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, Hydromorphone *(preferred in AKI, CKD, and RRT)*
- **Alternative:** Remifentanil, Ketamine

**Adjunct therapy:** Enteral acetaminophen, tramadol, gabapentin, oxycodone, methadone

**Sedation Management** *(optimize pain management, current inventory may determine selection)*

- **Preferred:** Dexametomidine *(not for deep level of sedation)*, Propofol
- **Alternative:** Midazolam *(use with caution in hepatic and renal dysfunction)*, Ketamine, 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)*.

**SEDATIVES**

**Neuromuscular blocking agents continuous infusion** *(adequate sedation and analgesia required prior to and during paralysis, current inventory may determine selection)*

- **Preferred:** Rocuronium, Cisatracurium *(preferred in AKI, CKD, RRT, and/or hepatic dysfunction)*
- **Alternative:** Atracurium *(preferred in AKI, CKD, RRT, and/or hepatic dysfunction)*

**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
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Dosing recommendation</th>
<th>Side effects and considerations</th>
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<tr>
<td><strong>ANALGESICS</strong> (continuous infusion therapy for mechanically ventilated patients)</td>
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</tbody>
</table>
| **Morphine** | 100 mg/100 mL (1 mg/mL) | MD: 1 - 10 mg/hr  
Titrate by: 1 mg/hr  
Frequency: No more than every 15 minutes  
Maximum dose: 10 mg/hr  
IV Bolus: 2-4 mg IV q 4 hr PRN or scheduled | Hypotension and bradycardia can occur due to histamine release.  
Avoid in renal dysfunction due to accumulation of active metabolite.  
Use with caution in hepatic dysfunction.  
Can cause respiratory depression, CNS depression, constipation, and ileus. |
| **Hydromorphone** | 40 mg/100 mL (0.4 mg/mL) | MD: 0.2 – 5 mg/hr  
Titrate by: 0.2 mg/hr  
Frequency: No more than every 30 minutes  
Maximum Dose: 5 mg/hr  
IV Bolus: 0.5 – 1 mg IV q 2 hr PRN or scheduled | Hydromorphone is 5 - 7 times MORE POTENT than morphine.  
Use lower doses in opioid-naïve patients.  
Use with caution in hepatic dysfunction.  
Can cause respiratory depression, CNS depression, constipation, and ileus. |
| **Remifentanil** | 5000 mcg/100 mL (50 mcg/mL) | MD: 0.5 – 12.5 mcg/kg/hr  
Titrate by: 1.5 mcg/kg/hr  
Frequency: No more than every 5 minutes  
Maximum dose: 12.5 mcg/kg/hr  
Use actual body weight. Use ideal body weight (IBW) if patient’s actual weight is 130% > IBW  
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.  
Can cause chest wall rigidity.  
Drug clearance occurs by blood and tissue esterases.  
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  
Maximum dose: 400 mg/day | Avoid in patients with seizure disorder.  
Associated with serotonin syndrome  
Hepatically metabolized to active metabolite O-desmethyltramadol that is renally eliminated.  
Requires dose adjustment in renal failure |
| **Gabapentin** | Inhibits alpha 2-delta subunit of voltage-gated calcium channels → reduce neuronal hyperexcitability | PO: 300 mg – 1200 mg three times daily | Preferred therapeutic option for neuropathic pain.  
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)  
Dose-dependent QTc prolongation |
| **SEDATIVES**  
(Continuous infusion for mechanically ventilated patients, optimize pain management) |
|---------------------------------------------------------------|
| **Propofol**  
1000 mg in 100 mL (10 mg/mL)  
500 mg in 50 mL (10 mg/mL)  |
| LD: Not recommended outside RSI  
MD: 5-80 mcg/kg/min  
Start: 5 mcg/kg/min  
Titrater by: 5 mcg/kg/min  
Frequency: No more than every 5 minutes  
Maximum Dose: 80 mcg/kg/min  |
| Bolus and rapid dose titration can cause cardiac and respiratory depression.  
Propofol-related infusion syndrome (PRIS) at doses >65 mcg/kg/min for >48 hours.  
Tubing should be changed every 12 hours.  
Avoid in patient allergic to egg or soy products.  |
| **GABA modulator**  
**Midazolam**  
50 mg/50 ml NS (1 mg/mL)  
100 mg/100 ml NS (1 mg/mL) |
| LD: 0.5-1 mg  
MD: 0.5-20 mg/hr  
Start: 0.5 mg/hr  
Titrater by: 0.25 mg/hr  
Frequency: No more than every 5 minutes  
Maximum Dose: 20 mg/hr  |
| Respiratory depression  
Use with caution in renal and hepatic impairment.  
Monitor for CYP-enzyme drug-drug interactions.  |
| **Lorazepam**  
50 mg/50 ml D5W (1 mg/mL)  
100 mg/100 ml D5W (1 mg/mL) |
| LD: 0.5-1 mg  
MD: 1-20 mg/hr  
Start: 1 mg/hr  
Titrater by: 0.5 mg/hr  
Frequency: No more than every 15 minutes  
Maximum Dose: 20 mg/hr  |
| Respiratory depression  
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.  
Use with caution in hepatic and renal (mild and moderate) impairment.  |
| **Dexmedetomidine**  
200 mcg/50 mL D5W (4 mcg/mL)  
400 mcg/100 mL D5W (4 mcg/mL)  
1000 mcg/250 mL NS (4 mcg/mL)- pharmacist order entry only |
| α2-Adrenergetic receptor agonist  
LD: 0.2-1.4 mcg/Kg/hr  
MD: 0.2 mcg/kg/hr  
Start: 0.2 mcg/kg/hr  
Titrater by: 0.1 mcg/kg/hr  
Frequency: No more than every 30 minutes  
Maximum Dose: 1.4 mcg/kg/hr  |
| Dexmedetomidine doesn’t provide deep sedation (RASS <-3)  
LD is not recommended, as IV push is associated with hypotension and bradycardia.  
Does not cause respiratory depression  
Can cause hypotension, bradycardia  
Caution with use in hepatic dysfunction  
Withdrawals symptoms can occur. Consider oral clonidine to taper off dexmedetomidine.  |
| **Ketamine**  
5000 mg in NS 500 mL (10 mg/mL) |
| LD: 1 mg/Kg  
MD: 0.3 – 2 mg/kg/hr  
Start: 0.3 mg/kg/hr  
Titrater by: 0.1 mg/kg/hr  
Frequency: No more than every 15 minutes  
Maximum Dose: 2 mg/kg/hr  |
| Contraindicated in acute decompensated heart failure.  
Use with caution in cerebral vascular accident and elevated intra-cranial pressures, and pulmonary hypertension.  
Associated with dissociative “emergence reaction”  
Can cause hypersalivation, lacrimation, and tachycardia  
Monitor for CYP-enzyme drug-drug interactions  |
### SEDATIVES
(consider adjunct therapy to lower continuous infusion sedation requirements)

| **PHENobarbital** | **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** | Respiratory depression
| | **Maximum 400 mg/day** | May cause hypotension.
| | **IV formulation contains propylene glycol; may cause metabolic acidosis.** | IV formulation contains propylene glycol; may cause metabolic acidosis.
| | **Monitor for CYP-enzyme drug-drug interactions** | Monitor for CYP-enzyme drug-drug interactions |
| **PHENobarbital** | 65 mg/mL and 130 mg/mL vials | Long-acting barbiturate
| **Clonidine (PO)** | Oral: 0.1-0.3 mg q 6-8 hr | Can cause bradycardia, hypotension, and xerostomia.
| | Titrated to achieve sedation, 0.2 to 0.5 mg every 6 hours | Can prolong effect in renal impairment.
| | Consider as an adjunct to other sedatives | Consider to prevent dexmedetomidine withdrawal symptoms. |
| **Olanzapine (PO/IV/IM)** | Use as adjunct therapy | May alter cardiac conduction and prolong the QT interval
| | PO: 5 – 10 mg every 2 hours | Avoid concomitant use of IV benzodiazepines as they may enhance the adverse effect of benzodiazepines (cardiorespiratory depression)
| | IV/IM: 1.25-10 mg repeat every 2-4 hours | May alter cardiac conduction and prolong the QT interval
| | Maximum daily dose of 30 mg | |
| **Quetiapine (PO)** | PO: 50 mg BID, increase by 100 mg/day to a total dose of 400 mg/day | |

### PARALYTICS
(adequate sedation and analgesia required prior to paralysis)

| **Rocuronium** | Initial bolus: 0.6 – 1 mg/kg | Appropriate alternative to succinylcholine for RSI
<p>| | MD: 5 – 12 mcg/kg/min | Avoid in hepatic and renal dysfunction |
| | Titrate by: 1 mcg/kg/min | Can cause tachycardia |
| | Frequency: No more than every 20 minutes | |
| | Maximum dose: 12 mcg/kg/min | |
| | RSI: 1 to 1.2 mg/kg followed by 20 ml of NS flush | |
| <strong>Vecuronium</strong> | Initial bolus with rocuronium | Active hepatic and renal metabolites, avoid in hepatic and renal dysfunction |
| | MD: 0.8 – 1.2 mcg/kg/min | |
| | Titrate by: 0.1 mcg/kg/min | |
| | Frequency: No more than every 30 minutes | |
| | Maximum dose: 1.2 mcg/kg/min | |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Administration Instructions</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisatracurium</td>
<td>40 mg/100 mL (0.4 mg/mL)</td>
<td>Initial bolus with rocuronium MD: 0.5 - 10 mcg/kg/min</td>
<td>Can cause bronchospasm, bradycardia</td>
</tr>
<tr>
<td></td>
<td>200 mg/100 mL (2 mg/mL)</td>
<td>Titrate by: 0.5 mcg/kg/min</td>
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<tr>
<td></td>
<td>pharmacist order entry only</td>
<td>Frequency: No more than every 15 minutes</td>
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<tr>
<td></td>
<td></td>
<td>Maximum dose: 10 mcg/kg/min</td>
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<tr>
<td></td>
<td></td>
<td>Can cause bronchospasm, bradycardia</td>
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<tr>
<td>Atracurium</td>
<td>500 mg/100 mL (5 mg/mL)</td>
<td>Initial bolus with rocuronium MD: 5 - 20 mcg/kg/min</td>
<td>Fast administration can cause hypotension, flushing, and bronchospasm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Titrate by: 1 mcg/kg/min</td>
<td>Tachyphylaxis can occur at high dose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frequency: No more than every 15 minutes</td>
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<tr>
<td></td>
<td></td>
<td>Maximum dose: 20 mcg/kg/min</td>
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<tr>
<td>Succinylcholine</td>
<td>20 mg/mL (10 mL vials)</td>
<td>RSI: 1-1.5 mg/kg</td>
<td>Avoid in hyperkalemia</td>
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<tr>
<td></td>
<td></td>
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<td>May cause a transient increase in intracranial pressure.</td>
</tr>
</tbody>
</table>

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