

Neuromuscular blocking agents (NMBAs) may facilitate various medical interventions. The following guidelines were designed for the long-term use of NMBAs ( $\geq 24$  hours) in the ICU. These guidelines are not intended for patients receiving NMBAs for short-term or occasional use.

**A. INDICATIONS:**

NMBAs to produce muscle paralysis in the ICU are indicated, but not limited to:

- 1) Early severe acute respiratory distress syndrome (ARDS) ( PaO<sub>2</sub>/FiO<sub>2</sub> less than 150)
- 2) Status asthmaticus with life-threatening situations (profound hypoxemia, respiratory acidosis, hemodynamic compromise) when other measures such as deep sedation fails
- 3) Management and facilitation of mechanical ventilation and decrease oxygen consumption
- 4) Management of muscle spasm, shivering (e.g., tetanus, therapeutic hypothermia), when underlying cause is not reversible and causes excessive oxygen consumption
- 5) Prevent patient interference with surgical repairs and devices (e.g. open chest, ECMO)
- 6) Acute pulmonary hypertension in pediatric patients

**NOTE: NMBAs provide no analgesia or sedation. All patients should be receiving concurrent analgesia and/or sedation prior to initiation of neuromuscular blockade.**

**B. NMBAs FOR PROLONGED ( $\geq 24$  hours) ICU PARALYSIS:**

For most adult and pediatric patients, paralysis can be achieved with the use of vecuronium or rocuronium. The preferred method of administration for both agents is scheduled intermittent bolus dosing. However, either may be administered by continuous infusion.

Cisatracurium is preferred in patients with ARDS or in patients with renal and/or hepatic failure

For all NMBA orders, a goal train-of-four (TOF) should be specified. For most ICU patients, the goal level of paralysis is 1 to 2 twitches (TOF 1 to 2 out of 4; see section C for train-of-four monitoring).

*Dosing of Neuromuscular Blocking Agent*

	<b>Vecuronium</b>	<b>Rocuronium</b>	<b>Cisatracurium</b>
<b>Adult Dosing*</b>			
<b>Loading/Bolus Dose</b>	0.08 – 0.1 mg/kg	0.6 – 1 mg/kg	0.1 – 0.2 mg/kg <u>For severe ARDS:</u> 15 mg IV bolus followed by infusion
<b>Maintenance Dose</b>			
<b>Intermittent Dosing** (Preferred)</b>	0.1 – 0.2 mg/kg IV every 1 – 2 h prn	0.3 – 0.6 mg/kg IV every 30 min prn	N/A
<b>Continuous Infusion**</b>	0.8 – 1.2 mcg/kg/min	5 - 15 mcg/kg/min	Start at 1 – 3 mcg/kg/min Range 0.5 – 10 mcg/kg/min <u>For severe ARDS:</u> 37.5 mg/hr for 48 hours (not titrated) Bolus 20mg IV if patient has high plateau pressure (>32mmHg for >10 minutes); repeat dose if plateau pressure remains high. Maximum 2 bolus doses within 24 hours

	<b>Vecuronium</b>	<b>Rocuronium</b>	<b>Cisatracurium</b>
<i>Pediatric Dosing</i>			
<b>Loading Dose</b>	0.08 – 0.1 mg/kg	0.6 – 1 mg/kg	0.1 mg/kg
<b>Maintenance Dose</b>			
<b>Intermittent Dosing** (Preferred)</b>	0.1 – 0.2 mg/kg IV every 1 – 2 hr. prn	0.3 – 1 mg/kg IV every 30 - 60min prn	N/A
<b>Continuous Infusion**</b>	0.05 – 0.2 mg/kg/hr.	5 – 15 mcg/kg/min	1 – 4 mcg/kg/min

\* Use **ideal body weight** for dose calculation of NMBAs in adult patients

\*\* Titration: Use lowest dose for initial dose, then adjust to minimum effective dose based on TOF monitoring and clinical assessment (see below).

#### *Characteristics of Neuromuscular Blocking Agents*

	<b>Vecuronium</b>	<b>Rocuronium</b>	<b>Cisatracurium</b>
<b>Onset of Action (minutes)</b>	3 – 4	1 – 2	2 – 3
<b>Duration of Action (minutes)</b>	35 – 45	30 – 60	45 – 60
<b>Recovery Time (minutes)</b>	45 – 60	20 – 30	< 90
<b>Route of Elimination</b>	35 – 50% Hepatic 50% Renal	<75% Hepatic 33% Renal	5 – 10% Renal as unchanged drug Hoffman Elimination
<b>Notes</b>	Accumulates in patients with renal and/or hepatic insufficiency, use decreased dose and extended interval.	Dose adjustments needed in patients with hepatic and/or multiple organ dysfunction	Drug of choice in patients with ARDS, severe renal and/or hepatic impairment.

#### *Potential Complications from Prolonged Neuromuscular Blockade and Prevention Strategies*

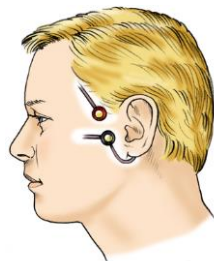
<b>Potential complications</b>	<b>Prevention strategies</b>
Skin breakdown, pressure ulcers	Frequent turning
Corneal drying/ulcers	Scheduled (not PRN) Lacrilube ointment to prevent corneal drying
Deep vein thrombosis	Pharmacological DVT prophylaxis, or SCDs if heparin contraindicated
Inadequate sedation and analgesia	Provide adequate sedation (RASS of -4 to-5) and analgesia <b>prior</b> to NMBA administration with regular assessments
Aspiration risk	Elevate head of bed if enteral feedings are used
Secretion accumulation	Regular suctioning
Muscle weakness	Ankle sprints and range of motion daily

### **C. MONITORING DURING NEUROMUSCULAR BLOCKADE**

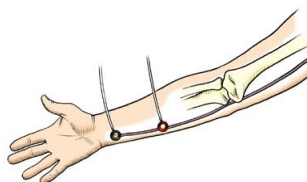
1. All patients receiving continuous neuromuscular blockade should be monitored with a peripheral nerve stimulator (train-of-four, TOF) **in conjunction with** clinical assessment.
2. Clinical assessment:
  - a) Ventilator synchrony
  - b) Airway pressures
  - c) Extremity movement
  - d) Degree of shivering

3. Procedure for peripheral nerve stimulator/ train-of four (TOF) monitoring:

- a) TOF may be performed at the ulnar or facial nerve. Ulnar nerve stimulation may become difficult if there is significant peripheral edema. Facial nerve stimulation may be more appropriate in this situation.
- b) Place 2 standard EKG electrodes at selected site, 2cm apart (for more detailed description on proper placement, refer to Peripheral Nerve Stimulation Section in Lippincott Procedures - <http://procedures.lww.com/lmp/view.do?pld=48137>).



Facial Nerve



Ulnar Nerve

- c) Attach alligator clips to the electrodes (polarity unimportant).
  - d) Determine the supramaximal stimulus (mAmps needed to produce 4 strong twitches).  
**This step should be done prior to initiation of NMBA.**
    - i. Set the peripheral nerve stimulator to 20-30 mAmps and depress TOF pad on the stimulator.
    - ii. Watch for twitches or feel for twitches in the thumb or hand or eyebrow.
    - iii. Increase the mAmps until 4 strong twitches of the same magnitude are seen/felt. (allow 10 seconds before repeating)
    - iv. Document the mAmps on ICU Vital Signs Flowsheet (Advanced Monitoring: Train of Four) to correspond to the supramaximal stimulus; do not increase mAmps and continue to use baseline mAmps during NMBA therapy
  - e) Retest the TOF 10 – 15 minutes after the bolus dose of NMBA is given and/or the continuous infusion is initiated.
  - f) If no twitches are seen/felt, perform troubleshooting procedures (i.e. reverse alligator clips, check electrode placement, check batteries). If no technical problems are discovered, hold NMBA until 1-2 twitches return, then restart at a decreased dose.
4. Frequency of TOF monitoring:
- a) For intermittent dosing, perform TOF before every dose and 15 min post dose, titrate dose until desired level of blockade achieved.
  - b) For continuous infusion, check TOF 10 – 15 minutes after bolus dosing, then check TOF every 30 minutes x 4 after infusion manipulation, titrate dose until desired level of blockade achieved.
  - c) Once achieved stable blockade (4 consecutive stable TOF assessment), TOF can be done every 4 hours.
  - d) Frequent monitoring with TOF should be done with each dose adjustments.
5. Record results of TOF monitoring in the **ICU Vital Signs Flowsheet (In Advanced Monitoring: Train of Four)** along with any dose adjustments. Format of documentation: TOF x/4 @ x mAmps (e.g., TOF 2/4 @ 20mAmps)

### Train-Of-Four Interpretation and NMBAs Suggested Dose Adjustments

# of Twitches	Degree of Paralysis	Suggested Dose Adjustments
0	100%- complete blockade  Drug accumulation <b>or</b> electrical current during nerve stimulation not transmitted.	Hold dose until 1 out of 4 twitches returns on TOF and restart at 75% of previous rate/dose or extend the interval (extend interval from q2hr to q3-4hr)
1	90% blockade  Goal for paralysis of diaphragm.	Continue current dose
2	≈ 85% blockade  Acceptable goal for most patients.	Continue current dose <b>or</b> rebolus with initial bolus dose and increase maintenance dose by 10% if 1:4 twitches is desired
3	≈ 80% blockade  Acceptable for some patients.	Rebolus with initial bolus dose and increase maintenance dose by 10% for more paralysis
4	< 75% blockade  Residual blockade may be present.	Rebolus with initial bolus and increase rate/dose by 20%  If patient is recovering from the NMBA, may use a 5 second head-lift to check for residual paralysis

6. Appropriate sedation/analgesia should be evaluated regularly by assessment of changes in parameters that may indicate stress or pain. Unexplained elevations in heart rate or blood pressure, diaphoresis, or tearing may indicate anxiety or wakefulness in the patient receiving NMBAs. Sedation/analgesia should not be titrated down, until the patient's TOF is 4 out of 4 (not paralyzed).

#### D. DRUG-DRUG INTERACTIONS:

1. Medications that potentiate the effects of neuromuscular blocking agents:
  - Antiarrhythmics (procainamide, quinidine)
  - Antimicrobials (aminoglycosides, polymyxin B, colistimethate, clindamycin, tetracycline)
  - Corticosteroids
  - Lidocaine
  - Magnesium
  - Calcium channel blockers
  - $\beta$ -Adrenergic blockers
  - Immunosuppressive agents (cyclosporine)
  - Dantrolene
  - Diuretics
  - Lithium carbonate
2. Medications that decrease the effects of neuromuscular blocking agents:
  - Phenytoin
  - Carbamazepine
  - Theophylline
  - Calcium
3. Conditions that may prolong neuromuscular blockade:
  - Hypothermia
  - Hypokalemia
  - Acidemia

## **E. ADVERSE EFFECTS:**

1. Histamine release: generally, insignificant clinically but may occur with all the NMBAs in large bolus doses, administered rapidly. Histamine release predominantly occurs with use of atracurium, minimal to none with use of cisatracurium, vecuronium and rocuronium.
2. Cardiovascular: tachycardia (vagolytic effect – minimal to none with vecuronium and cisatracurium, some with high dose rocuronium), bradycardia, mild hypotension.
3. Tachyphylaxis: therapeutic resistance may occur with all NMBAs due to up regulation of the receptors; may occur less with bolus dosing; may need to increase dose or switch to a different agent.
4. Prolonged neuromuscular blockade from accumulation: minimized with regular TOF monitoring, using lowest effective dose, and decreasing cumulative dose.
5. Acute quadriplegic myopathy syndrome (AQMS):
  - a. Occurs with all agents, unpredictable.
  - b. Risk factors: concurrent corticosteroids, aminoglycosides, immunosuppressive agents, hyperglycemia, nutritional deficiencies
  - c. Diffuse weakness may persist long after the discontinuation of neuromuscular blockade. Affected muscles include both upper and lower extremities, but extraocular muscles are normally preserved. Sensory function is preserved
  - d. Severity can range from mild weakness to quadriplegia

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