Vecuronium
Newborn use only

2024

Alert	High-alert medication: High risk of causing significant patient harm when used in error.[1] This drug should be administered in the presence of personnel trained in advanced airway management. Reversal agents should be immediately available (see Special Comments). Suggest regular cessation of infusion for a few to several hours, possibly every 24 hours (commonly referred to as a 'drug holiday') to assess the need for continued paralysis and adequacy of sedation or analgesia. Following cessation, the line should be adequately flushed to avoid unintended paralysis during later use of the line. Eye lubricant should be used whilst patient is receiving vecuronium.
Indication	1. Skeletal muscle relaxation or paralysis in mechanically ventilated infants. 2. For elective endotracheal intubation.
Action	Nondepolarizing neuromuscular blockers are competitive acetylcholine (ACh) antagonists that bind directly to nicotinic receptors on the postsynaptic membrane, thus blocking the binding of ACh so the motor endplate cannot depolarize. Onset of action is 1-2 minutes; duration of action is 30-40 minutes.
Drug Type	Non-depolarising neuromuscular blocking agent.
Trade Name	Vecure Powder for injection, Vecure Sun Powder for injection
Presentation	10 mg of vecuronium bromide in glass vial (powder for reconstitution)
Dose	**Intubation** IV bolus – 0.1 mg/kg **Muscle relaxation*#** **Intermittent IV bolus** 0.1 mg/kg (0.03-0.15 mg/kg) IV push every 1-2 hours as required. **Continuous IV infusion (with or without loading dose)** 100 microgram/kg/hour (60-200 microgram/kg/hour). Start 20 minutes post bolus recovery. Titrate in 10% dose increments until desired neuromuscular blockade is achieved. * Provide eye protection and instil lubricating eye drops every 2 hours. # Sensation remains intact; additional sedation & analgesia should be used for painful procedures.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No specific dose adjustment. However, duration of action may be prolonged. Hepatic impairment – No specific dose adjustment. However, hepatic impairment decreases clearance resulting in prolonged duration of action.
Route	IV
Maximum Dose	IV bolus: 0.2 mg/kg IV infusion: 0.2 mg/kg/hour.
Total cumulative dose	
Preparation	**IV bolus:** Add 5 mL water for injection to 10 mg of vecuronium powder for reconstitution vial to make a 2 mg/mL solution. **Further dilute**: From this vial, draw up 2 mL (4 mg of vecuronium) and add to 2 mL of sodium chloride 0.9% to make a final volume of 4 mL with a concentration of 1 mg/mL. **IV infusion:** Infusion rate: 1 mL/hour = 100 microgram/kg/hour; Prescribed amount: 5 mg/kg vecuronium and make up to 50 mL Add 5 mL water for injection to 10 mg vecuronium powder for reconstitution vial to make a 2 mg/mL solution. **Further dilute**: From this vial, draw up 2.5 mL/kg of solution (5 mg/kg of vecuronium) and dilute to 50 mL with sodium chloride 0.9% or glucose 5%. Infusing at a rate of **1 mL/hour = 100 microgram/kg/hour**.

Administration	IV bolus: Administer over several seconds. IV infusion via syringe pump. Flush line adequately after each dose with sodium chloride 0.9% to avoid unintended paralysis and/or incompatibility with other medications during later use of the line.
Monitoring	Continuous cardio-respiratory and pulse oximetry monitoring. Close monitoring of neuromuscular function, sedation, and blood pressure (invasive or non-invasive). Monitor electrolytes and renal function. Monitor injection site for signs of extravasation.
Contraindications	Hypersensitivity to vecuronium 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. Severe electrolyte abnormalities.
Precautions	Avoid prolonged usage. **Factors which can increase duration of neuromuscular blockade:** Acidosis, hypothermia, neuromuscular disease, hepatic disease, hypokalaemia, hypermagnesaemia, renal failure, and younger age. Vecuronium is lipid soluble and is predominantly excreted via the liver so poor liver function can cause prolonged effects. **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. Suggest regular cessation of infusion, possibly every 24 hours (commonly referred to as 'drug holiday') to assess the need for continued paralysis and adequacy of sedation or analgesia. Monitoring of fluid balance is essential due to risk of fluid retention. Aminoglycosides & general anaesthetics can increase (potentiate) duration of neuromuscular blockade. **Corticosteroids:** Concomitant use with corticosteroids has been reported to be associated with development of acute quadriplegic myopathy syndrome (AQMS) in adults.[3] However, Recent trials provided no evidence for increased risk of neuromyopathy in patients with sepsis or acute respiratory distress syndrome (ARDS) with the use of corticosteroids or neuromuscular blockers.[17] Adrenaline (epinephrine) can reduce (antagonise) duration of neuromuscular blockade.
Drug Interactions	Antimicrobials like aminoglycosides, tetracyclines, polymyxins, and clindamycin can potentiate neuromuscular blockade.[3] Inhaled anaesthetics can potentiate neuromuscular blockade.[3] Anti-epileptics can make patients resistant to vecuronium.[3] Local anaesthetics can potentiate neuromuscular blockade.[3] Aminoglycosides & general anaesthetics can increase duration of neuromuscular blockade. **Corticosteroids:** Concomitant use with corticosteroids has been reported to be associated with development of acute quadriplegic myopathy syndrome (AQMS) in adults.[3] However, Recent trials provided no evidence for increased risk of neuromyopathy in patients with sepsis or acute respiratory distress syndrome (ARDS) with the use of corticosteroids or neuromuscular blockers.[17] Dexamethasone and hydrocortisone may result in decreased vecuronium effectiveness, prolonged muscle weakness, and myopathy.[3] Adrenaline (epinephrine) can reduce (antagonise) duration of neuromuscular blockade.
Adverse Reactions	Hypoxaemia 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 and tachycardia.

Overdose	Supportive measure: Ventilatory support and sedation. Reversal of neuromuscular blockade can be achieved by neostigmine (refer to special comments). For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).
Compatibility	Fluids: [3] glucose 5%, sodium chloride 0.9%. Y-site:[3] glucose/amino acid solutions, adrenaline (epinephrine), alprostadil, amikacin sulfate, aminophylline, amiodarone, ampicillin, atenolol, azithromycin, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, ceftazidime, ceftriaxone, ciprofloxacin, clindamycin, dexamethasone sodium phosphate, dexmedetomidine, digoxin, diltiazem, dobutamine, dopamine, enalaprilat, adrenaline (epinephrine), erythromycin lactobionate, esmolol, fentanyl, fluconazole, fluorouracil, fosphenytoin, gentamicin, glycopyrrolate, heparin, hydralazine, hydrocortisone sodium succinate, insulin (regular), isoprenaline, labetalol, lidocaine, linezolid, lorazepam, magnesium sulfate, meropenem, metaprolol, metronidazole, midazolam, milrinone, morphine, naloxone, nicardipine, nitroglycerin, norepinephrine, octreotide, ondansetron, pamidronate, pentoxifylline, phenobarbital, phenylephrine, potassium acetate, potassium chloride, propofol at vecuronum concentrations of ≤1 mg/mL, propranolol hydrochloride, ranitidine hydrochloride, remifentanil, sodium acetate, sodium bicarbonate, sodium nitroprusside, sodium phosphate, streptozocin, succinylcholine, tacrolimus, theophylline, ticarcillin disodium/clavulante potassium, tigecycline, tobramycin, sulfamethoxazole/trimethoprim, and vancomycin hydrochloride, vasopressin, verapamil, voriconazole, zidovudine, and zoledronic acid.
Incompatibility	Fluids: No information. No information on lipid emulsions. Y site:[3] Aciclovir, amphotericin B (all compounds), cefepime, cefotaxime, diazepam, furosemide, ganciclovir, ibuprofen lysine, imipenem/cilastatin sodium, methylprednisolone sodium succinate, micafungin sodium, pantoprazole, phenytoin, piperacillin sodium, piperacillin-tazobactam, propofol at vecuronium concentrations >1 mg/mL, sulbactam/durlobactam, and thiopental sodium.
Stability	Diluted solution stable for up to 24 hours. Protect from light. Discard any unused solution.
Storage	Store below 25°C. Protect from light. Store in accordance with local policies.
Excipients	Citric acid, dibasic sodium phosphate, sodium hydroxide and/or phosphoric acid, and mannitol.
Special Comments	Muscle relaxation is reversed by neostigmine (50 microgram/kg) and atropine (20 microgram/kg). Sugammadex is being increasingly used with extrapolated information from other populations. Sensation remains intact: sedation & analgesia should be used for painful procedures. Provide eye protection and instil lubricating eye drops every 2 hours. Vecuronium produces less tachycardia and hypotension when compared with pancuronium.[15,16] The neuromuscular blockade of vecuronium is of shorter duration than that of pancuronium.[15,16] Prior administration of suxamethonium shortens onset and may increase depth of blockade; reduce dose and give vecuronium only after recovery from suxamethonium-induced neuromuscular blockade.
Evidence	**Background** Nondepolarizing neuromuscular blocking agents (NMBA) can be classified into 2 classes: steroidal (rocuronium, vecuronium, pancuronium) or benzylisoquinoline (mivacurium, atracurium, cisatracurium). Nondepolarizing neuromuscular blockers are competitive acetylcholine (ACh) antagonists that bind directly to nicotinic receptors on the postsynaptic membrane, thus blocking the binding of ACh so the motor endplate cannot depolarize. This leads to skeletal muscle paralysis.[2] Paralysis occurs sequentially because of the differing sensitivity of muscles to NMBAs as well as blood flow to the area. Generally, paralysis begins with smaller, fast twitch muscles such as the eyes and larynx, then affects the limbs, neck, trunk, and upper airway, and eventually progresses to the intercostals and diaphragm until respiration terminates. Recovery from paralysis occurs in the reverse order with function of the diaphragm returning first.[4] **Vecuronium:** vecuronium is structurally related to pancuronium. It has a greater potency, shorter duration of action, lack significant cardiovascular effects (tachycardia), and less cumulative properties. Vecuronium produces less tachycardia and hypotension when compared with pancuronium.[15,16] The

	neuromuscular blockade of vecuronium is of shorter duration than that of pancuronium.[15,16] Time of onset of action is 90-120 seconds after IV bolus, with a duration of effect that lasts only 30-40 minutes. Intermittent bolus dosing would need to be so frequent (i.e., every 30 to 60 minutes) that continuous IV infusion is preferred over intermittent boluses to maintain paralysis in ventilated infants.[5] In comparison, rocuronium is an analogue of vecuronium with a more rapid onset of action (20-100 seconds), but less potent than vecuronium, and hence larger doses (example, 600 microgram/kg of rocuronium, compared to 100 microgram/kg of vecuronium). Tachycardia is more frequent with rocuronium, while vecuronium lacks this effect in regular doses.[4] The neuromuscular blockade effect of vecuronium is stronger and lasts longer in neonate than infant or adult.[6] The 95% effective dose (ED_{95}) for NMBDs specifies the dose that produces 95% twitch depression in 50% of individuals. ED_{95} of vecuronium in neonates (47 microgram/kg) is 40% less than in children (81 microgram/kg) meaning less dose is needed in neonates compared to children.[7] **Efficacy** <u>Muscle relaxation</u> Two prospective studies by Meretoja et al in 1988 and 1989 determined the dose responses with vecuronium bolus and continuous infusion in paediatric population.[7,8] The bolus dose required to achieve effective neuromuscular blockade in neonates was 40% less than in children. The median maintenance dose of 0.1 mg/kg is required in neonates to maintain 1 hour of neuromuscular blockade, in comparison to 0.217 mg/kg/hour in children 3-10 years old. Fitzpatrick et al studied vecuronium to facilitate paralysis in mechanically ventilated paediatric population (4 neonates, and 11 infants and children). A loading dose of 0.1 mg/kg was followed by an infusion of 0.1 mg/kg/hour. The titration rate was adjusted to maintain a neuromuscular block of approximately 90% as assessed by the presence of one response to a train of four (TOF) stimulation. The duration of the infusions varied from 9.5 to 179 hours. Mean recovery times after stopping the infusion were 5I.7 (±17.6) and 46.8 (± 16.5) minutes for the children and neonates respectively. No adverse cardiovascular or toxic effects were noted.[9] Fisher et al determined the recovery period (time from injection to 90% recovery) after a bolus of vecuronium. Recovery was longest for infants (73±27 minutes), compared to children (35±6 minutes).[10] The longer recovery period in neonates is thought to be due higher volume of distribution. Hodges et al evaluated the appropriate vecuronium infusion rates in 12 neonates/infants and 18 children using train of four (TOF) monitoring. Neonates and infants required 45% less vecuronium (mean infusion rate 0.54 mg/kg/hour) than older children (0.99 mg/kg/hour) and had faster recovery (45 min vs 65 min), with no evidence of prolonged weakness.[11] **Safety** Adults with hepatic and renal failure have been shown to experience prolonged neuromuscular blockade.[12,13] **Pharmacokinetics** Hepatobiliary clearance is the primary route of elimination, accounting for approximately 50% of the dose. Vecuronium is metabolised rapidly in the liver to 3-desacetyl-vecuronium, which is 50–70% as potent as the parent compound. This metabolite is cleared primarily by renal elimination. Approximately 20–30% of vecuronium is excreted unchanged in urine.[9,11,12] Time of onset of action is 90-120 seconds after IV bolus, with a duration of effect that lasts only 30-40 minutes. (prolonged with higher doses and in preterm infants).[5,14]
Practice points	Eye lubrication should be applied to all patients.
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