3.47 ± 1.48	6.64 ± 2.33*

* 0 to 8 hr

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate carcinogenic potential. Studies to evaluate the mutagenic potential of glycopyrrolate have not been conducted. In reproduction studies in rats, dietary administration of glycopyrrolate resulted in diminished rates of conception in a dose-related manner. Other studies in dogs suggest that this may be due to diminished seminal secretion which is evident at high doses of glycopyrrolate.

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

Glycopyrrolate Injection, USP 0.2 mg per mL without preservative is available as:

Product Code	Unit of Sale	Strength	Each
720330	NDC 76045-023-30 Unit of 10	0.6 mg/3 mL (0.2 mg/mL)	NDC 76045-023-00 3 mL Pre-filled disposable syringe

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature.]

Sensitive to heat – Do not autoclave.

Do not place syringe on a sterile field.

17 PATIENT COUNSELING INFORMATION

Because glycopyrrolate injection may produce drowsiness or blurred vision, the patient should be cautioned not to engage in activities requiring mental alertness and/or visual acuity such as operating a motor vehicle or other machinery, or performing hazardous work while taking this drug [see *Warnings and Precautions (5)*].

The patient also should be cautioned about the use of this drug during exercise or hot weather since overheating may result in heat stroke.

The patient may experience a possible sensitivity of the eyes to light.

INSTRUCTIONS FOR USE:

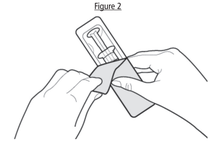
Figure 1: Outer Packaging and Prefilled Syringe

NOTES:

- Do not introduce any other fluid into the syringe at any time.
- Do not dilute for IV push.
- Do not re-sterilize the syringe.
- Do not use this product on a sterile field.
- This product is for single dose only.

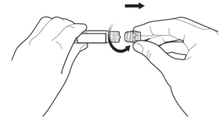
1. Inspect the outer packaging (blister pack) to confirm the integrity of the packaging. Do not use if the blister pack or the prefilled syringe has been damaged.
2. Remove the syringe from the outer packaging. (See Figure 2)

Figure 2



3. Visually inspect the syringe. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
4. Twist off the syringe tip cap. Do not remove the label around the luer lock collar. (See Figure 3)

Figure 3



5. Expel air bubble(s). Adjust the dose (if applicable).
6. Administer the dose ensuring that pressure is maintained on the plunger rod during the entire administration.
7. Discard the used syringe into an appropriate receptacle.

For more information concerning this drug, please call Fresenius Kabi USA, LLC at 1-800-551-7176.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

U.S. Patent 9,731,082 and 10,661,018

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