PREVDUO™ (neostigmine methylsulfate and glycopyrrolate) Injection

STANDARD DOSING RATIO,[1] SIMPLIFIED

When used for reversal of nondepolarizing neuromuscular blocking agents (NMBAs), the standard dose of glycopyrrolate injection is 0.2 mg for each 1.0 mg of neostigmine, as stated in the FDA-approved glycopyrrolate prescribing information.[2] PREVDUO™ delivers the standard dosing ratio of neostigmine methylsulfate and glycopyrrolate in one prefilled syringe.

In a survey of anesthesiologists[3]*:

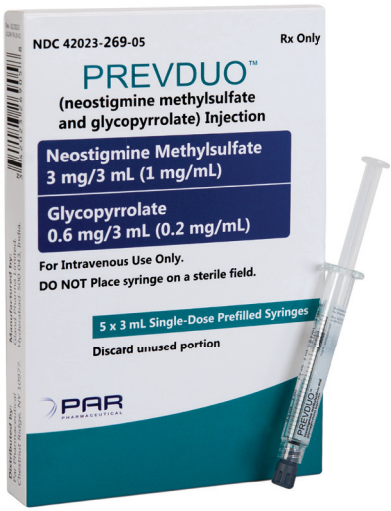
83% **The standard dosing ratio is used in 83% of NMBA reversal cases.†**

70% **Up to 70%‡ of anesthesiologists have reported combining neostigmine methylsulfate and glycopyrrolate into one syringe.**

*Results of an online survey from January 2023 completed by US anesthesiologists who have at least 5 anesthesiology reversal cases in an average week and who use neostigmine-glycopyrrolate in at least 15% of those cases (N=112).

†When anesthesiologists or certified registered nurse anesthetists (CRNAs) were asked what ratio is usually used to prepare neostigmine-glycopyrrolate in the operating room (N=112).

‡Among those who have received standard vials for both neostigmine and glycopyrrolate and were asked how they usually prepare the medication for administration, 49% of respondents reported usually using 1 syringe, 21% reported sometimes using 1 syringe, and 30% reported usually using 2 individual syringes (N=91).



PREVDUO™ combines the standard dosing ratio of neostigmine methylsulfate and glycopyrrolate in one prefilled syringe.

To learn more about PREVDUO™:

- **Contact your Par Pharmaceutical representative**
- **Visit PREVDUO.com**

CHOOSE THE FIRST AND ONLY FDA-APPROVED NEOSTIGMINE-GLYCOPYRROLATE PREFILLED SYRINGE AVAILABLE IN THE US[4]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

PREVDUO™ is contraindicated in patients with:

- known hypersensitivity to neostigmine methylsulfate (known hypersensitivity reactions have included urticaria, angioedema, erythema multiforme, generalized rash, facial swelling, peripheral edema, pyrexia, flushing, hypotension, bronchospasm, bradycardia and anaphylaxis) and glycopyrrolate or any inactive ingredients.

See additional Important Safety Information on next page.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS (continued)

PREVDUO™ is contraindicated in patients with:

- peritonitis or mechanical obstruction of the intestinal or urinary tract.
- 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.

WARNINGS AND PRECAUTIONS

Bradycardia: Neostigmine, a component of PREVDUO™, is associated with bradycardia. Consideration should be given to administration of glycopyrrolate prior to neostigmine (i.e., as separate products) in patients with bradycardia or in patients in whom bradycardia, a known risk of neostigmine methysulfate, may cause hemodynamic instability.

Serious Adverse Reactions in Patients with Certain Coexisting Conditions: PREVDUO™ should be used with caution in patients with coronary artery disease, congestive heart failure, cardiac arrhythmias, recent acute coronary syndrome, hypertension, myasthenia gravis and hyperthyroidism. Because of the known pharmacology of neostigmine methylsulfate as an acetylcholinesterase inhibitor, cardiovascular effects such as bradycardia, hypotension or dysrhythmia would be anticipated. In patients with acute cardiovascular conditions such as coronary artery disease, cardiac arrhythmias or recent acute coronary syndrome, the risk of blood pressure and heart rate complications may be increased. Risk of these complications may also be increased in patients with myasthenia gravis.

Hypersensitivity: Because of the possibility of hypersensitivity, medications to treat anaphylaxis should be readily available.

Neuromuscular Dysfunction: Large doses of PREVDUO™ administered when neuromuscular blockade is minimal can produce neuromuscular dysfunction. The dose of PREVDUO™ should be reduced if recovery from neuromuscular blockade is nearly complete.

Cholinergic Crisis: It is important to differentiate between myasthenic crisis and cholinergic crisis caused by overdosage of neostigmine. Both conditions result in extreme muscle weakness but require radically different treatment.

Precipitation of Acute Glaucoma: Glycopyrrolate, a component of PREVDUO™, is contraindicated in patients with glaucoma because it may cause mydriasis and increase intraocular pressure. Advise patients with glaucoma to promptly seek medical care in the event that they experience symptoms of acute angle closure glaucoma (pain and reddening of the eyes, accompanied by dilated pupils).

Drowsiness and Blurred Vision: Glycopyrrolate, a component of PREVDUO™, may cause drowsiness or blurred vision. Warn patients not to participate in activities requiring mental alertness, such as operate a motor vehicle or other machinery or perform hazardous work until these issues resolve.

Heat Prostration: Glycopyrrolate, a component of PREVDUO™, may cause heat prostration (due to decreased sweating) in presence of fever, high environmental temperature, and/or during physical exercise, particularly in children and the elderly. Advise patients to avoid exertion and high environmental temperature after receiving PREVDUO™.

Intestinal Obstruction: Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with Glycopyrrolate, a component of PREVDUO™, is inappropriate and possibly harmful. Avoid use in patients with these conditions.

Tachycardia: Investigate any tachycardia before giving Glycopyrrolate, a component of PREVDUO™ 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.

ADVERSE REACTIONS

- Most common adverse reactions to neostigmine during treatment: bradycardia, nausea, vomiting, blurred vision and photophobia.
- Most common adverse reactions to glycopyrrolate are related to anticholinergic pharmacology and 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; bradycardia; palpitation; and decreased sweating.

DRUG INTERACTIONS

Neostigmine Methylsulfate: The pharmacokinetic interaction between neostigmine methylsulfate and other drugs has not been studied. Neostigmine methylsulfate is metabolized by microsomal enzymes in the liver. Use with caution when using neostigmine methylsulfate with other drugs which may alter the activity of metabolizing enzymes or transporters.

Glycopyrrolate: The concurrent use of glycopyrrolate 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.

INDICATION AND USAGE

PREVDUO™, a fixed dose combination of cholinesterase inhibitor and antimuscarinic agent, is indicated in patients age two years and above for the reversal of the effects of nondepolarizing neuromuscular blocking agents (NMBA) after surgery, while decreasing the peripheral muscarinic effects (e.g., bradycardia and excessive secretions) associated with cholinesterase inhibition following NMBA reversal administration.

Please click for full Prescribing Information.

References: 1. Howard J, Wigley J, Rosen G, D'mello J. Glycopyrrolate: it's time to review. *J Clin Anesth.* 2017;36:51-53. **2.** Glycopyrrolate Injection. Prescribing Information. Fresenius Kabi USA LLC. **3.** InCrowd, Inc. Neostigmine-Glycopyrrolate Online Quantitative Market Research Study. January 2023. **4.** US Food and Drug Administration. Prescription and over-the-counter drug product list, 43rd edition. Cumulative Supplement Number 02: February 2023. https://www.fda.gov/media/166160/download. Accessed September 5, 2023.

PAR PHARMACEUTICAL
an endo international company

TRU DELIVERY™

PSP-PRVD-05021/September 2023 www.parpharm.com