# MEMO

**To:** YNHHS Medical Staff

**From:** YNHHS ICU Committee

**Subject:** SBAR: Alternative Drug Shortage Guide (Sedatives, Analgesics, Paralytics)

**Date:** May 18, 2020

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**Situation:** There is a need to provide guidance on currently available and alternative therapies for sedation, analgesia and paralysis.

**Background**: As a result of the increase in volume of COVID-19 critically ill patients, there is a nationwide shortage in commonly used sedatives, analgesics and paralytics. Several alternative medications have been acquired to meet the increased demand for these therapies. Additionally, there is an ongoing expansion of critical care units and familiarizing staff with these newly added agents is warranted.

**Assessment:** There is a need for an alternative therapy guide to familiarize clinicians with available therapies for sedation, analgesia, and paralysis.

**Recommendation**: The alternative drug therapy guide below will provide guidance to clinicians on existing and alternative therapies.

**Sedatives, Analgesics, Neuromuscular Blocking Agents – Alternative Drug Shortage Guide**

**Drug supply is inconsistent and changes frequently, alternative therapies will be guided based on drug availability**

**ANALGESICS**

**Analgesia Management** (current inventory may determine selection)
**Preferred**: Morphine, fentanyl (preferred in AKI, CKD, and RRT)
**Alternative**: Hydromorphone (continuous infusion) -pharmacist order entry (patients with high opioid requirements; receiving 10 mg IV morphine per hour for at least 2 hours)
Remifentanil - pharmacist order entry
Ketamine - pharmacist order entry (patient with adverse reaction to hydromorphone and when remifentanil not available)
**Adjunct therapy**: Enteral acetaminophen, tramadol, gabapentin, oxycodone, methadone

**SEDATIVES**

**Sedation Management** (optimize pain management, current inventory may determine selection)
**Preferred**: Dexmedetomidine (not for deep level of sedation)
Propofol
**Alternative**:Midazolam (use with caution in hepatic and renal dysfunction)
Ketamine - pharmacist order entry, third-line agent, restricted to the following:
- Escalating doses or contraindication to propofol (≥65 mcg/kg/min or TG >600 mg/dL)
- Escalating doses to midazolam/lorazepam (≥10mg/hr) or contraindication to midazolam (cirrhosis, AST/ALT >5xULN) and lorazepam (Osmol gap >10 mOsm/kg)

Phenobarbital monotherapy for management of alcohol withdrawal syndrome
**Critical shortage**: Lorazepam (use with caution in hepatic and renal dysfunction)
**Adjunct therapy**: to lower sedation requirements; phenobarbital, enteral clonidine, atypical antipsychotic (quetiapine, olanzapine)

**PARALYTICS**

**Neuromuscular blocking agents continuous infusion** (adequate sedation and analgesia required prior to and during paralysis, current inventory may determine selection)
**Preferred**: Rocuronium
Cisatracurium - pharmacist order entry (preferred in AKI, CKD, RRT, and/or hepatic dysfunction)
**Alternative**: Atracurium - pharmacist order entry (preferred in AKI, CKD, RRT, and/or hepatic dysfunction and cisatracurium not available)
**Critical shortage**: Vecuronium

**Neuromuscular blocking agents for rapid sequence intubation** current inventory may determine selection
**Preferred**: Succinylcholine
**Alternative**: Rocuronium

*AKI: acute kidney injury; CKD: chronic kidney disease (CrCl <30 mL/min); RRT: renal replacement therapy; TG: serum triglyceride (mg/dL); ULN: upper lower limit of normal*

| Drug | Mechanism of action | Dosing recommendation | Side effects and considerations |
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| **ANALGESICS (continuous infusion therapy for mechanically ventilated patients)** | | | |
| **Morphine**<br><br>100 mg/100 mL (1 mg/mL) | Opioid (mu)-receptor agonist | MD: 1 -10 mg/hr<br>Titrate by: 1 mg/hr<br>Frequency: No more than every 15 minutes<br>Maximum dose: 10 mg/hr<br><br>IV Bolus: 2-4 mg IV q 4 hr PRN or scheduled | Hypotension and bradycardia can occur due to histamine release.<br><br>Avoid in renal dysfunction due to accumulation of active metabolite.<br><br>Use with caution in hepatic dysfunction.<br><br>Can cause respiratory depression, CNS depression, constipation, and ileus. |
| **Hydromorphone**<br><br>40 mg/100 mL (0.4 mg/mL) | | MD: 0.2 – 5 mg/hr<br>Titrate by: 0.2 mg/hr<br>Frequency: No more than every 30 minutes<br>Maximum Dose: 5 mg/hr<br><br>IV Bolus: 0.5 – 1 mg IV q 2 hr PRN or scheduled | Hydromorphone is 5 - 7 times MORE POTENT than morphine.<br><br>Use lower doses in opioid-naïve patients.<br><br>Use with caution in hepatic dysfunction.<br><br>Can cause respiratory depression, CNS depression, constipation, and ileus. |
| **Remifentanil**<br><br>5000 mcg/100 mL (50 mcg/mL) | | MD: 0.5 – 12.5 mcg/kg/hr<br>Titrate by : 1.5 mcg/kg/hr<br>Frequency: No more than every 5 minutes<br>Maximum dose: 12.5 mcg/kg/hr<br><br>Use actual body weight. Use ideal body weight (IBW) if patient's actual weight is 130% > IBW<br><br>IV Bolus: 25 – 100 mcg every 30 min PRN | Monitor for opiate withdrawal symptoms for 24 hours after discontinuing Remifentanil. Consider x1 dose of morphine/hydromorphone injection prior to remifentanil infusion discontinuation.<br><br>Can cause chest wall rigidity.<br><br>Drug clearance occurs by blood and tissue esterases.<br><br>Can cause respiratory depression, CNS depression, constipation, and ileus. |
| **ANALGESIA ADJUNCT THERAPY (consider adjunct therapy to lower continuous infusion analgesia requirements)** | | | |
| **Oxycodone** | Opioid (mu)-receptor agonist | PO: 2.5 – 10 mg PO q 4 hr PRN or scheduled | |
| **Tramadol** | Opioid (mu)-receptor agonist, inhibit norepinephrine and serotonin reuptake, and NMDA receptor antagonist | PO: 25 – 100 mg PO q6 hr<br>Maximum dose: 400 mg/day | Avoid in patients with seizure disorder.<br><br>Associated with serotonin syndrome<br><br>Hepatically metabolized to active metabolite O-desmethyltramadol that is renally eliminated.<br><br>Requires dose adjustment in renal failure |
| **Gabapentin** | Inhibits alpha 2-delta subunit of voltage-gated calcium channels → reduce neuronal hyper-excitability | PO: 300 mg – 1200 mg three times daily | Preferred therapeutic option for neuropathic pain.<br><br>Adjust dose based on renal function. |
| **Methadone** | Mu-receptor agonist, NMDA-receptor antagonist | PO: 5 – 10 mg PO q8 – 12 hr scheduled | Very long half-life (up to 60 hours)<br><br>Dose-dependent QTc prolongation |

| SEDATIVES<br>(Continuous infusion for mechanically ventilated patients, optimize pain management) | | | |
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| **Propofol**<br><br>1000 mg in 100 mL (10 mg/mL)<br><br>500 mg in 50 mL (10 mg/mL) | GABA modulator | LD: Not recommended outside RSI<br>MD: 5-80 mcg/kg/min<br>Start: 5 mcg/kg/min<br>Titrate by: 5 mcg/kg/min<br>Frequency: No more than every 5 minutes<br>Maximum Dose: 80 mcg/kg/min | Bolus and rapid dose titration can cause cardiac and respiratory depression.<br><br>Propofol-related infusion syndrome (PRIS) at doses >65 mcg/kg/min for >48 hours.<br><br>Tubing should be changed every 12 hours.<br><br>Avoid in patient allergic to egg or soy products. |
| **Midazolam**<br><br>50 mg/50 ml NS (1 mg/mL)<br><br>100 mg/100 mL NS (1 mg/mL) | | LD: 0.5-1 mg<br>MD: 0.5-20 mg/hr<br>Start: 0.5 mg/hr<br>Titrate by: 0.25 mg/hr<br>Frequency: No more than every 5 minutes<br>Maximum Dose: 20 mg/hr | Respiratory depression<br><br>Use with caution in renal and hepatic impairment.<br><br>Monitor for CYP-enzyme drug-drug interactions. |
| **Lorazepam**<br><br>50 mg/50 ml D5W (1 mg/mL)<br><br>100 mg/100 mL D5W (1 mg/mL) | | LD: 0.5-1 mg<br>MD: 1-20 mg/hr<br>Start: 1 mg/hr<br>Titrate by: 0.5 mg/hr<br>Frequency: No more than every 15 minutes<br>Maximum Dose: 20 mg/hr | Respiratory depression<br><br>At high doses, propylene glycol excipient can cause hypotension, metabolic acidosis, increase in osmolality (>320 mOsm/Kg), acute tubular necrosis. Monitor arterial blood gas pH, osmolar gap, serum creatinine, and urine output.<br><br>Use with caution in hepatic and renal (mild and moderate) impairment. |
| **Dexmedetomidine**<br><br>200 mcg/50 mL D5W (4 mcg/mL)<br><br>400 mcg/100 mL D5W (4 mcg/mL)<br><br>1000 mcg/250 mL NS (4 mcg/mL)-pharmacist order entry only | $\alpha_2$-Adrenergic receptor agonist | MD: 0.2-1.4 mcg/Kg/hr<br>Start: 0.2 mcg/kg/hr<br>Titrate by: 0.1 mcg/kg/hr<br>Frequency: No more than every 30 minutes<br>Maximum Dose: 1.4 mcg/kg/hr | Dexmedetomidine doesn't provide deep sedation (RASS <-3)<br><br>LD is not recommended, as IV push is associated with hypotension and bradycardia.<br><br>Does not cause respiratory depression<br><br>Can cause hypotension, bradycardia<br><br>Caution with use in hepatic dysfunction<br><br>Withdrawals symptoms can occur. Consider oral clonidine to taper off dexmedetomidine. |
| **Ketamine**<br><br>5000 mg in NS 500 mL (10 mg/mL)<br><br>2500 mg in NS 250 mL (10 mg/mL) | NMDA receptor antagonist | LD: 1 mg/Kg<br>MD: 0.3 – 2 mg/kg/hr<br>Start: 0.3 mg/kg/hr<br>Titrate by: 0.1 mg/kg/hr<br>Frequency: No more than every 15 minutes<br>Maximum Dose: 2 mg/kg/hr | Contraindicated in acute decompensated heart failure.<br><br>Use with caution in cerebral vascular accident and elevated intra-cranial pressures, and pulmonary hypertension.<br><br>Associated with dissociative "emergence reaction"<br><br>Can cause hypersalivation, lacrimation, and tachycardia<br><br>Monitor for CYP-enzyme drug-drug interactions |

| ADJUNCT SEDATIVES<br>(consider adjunct therapy to lower continuous infusion sedation requirements) | | | |
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| **PHENobarbital**<br><br>65 mg/mL and 130 mg/mL vials | Long-acting barbiturate | Dose IV/IM (adjunct for sedation): 30 to 120 mg/day IV in 2 or 3 divided doses; do not exceed a rate of 60 mg/min<br><br>Maximum 400 mg/day | Respiratory depression<br><br>May cause hypotension.<br><br>IV formulation contains propylene glycol; may cause metabolic acidosis.<br><br>Monitor for CYP-enzyme drug-drug interactions |
| **Clonidine (PO)**<br><br>0.05 mg, 0.1 mg, 0.3 mg, 0.6 mg | $\alpha_2$-Adrenergic receptor agonist | Oral: 0.1-0.3 mg q 6-8 hr<br><br>Titrate to achieve sedation, 0.2 to 0.5 mg every 6 hours<br><br>Consider as an adjunct to other sedatives | Can cause bradycardia, hypotension, and xerostomia.<br><br>Can prolong effect in renal impairment.<br><br>Consider to prevent dexmedetomidine withdrawal symptoms. |
| **Olanzapine (PO/IV/IM)**<br><br>2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg<br>10 mg/vial | Atypical antipsychotic<br><br>Affects central dopamine, muscarinic, serotonin receptors, and peripheral α-1 receptors | Use as adjunct therapy<br>PO: 5 – 10 mg every 2 hours<br>IV/IM: 1.25-10 mg repeat every 2-4 hours<br>Maximum daily dose of 30 mg | May alter cardiac conduction and prolong the QT interval<br><br>Avoid concomitant use of IV benzodiazepines as they may enhance the adverse effect of benzodiazepines (cardiorespiratory depression) |
| **Quetiapine (PO)**<br><br>12.5 mg, 25 mg, 50 mg, 100 mg, 200 mg, 300mg, 400 mg | Atypical antipsychotic<br><br>Affects Serotonin, dopamine, histamine , and adrenergic receptors | PO: 50 mg BID, increase by 100 mg /day to a total dose to 400 mg/day | May alter cardiac conduction and prolong the QT interval |
| **PARALYTICS**<br>**(adequate sedation and analgesia required prior to paralysis)** | | | |
| **Rocuronium**<br><br>10 mg/mL (5 ml vials)<br><br>100 mg/100 mL (1 mg/mL)<br><br>500 mg/100 mL (5 mg/mL) | Inhibit acetylcholine at motor endplate | Initial bolus: 0.6 – 1 mg/kg<br>MD: 5 – 12 mcg/kg/min<br>Titrate by: 1 mcg/kg/min<br>Frequency: No more than every 20 minutes<br>Maximum dose: 12 mcg/kg/min<br><br>RSI: 1 to 1.2 mg/kg followed by 20 ml of NS flush | Appropriate alternative to succinylcholine for RSI<br><br>Avoid in hepatic and renal dysfunction<br><br>Can cause tachycardia |
| **Vecuronium**<br><br>40 mg/100 mL (0.4 mg/mL) | | Initial bolus with rocuronium<br>MD: 0.8 – 1.2 mcg/kg/min<br>Titrate by: 0.1 mcg/kg/min<br>Frequency: No more than every 30 minutes<br>Maximum dose: 1.2 mcg/kg/min | Active hepatic and renal metabolites, avoid in hepatic and renal dysfunction |

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| **Cisatracurium**<br><br>40 mg/100 mL (0.4 mg/mL)<br><br>200 mg/100 mL (2 mg/mL), pharmacist order entry only | | Initial bolus with rocuronium<br>MD: 0.5 -10 mcg/kg/min<br>Titrate by: 0.5 mcg/kg/min<br>Frequency: No more than every 15 minutes<br>Maximum dose: 10 mcg/kg/min | Can cause bronchospasm, bradycardia |
| **Atracurium**<br><br>500 mg/100 mL (5 mg/mL) | | Initial bolus with rocuronium<br>MD: 5 - 20 mcg/kg/min<br>Titrate by: 1 mcg/kg/min<br>Frequency: No more than every 15 minutes<br>Maximum dose: 20 mcg/kg/min | Fast administration can cause hypotension, flushing, and bronchospasm<br><br>Tachyphylaxis can occur at high dose. |
| **Succinylcholine**<br><br>20 mg/mL (10 mL vials) | | RSI: 1-1.5 mg/kg | Avoid in hyperkalemia<br><br>May cause a transient increase in intracranial pressure. |

*CYP: cytochrome; GABA: gamma aminobutyric acid; IV: intravenous; IM: intramuscular; LD: initial loading dose; MD: maintenance dose; NMDA: N-methyl-D-aspartate receptor; PO: oral; RSI: rapid sequence intubation*