ROCURONIUM - STANDARD CONCENTRATION

Newborn use only

2025

Alert	High-risk medicine: High risk of causing significant patient harm when used in error. This drug should be administered in the presence of personnel trained in advanced airway management. Suggest regular cessation of infusion for a few to several hours, possibly every 24 hours (commonly referred to as 'drug holiday'[1]) to assess the need for continued paralysis and adequacy of sedation or analgesia. Line should be adequately flushed to avoid unintended paralysis during later use of the line.
Indication	1. Intubation 2. Muscle relaxation
Action	Non-depolarising muscle relaxant that competitively antagonises nicotinic acetylcholine receptors at the neuromuscular junction. Also competitively antagonises autonomic nicotinic acetylcholine receptors and may result in increased heart rate and reduced blood pressure.
Drug type	Non-depolarising neuromuscular blocking agent
Trade name	DBL Rocuronium Bromide, Rocon, Rocuronium Baxter, Rocuronium Bromide Medsurge, Rocuronium Sandoz, Rocuronium-hameln
Presentation	50 mg/5 mL vial
Dose	**Intubation** ***IV bolus:*** 600 microgram/kg (400-1000 microgram/kg) **Muscle relaxation** ***Intermittent IV bolus***: 600 microgram/kg (400 – 1000 microgram) every 30 to 60 minutes as needed. ***Continuous IV infusion*** OPTIONAL LOADING DOSE: 600 microgram/kg Continuous maintenance infusion: 600 microgram/kg/hour (400–1000 microgram/kg/hour). Titrate until desired neuromuscular blockade is achieved.
Dose adjustment	No information.
Maximum dose	2000 microgram/kg/dose
Route	IV bolus, IV infusion
Preparation	**IV bolus**: Draw up 1 mL (10 mg) of rocuronium and add 4 mL of sodium chloride 0.9% to make a 5 mL solution [2 mg/mL]. **IV infusion**: **Note: Refer to Appendix for tables to assist with concentration selection.** **Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24-hour fluid volumes**

Infant weight	<2 kg	2 to 5 kg	>5 kg
Suggested rocuronium concentration	**1.5 mg/mL**	**5 mg/mL**	**10 mg/mL**
600 microgram/kg/hour is equal to	0.4 mL/kg/hour	0.12 mL/kg/hour	0.06 mL/kg/hour
IV bolus of 600 microgram/kg	0.4 mL/kg	0.12 mL/kg	0.06 mL/kg

20mL Syringe

Draw up rocuronium and add compatible fluid* as per table below to make a final volume of 20 mL

Rocuronium concentration	**1.5 mg/mL**	**5 mg/mL**	**10 mg/mL**
Volume of rocuronium (10 mg/mL)	3 mL (30 mg)	10 mL (100 mg)	20 mL (200 mg)
Volume of compatible fluid*	17 mL	10 mL	Nil
Total volume	20 mL	20 mL	20 mL

*Compatible fluid: glucose 5% or sodium chloride 0.9%

<table>
<tr><td></td><td>

40mL Syringe

Draw up rocuronium and add compatible fluid* as per table below to make a final volume of 40 mL

Rocuronium concentration	1.5 mg/mL	5 mg/mL	10 mg/mL
Volume of rocuronium (10 mg/mL)	6 mL (60 mg)	20 mL (200 mg)	40 mL (400 mg)
Volume of compatible fluid*	34 mL	20 mL	undiluted
Total volume	40 mL	40 mL	40 mL

*Compatible fluid: glucose 5% or sodium chloride 0.9%.
</td></tr>
<tr><td>Administration</td><td>IV bolus over 5–10 seconds
IV continuous infusion
Line should be adequately flushed upon cessation of treatment to avoid unintended paralysis during later use of the same line.</td></tr>
<tr><td>Monitoring</td><td>Continuous cardiorespiratory and pulse oximetry monitoring.
Close monitoring of neuromuscular function, sedation and blood pressure (invasive or non-invasive) is essential.
Electrolytes and renal function.</td></tr>
<tr><td>Contraindications</td><td>Hypersensitivity to rocuronium or any component of the formulation.
Cross-sensitivity with other neuromuscular-blocking agents may occur; use with extreme caution in patients with previous anaphylactic reactions.</td></tr>
<tr><td>Precautions</td><td>Factors which can increase duration of neuromuscular blockade:
Acidosis, hypothermia, neuromuscular disease, hepatic disease, hypokalaemia, hypermagnesaemia, renal failure and younger age.
Factors which can decrease duration of neuromuscular blockade:
Alkalosis and hyperkalaemia

Use cautiously in neonates with hepatic or renal impairment and in neonates with fluid and electrolyte imbalance.
In the first week after birth, use cautiously in neonates whose mothers received magnesium sulfate infusion for pre-eclampsia or fetal neuroprotection.

Assess regularly (at least every 24 hours) the need for ongoing use of muscle relaxant and neuromuscular function/blockade. Consider “drug holiday” in case of prolonged usage of >24 hours.
Drug Holiday: A drug holiday refers to cessation of the NMBA for a period of time (at least until neuromuscular function begins to return) on a daily basis. At this point, clinicians should reassess need for ongoing treatment and restart the NMBA only when clinically necessary.[1, 2]</td></tr>
<tr><td>Drug interactions</td><td>Aminoglycosides and general anaesthetics can increase (potentiate) duration of neuromuscular blockade.
Corticosteroids: In addition to prolonging recovery from neuromuscular blockade, concomitant use with corticosteroids has been associated with development of acute quadriplegic myopathy syndrome (AQMS). Current adult guidelines recommend neuromuscular blockers be discontinued as soon as possible in patients receiving corticosteroids or interrupted daily until necessary to restart them based on clinical condition.[3]

Adrenaline (epinephrine) can reduce (antagonise) duration of neuromuscular blockade.</td></tr>
<tr><td>Adverse reactions</td><td>Hypoxaemia/hypercarbia may occur because of inadequate ventilation and deterioration in pulmonary mechanics
Hypotension and bradycardia, particularly when used in combination with opioids
Prolonged paralysis after long-term use
Rare—anaphylactic reaction.</td></tr>
<tr><td>Compatibility</td><td>Fluids: Glucose 5%, sodium chloride 0.9%, Hartmann’s.
Amino acids at Y site: Compatible with 2 in 1 solution (Amino acid-glucose-trace element mixture not containing lipid emulsion)
Y site: Acetaminophen, aciclovir, adrenaline (epinephrine), alfentanil, amikacin sulfate, amiNOPHYLLine, amiODAROne, ampicillin, anidulafungin, atenolol, aziTHROMYCIN, aztreonam, bivalirudin, calcium chloride, calcium gluconate, caspofungin, cefEPIME, cefOTAXIME, cefotetan, cefOXITIN, cefTAZIDIME, ceftizoxime, cefuroxime, ciPROFLOXAcin, clindamycin, digoxin, diltiazem, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, fentanyl, flucONAZOLe, foscarnet, Fosfomycin, fosphenytoin, ganciclovir, gentamicin sulfate, glycopyrrolate, heparin, labetolol, lidocaine, linEZOLID, magnesium sulfate, meropenem, metronidazole, midazolam, milrinone, morphine, naloxone, nicardipine, nitroglycerin,</td></tr>
</table>

	octreotide, ondansetron, pamidronate, phenobarbital, phenylephrine, potassium acetate, potassium chloride, propRANOLol, ranitidine, remifentanil, sodium acetate, sodium bicarbonate, sodium nitroprusside, sodium phosphate, TACrolimus, ticarcillin, tobramycin, vasopressin, verapamil, voriconazole, zidovudine
Incompatibility	**Fluids**: No information. **Lipid at Y site:** Lipid emulsion **Y site**: Amoxicillin, amphotericin B (amphotericin), azATHIOPRINE, cefaZOLin, cefiderocol, cefoperazone, cloxacillin, dexAMETHASOne, dexMEDETOMIDine, DIAzepam, ERYthromycin, famotidine, furosemide, hydrocortisone sodium succinate, insulin, ketamine, ketOROLAC, lorazepam, methylprednisolone, micafungin, pantoprazole, pentobarbital, phenytoin, piperacillin, piperacillin/tazobactam, prednisolone, piperacillin-tazobactam, sulfamethoxazole/trimETHOPRIM, thiopental, vancomycin.
Stability	Diluted solution is stable for up to 24 hours at 2–8°C
Storage	Refrigeration at 2–8°C. Stable for 12 weeks below 30°C (note the date of removal from fridge and do not return to the fridge).
Excipients	Sodium acetate trihydrate, sodium chloride, glacial acetic acid, water for injections.
Special comments	Muscle relaxation is reversed by neostigmine (60 microgram/kg) and atropine (20 microgram/kg). Sugammadex is also effective for rocuronium reversal in older patients but has not been systematically studied in neonates or infants. Sensation remains intact; sedation should be used in all patients and analgesia should be used for painful procedures. Provide eye protection and instil lubricating eye drops every 2 hours. Rocuronium produces significantly less tachycardia and hypotension when compared with pancuronium although more commonly than with vecuronium. The neuromuscular blockade of rocuronium is more rapid in onset than that of pancuronium and vecuronium. The duration of action is dose dependent and similar to vecuronium. Its action is prolonged in neonates compared to children and adults and therefore is similar to long-acting NMBAs in this population.[7]
Evidence	**Efficacy** <u>Muscle relaxation</u> The potency of rocuronium is significantly less (approximately one sixth) than that of pancuronium or vecuronium.[7, 8, 9] Rocuronium, although known to be shorter acting than pancuronium in older patients, tends to have a duration of action similar to that of a long-acting neuromuscular blocking agent in neonates. This may be because infants require lower plasma drug concentrations for 50% depression of neuromuscular function and because their volume of distribution is larger than children or adults.[10] In newborn and small infants up to 3 or 4 months, a dose of 0.45 mg/kg rocuronium bromide is sufficient for good neuromuscular blockade and satisfactory recovery times[7]. The majority of research regarding use of rocuronium in neonates and infants is in the setting of general anaesthesia. Therefore, given the known ability for anaesthetic agents to potentiate the effects of neuromuscular blocking agents, information on the pharmacodynamics of rocuronium in the NICU setting is limited.[7] In the anaesthetic setting, rocuronium is reported to rapidly induce paralysis and good intubating conditions, usually within 1 minute (faster than other non- depolarising agents).[11, 12] Time to recovery has not been consistently measured and, therefore, adult data are unlikely to be comparable. However, in neonatal patients it is dose dependent and up to 100 min.[7, 13] <u>Intubation</u> A randomised, controlled trial of rocuronium 0.5 mg/kg for elective intubation of neonates with fentanyl and atropine (control group fentanyl and atropine without muscle relaxation) showed 80% effectiveness in complete relaxation with the remaining 20% of infants having only minimal muscle activity. Onset of paralysis was between 4 and 178 seconds after administration and duration of action between 1 and 60 minutes.[14] There are limited data on the use of rocuronium infusion in newborn infants. In a study of 20 patients (age 2 months to 16 years), rocuronium infusion provided satisfactory neuromuscular blockade.[1] **Safety**

	Rocuronium is excreted in both urine and bile; however, unlike vecuronium, it is not reported to have active metabolites which may prolong the duration of action. In adult patients, prolonged duration of action has been observed in the presence of hepatic or renal impairment. A study comparing children with renal failure (most on dialysis) to healthy children undergoing elective procedures compared the onset and duration of action of rocuronium during anaesthesia and found a longer time to onset of action but not prolongation of action in the group with renal failure. A low dose (0.3 mg/kg) was used in this study which may have influenced the results.[15] Significant adverse events have not been reported in neonates with the exception of prolonged duration of action. Sugammadex has been reported to reverse the presumed central nervous effects of rocuronium in a neonate.[17] In older patients, immediate hypersensitivity reactions, prolonged duration of action and injection site reactions are the commonest adverse effects.[4] Transient tachycardia has been reported with higher doses.[16] **Pharmacokinetics** Clearance of rocuronium is via both urine and bile with approximately half via each route. Rocuronium has no active metabolites and approximately 50% of the drug is recovered unchanged.[4] Onset of action is dose dependent and 15 seconds to 2 minutes; duration of action is 30–60 minutes (prolonged with higher doses and in preterm infants).
Practice points	
References	1. Johnson PN, Miller J, Gormley AK. Continuous-Infusion Neuromuscular Blocking Agents in Critically Ill Neonates and Children. Pharmacotherapy 31 (6): 609-620 2011 2. Playfor S, Jenkins I, Boyles C, et al. Consensus guidelines for sustained neuromuscular blockade in critically ill children. Paediatr Anaesth 2007;17:881–7. 3. Murray MJ, Cowen J, DeBlock H, et al, Clinical Practice Guidelines for Sustained Neuromuscular Blockade in the Adult Critically Ill Patient. Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists, American College of Chest Physicians. Crit Care Med 2002;30(1):142-56. 4. Product information. MIMS Online, MIMS Australia Pty Ltd, (online) Last updated 19/2/2015, Accessed 9/3/2017. 5. Micromedex solutions. Accessed on 9 March 2017. 6. Australian Injectable Drugs Handbook. 6th edition. Accessed on 10 April 2017. 7. Rapp HJ, Altenmueller CA, Waschke C. Neuromuscular recovery following rocuronium bromide single dose in infants. Pediatric Anaesthesia, 2004, 14 (4): 329-335. 8. Hunter JM. Rocuronium: the newest aminosteroid neuromuscular blocking drug. British Journal of Anaesthesia 1996, 76 (4): 481-483 9. Parasa M, Vemuri NN, Shaik MS. Comparison of equipotent does of rocuronium and vecuronium. Anaesthetic Essays and Researches 2015, 9 (1): 88-91. 10. Meretoja OA. Is vecuronium a long-acting neuromuscular blocking agent in neonates and infants? Br J Anaesth 1989;62:184-187. 11. Scheiber G, Ribeiro FC, Marichal A, Bredendiek M, Renzing K. Intubating conditions and onset of action after rocuronium, vecuronium and atracurium in young children. Pediatric Anaesthesia 1996, 83 (2): 320-324 12. Ribeiro FC, Scheiber G, Marichal, A. Comparison of time course of neuromuscular blockade in young children following rocuronium and atracurium. European Journal of Anaesthesiology 1998, 15 (3): 310-313. 13. Driessen JJ, Robertson EN, Booij DJ. Acceleromyography in neonates and small infants: baseline calibration and recovery of the responses after neuromuscular blockade with rocuronium. European Journal of Anaesthesiology 2005, 22 (1): 11-15. 14. Feldman DM, Weiss MG, Nicoski P, Sinacore J. Rocuronium for nonemergent intubation of term and preterm neonates. Journal of Perinatology 2011, 31 (1): 38-43 15. Driessen JJ, Robertson EN, van Egmond J, Booij DJ. Time-course of action of rocuronium 0.3mg/kg in children with and without end stage renal failure. Paediatric Anaesthesia 2002, 12: 507-510 16. Woelfel SK, Brandom BW, Cook DR, Sarner JB. Effects of bolus administration of ORG-9426 in children during nitrous oxide-halothane anaesthesia. Anaesthesiology 1992, 76: 939-942 17. Langley RJ, McFadzean J, McCormack J. The presumed central nervous system effects of rocuronium in a neonate and its reversal with sugammadex. Paediatric anaesthesia. Jan 2016;26(1):109-111.

Appendix

Infusion tables to assist concentration selection

Table 1: Infusion rates when using rocuronium concentration **1.5 mg/mL**
(suggested weight <2kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate microgram/kg/hour**									
0.5	300	600	900	1200	1500	1800	2100	2400	2700	3000
1	150	300	450	600	750	900	1050	1200	1350	1500
1.5	100	200	300	400	500	600	700	800	900	1000
2	75	150	225	300	375	450	525	600	675	750
2.5	60	120	180	240	300	360	420	480	540	600
3	50	100	150	200	250	300	350	400	450	500
3.5	43	86	129	171	214	257	300	343	386	429
4	38	75	113	150	188	225	263	300	338	375
4.5	33	67	100	133	167	200	233	267	300	333
5	30	60	90	120	150	180	210	240	270	300

Table 2: Infusion rates when using rocuronium concentration **5 mg/mL**
(suggested weight 2 to 5 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate microgram/kg/hour**									
0.5	1000	2000	3000	4000	5000	6000	7000	8000	9000	10000
1	500	1000	1500	2000	2500	3000	3500	4000	4500	5000
1.5	333	667	1000	1333	1667	2000	2333	2667	3000	3333
2	250	500	750	1000	1250	1500	1750	2000	2250	2500
2.5	200	400	600	800	1000	1200	1400	1600	1800	2000
3	167	333	500	667	833	1000	1167	1333	1500	1667
3.5	143	286	429	571	714	857	1000	1143	1286	1429
4	125	250	375	500	625	750	875	1000	1125	1250
4.5	111	222	333	444	556	667	778	889	1000	1111
5	100	200	300	400	500	600	700	800	900	1000

Table 3: Infusion rates when using rocuronium concentration **10 mg/mL**
(suggested weight >5kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate microgram/kg/hour**									
0.5	2000	4000	6000	8000	1000	1200	1400	1600	1800	20000
1	1000	2000	3000	4000	5000	6000	7000	8000	9000	10000
1.5	667	1333	2000	2667	3333	4000	4667	5333	6000	6667
2	500	1000	1500	2000	2500	3000	3500	4000	4500	5000
2.5	400	800	1200	1600	2000	2400	2800	3200	3600	4000
3	333	667	1000	1333	1667	2000	2333	2667	3000	3333
3.5	286	571	857	1143	1429	1714	2000	2286	2571	2857

4	250	500	750	1000	1250	1500	1750	2000	2250	2500
4.5	222	444	667	889	1111	1333	1556	1778	2000	2222
5	200	400	600	800	1000	1200	1400	1600	1800	2000

$$\text{Dose (microgram/kg/hour)} = \frac{\text{Rate (mL/hr)} \times \text{Concentration (mg/mL)} \times 1000}{\text{Weight (kg)}}$$

$$\text{Rate (mL/hr)} = \frac{\text{Dose (microgram/kg/hour)} \times \text{Weight (kg)}}{\text{Concentration (mg/mL)} \times 1000}$$

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