Neostigmine
Newborn use only

2025

Alert	Atropine or glycopyrrolate should be given before or with neostigmine to counteract any severe cholinergic reactions.[1,2]
Indication	1. Reversal of residual neuromuscular blockade by **non-depolarizing** neuromuscular blocking agents (e.g. rocuronium, vecuronium) * 2. Myasthenia gravis * Sugammadex and Neostigmine are currently regarded as clinically equivalent for reversal of neuromuscular blockade, except in situations where rapid reversal of blockade is required (under 5 minutes), in which case Sugammadex is the preferred agent (Refer to practice points)
Action	Neostigmine is a reversible cholinesterase inhibitor. It increases acetylcholine at the neuromuscular junction by inhibiting its breakdown by cholinesterase.
Drug Type	Neuromuscular blocking agent, cholinergic agent
Trade Name	Juno, Hameln (section 19A)
Presentation	Neostigmine methylsulfate 2.5mg (2500microgram) in 1mL ampoule
Dose	**Reversal of non-depolarising neuromuscular blockade** IV - 40 microgram/kg (0.04 mg/kg) – to be given only after witnessing signs of recovery from Neuromuscular blockade (NMB). NOT to GIVE TOO EARLY. **NOTE: Administer atropine (20 microgram/kg) before, or with neostigmine** to prevent muscarinic effects (e.g. bradycardia, hypotension).[2] **Myasthenia Gravis (MG)[3,4]** Note: Pyridostigmine is the preferred drug. Neostigmine is rarely used for diagnosis and treatment of neonatal MG. May be considered in rare situations with suspected neonatal MG where enteral treatment is not feasible. Some genetic causes of neonatal MG can be worsened by neostigmine. To be discussed with paediatric neurologist. Neostigmine is to be given with atropine (20 microgram/kg) to prevent muscarinic effects (e.g. bradycardia, hypotension) Dose: IM/IV (IM preferable) – 50 microgram/kg (0.05 mg/kg) every 3-4 hours, preferably 30 minutes before feeding to assist with dysphagia. Treatment is not usually required beyond 8 weeks of age. Condition is usually self-limiting, so daily dosage should gradually be weaned off
Dose adjustment	Therapeutic hypothermia - No information. ECMO – No information. Renal impairment – Prolonged action in severe renal impairment. Hepatic impairment – No dose adjustment.
Maximum Dose	
Route	IV bolus over 1 minute, IM - Anterolateral thigh.
Preparation	Draw up 1 mL (2500 microgram neostigmine) and add 9 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 250 microgram/mL.
Administration	For Neuromuscular reversal: IV bolus over 1 minute For Myasthenia Gravis: IM injection preferred. The maximum volume for intramuscular administration is 0.5mL per site, the dose should be administered 30 minutes before feed.
Monitoring	Cardiorespiratory monitoring Respiratory function (Breathing sufficiency, SaO2) for any residual neuromuscular blockade. Train of four monitoring where available. Recurrence of neuromuscular blockade
Contraindications	Mechanical obstruction of intestinal or urinary tract. Known hypersensitivity to neostigmine. Neostigmine should not be given in conjunction with suxamethonium as neostigmine potentiates the depolarising myoneural blocking effects of suxamethonium.
Precautions	Use with extreme caution in neonates who have undergone recent intestinal or bladder surgery. Use in patients with intestinal anastomosis may produce rupture or leakage of the anastomosis due to the sudden return of abdominal muscle tone. Neostigmine can induce significant bronchoconstriction.

	Use with caution in patients with cardiovascular disorders including arrhythmias and hypotension. Use with caution in patients with epilepsy, renal impairment, Addison's disease or hyperthyroidism.
Drug Interactions	Corticosteroids: Corticosteroids may decrease the anticholinesterase effects of neostigmine. Depolarising muscle relaxants: Neostigmine may prolong the effect of depolarising muscle relaxants such as suxamethonium. Atropine or glycopyrrolate: Atropine or glycopyrrolate reverses neostigmine's muscarinic effects (bradycardia, hypotension, bronchoconstriction, increased gut motility and salivation, bladder contraction) Aminoglycosides: Neostigmine can be effective in reversing neuromuscular block induced by aminoglycoside antibiotics.
Adverse Reactions	Inadequate reversal of neuromuscular blockade. Bradycardia (prevented by simultaneous administration of atropine or glycopyrrolate), hypotension, syncope, arrhythmias (bradycardia, tachycardia, AV block, abnormal ECG, Prolonged QTc interval/cardiac arrest[5-7] Diaphoresis, Miosis, tearing, Increased bronchial secretions, respiratory depression, bronchoconstriction, Pulmonary oedema[8](8) Muscle spasms, twitching and weakness Anaphylaxis[9] Gastrointestinal (nausea, vomiting, salivation, flatulence, diarrhea, stomach cramps)
Overdose	AUSTRALIA Contact the Poisons Information Centre on **13 11 26** for information on the management of overdose NEW ZEALAND Contact the National Poisons Centre on **0800 764 766** for information on the management of overdose.
Compatibility	Fluids:[1,10] Sodium chloride 0.9%. PN at Y-site: No information. Y-site: Palonosetron hydrochloride, Plasma-Lyte 148[10].
Incompatibility	Fluids: No information. PN at Y-site: No information. Y site: No information.
Stability	Stability varies between brands. Check product information.
Storage	Store below 25^{0}C. Protect from light. Discard unused potion.
Excipients	Sodium chloride, water for injections.
Special Comments	The maximum volume for intramuscular administration is 0.5mL per site, the dose should be administered 30 minutes before feed. In patients with bradycardia, after administration of atropine the pulse rate should increase to 80 bests/min before administering neostigmine.
Evidence	**Background** Neuromuscular blocking agents (NMBAs) are commonly used during paediatric anaesthesia and neonatal intensive care to facilitate intubation and muscle relaxation. Spontaneous recovery from neuromuscular blockade (NMB) can be slow and variable. Residual NMB refers to symptoms and signs of inadequate recovery from blockade, such as muscle weakness, apnoea and hypoxia. Residual NMB, which can be defined as the train-of-four (TOF) ratio <0.9, is a problem in the immediate (0-2hrs) post-operative period. The incidence of residual NMB in the post-operative period has been reported as high as 37%–82%.[11] Some anaesthesiologists use neostigmine to reverse NMB of **non-depolarising** muscle relaxants for paediatric surgical patients.[12,13] As an anticholinesterase, neostigmine mainly inhibits the breakdown of acetylcholine, increases acetylcholine in the neuromuscular junction, and enhances the availability of acetylcholine to compete with NMBAs.[11] Neostigmine has a broad-spectrum reversal of the effect of all nondepolarizing NMBAs.[11] However, it has a maximum effective dosage, and administering additional neostigmine will not produce further reversal. The maximum effective dose is in the range of 60-80 microgram/kg, and the recommended dose for blockade reversal in paediatric patients is 20-60 microgram/kg when combined with 20 microgram/kg atropine.[12,13]

	Efficacy Reversal of NMD A 2014 Cochrane review found no RCTs on the routine use of neostigmine to reverse NMB in paediatric patients.[13] However, neostigmine usage for reversal of NMB goes back many decades and it's unsurprising no RCT was found. One of the drawback of neostigmine is its inability to reverse profound and deep blockade, because its effect reaches a plateau (i.e. ceiling effect) when acetylcholinesterase inhibition is near 100%, and the maximal concentration of acetylcholine is achieved.[11] **Transient Neonatal Myasthenia Gravis (TNMG)** Transient neonatal myasthenia gravis (TNMG) is caused by pathogenic maternal autoantibodies that cross the placenta. TNMG affects 10–20% of children born to mothers with MG. The severity of symptoms ranges from minor feeding difficulties to life-threatening respiratory weakness. Acetylcholine-esterase inhibitors (e.g. neostigmine or pyridostigmine) and antibody-clearing therapies such as immunoglobulins can be used to treat TNMG, but most children do well with observation only. TNMG is self-limiting within weeks as circulating antibodies are naturally cleared from the blood. Symptomatic treatment with acetylcholine-esterase inhibitors can be used for TNMG. Neostigmine and pyridostigmine are usually well tolerated and are administered as needed every 3–4 hours parenterally (preferably IM or SC) or every 4–6 hours. Neostigmine (neostigmine methylsulfate: 50 microgram/kg IV/IM/SC) is usually preferred for parenteral use, while the slower-acting pyridostigmine is preferred for enteral use (50-150 microgram/kg IV/IM or 0.5–1.0 mg/kg PO, max. 10 mg/dose).[3,4] It is sensible to schedule the administration prior to feedings for maximal benefit. Muscarinic side effects (diarrhea, increased secretions, fasciculations, and flushing) are dose-dependent and usually manageable by altering the dosing regimen.[3,4] **Pharmacokinetics** neostigmine does not cross the blood-brain barrier to produce CNS effects. Neostigmine is excreted in urine as unchanged drug (50%) and metabolites. Following IV administration it's onset of clinical action is within 5-10 minutes and the elimination half-life ranges from 47 to 60 minutes and after IM administration 50 to 91 minutes.[1] **Renal impairment:** The duration of effect may be prolonged in patients with renal impairment since neostigmine is excreted mostly in the urine. Dosage adjustment may be needed for patients in renal failure.[1] **Safety** Anaphylactoid reaction, occasionally seen in adults, is very rarely reported in paediatric population.[9] Pulmonary oedema was reported in a 1-year-old child after administration of a neostigmine–glycopyrrolate mixture to reverse neuromuscular blockade during general anaesthesia.[8] There are case reports of prolonged Q-Tc interval and cardiac arrest in children and adults.[5-7]
Practice points	**Expert commentary (A/Prof Justin Skowno)** 1. Sugammadex acts quicker, and more effectively, with the trade-off a higher rate of anaphylaxis and a higher cost compared to neostigmine. 2. Neostigmine has a long history of clinical use, while sugammadex was introduced for the same purpose more recently. 3. Administer atropine (20 microgram/kg) before or with neostigmine to prevent bradycardia and hypotension.
References	1. Neostigmine Juno injection. MIMS online. Accessed on 12th April 2025. 2. Meakin GH. Neuromuscular blocking drugs in infants and children. Continuing Education in Anaesthesia, Critical Care & Pain. 2007;7(5):143-7. 3. Lindroos JLV, Bjørk M-H, Gilhus NE. Transient Neonatal Myasthenia Gravis as a Common Complication of a Rare Disease: A Systematic Review. Journal of Clinical Medicine. 2024;13(4):1136. 4. Norwood F, Dhanjal M, Hill M, James N, Jungbluth H, Kyle P, et al. Myasthenia in pregnancy: best practice guidelines from a U.K. multispecialty working group. J Neurol Neurosurg Psychiatry. 2014;85(5):538-43. 5. Nkemngu NJ. Asystole following neuromuscular blockade reversal in cardiac transplant patients. Annals of Cardiac Anaesthesia. 2017;20(3):385-6. 6. Sawasdiwipachai P, Laussen PC, McGowan FX, Smoot L, Casta A. Cardiac arrest after neuromuscular blockade reversal in a heart transplant infant. Anesthesiology. 2007;107(4):663-5.

	7. Tufek A, Yildirim B, Tokgoz O, Karaman H, Celik F, Aycan IO. Immediate cardiac arrest after neostigmine administration. JPMA J Pak Med Assoc. 2012;62(6):609-11. 8. Nagella AB, Bijapur MB, Shreyavathi S, Rao RR. Neostigmine and pulmonary oedema. BMJ Case Rep. 2014;08:08. 9. Iwasai S, Kinoshita Y, Asagoe Y, Matsuzaki T, Arai M, Sato T. [Anaphylactoid Reactions Suspected to Be Caused by Neostigmine in Pediatric Patients under General Anesthesia]. Masui. 2016;65(4):377-9. 10. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: Apr/13/2025). 11. Luo J, Chen S, Min S, Peng L. Reevaluation and update on efficacy and safety of neostigmine for reversal of neuromuscular blockade. Therapeutics and clinical risk management. 2018:2397-406. 12. Meretoja OA. Neuromuscular block and current treatment strategies for its reversal in children. Paediatric Anaesthesia. 2010;20(7):591-604. 13. Yang L, Yang D, Li Q, Zuo Y, Lu D. Neostigmine for reversal of neuromuscular block in paediatric patients. Cochrane Database of Systematic Reviews. 2014(5).

VERSION/NUMBER	DATE
Original 1.0	**29/05/2025**
REVIEW	**29/05/2030**

Authors Contribution of the current version

Current version authors	Srinivas Bolisetty, Mohammad Irfan Azeem
Evidence Review	Srinivas Bolisetty
Expert review	A/Prof Justin Skowno (Paediatric anaesthetist, Sydney Children's Hospital Network) Dr Richard Webster, Paediatric Neurologist, Sydney Children's Hospital Network.
Nursing Review	Bryony Malloy
Pharmacy Review	Mohammad Irfan Azeem, Michelle Jenkins
ANMF Group contributors	Bhavesh Mehta, Nilkant Phad, Amber Seigel, Rebecca Barzegar, Rebecca O'Grady, Thao Tran, Cindy Chen, Kerrie Knox, Jutta van den Boom, Susannah Brew, Renae Gengaroli, Samantha Hassall, Celia Cunha Brites, Tiffany Kwan
Final editing	Srinivas Bolisetty
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty

Citation for the current version

Bolisetty S, Azeem MI, Skowno J, Jenkins M, Mehta B, Malloy B, Phad N, Seigel A, Barzegar R, O'Grady R, Tran T, Chen C, Knox K, van den Boom J, Brew S, Brites CC, Gengaroli R, Hassall S, Kwan T, Callander I. Neostigmine. Consensus formulary by the Australasian Neonatal Medicines Formulary group. Version 1, dated 29 May 2025. www.anmfonline.org