COVID-19 Analgesia and Sedation Treatment Algorithms – IV with PO Analgesia

All patients receiving continuous analgesia and/or sedation should receive daily SATs/SBTs per institution-specific policies.

**Algorithm 1 – IV with PO Analgesia**

Assess patient for pain (Wong-Baker, CPOT ≥ 3, BPS >3)

- **Positive for pain**
  - Hydromorphone 1mg IV x 1 **PLUS** scheduled PO/NG Analgesia regimen* **PLUS** Hydromorphone 0.5 mg IV q30min PRN
  - OR
  - Morphine 4mg IV x 1 **PLUS** scheduled PO/NG Analgesia regimen* **PLUS** Morphine 2 mg IV q30min PRN
  - OR
  - Fentanyl 50mcg IV x 1 **PLUS** scheduled PO/NG Analgesia regimen* **PLUS** Fentanyl 50 mcg IV q30 min PRN
  - (DOC for renal failure or hemodynamic instability)

  Dose escalation should be performed for patients requiring 2 PRN doses per hour (e.g. Consider up to hydromorphone 1mg, morphine 4mg, fentanyl 100mcg)

- **Negative for pain**
  - Assess for need for sedation

If requiring > 4 PRN doses (after increases in dosing) in any 2-hour period

- **Fentanyl infusion^** **PLUS** scheduled, dose-escalated PO/NG Analgesia regimen* **PLUS**
  - Fentanyl 25-50mcg IV bolus PRN prior to titrating up on the infusion rate

  If fentanyl not available

- **Hydromorphone infusion PLUS** scheduled PO/NG Analgesia regimen* **PLUS**
  - Hydromorphone 0.5mg IV bolus PRN
  - (Hydromorphone preferred in renal dysfunction)
  - OR
  - Morphine infusion PLUS scheduled PO/NG Analgesia regimen PLUS
  - Morphine 1-2mg IV bolus PRN

  Refractory agitation

- **Assess for need for sedation**

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- Once pain has been controlled or ruled out as a cause of agitation, move to Algorithm 2 for sedative management.
- All patients receiving continuous analgesia and/or sedation should receive **DAILY** SATs/SBTs per institution-specific policies. If pain/sedation goals are met, attempt to decrease by 10-25% when resuming infusion after assessment – titrate up/down based on response.
- ^For patients on fentanyl infusion at rates above 150mcg/hr without ability to titrate down, providers can consider the addition of Fentanyl patches:
  - Initiate Fentanyl patch at 50% of current rate and reduce IV infusion rate by 50% 6 hours after application of the first transdermal patch
  - Continue to wean drip, based on patient assessment, to reduce overall IV drug consumption

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*Scheduled PO/NG Analgesia Regimens – Options include:
- Hydromorphone 4 mg PO/NG Q4H SCH
- Oxycodone IR 5 mg PO/NG Q4H SCH
- Hydrocodone/Acetaminophen 10/325mg PO/NG Q6H SCH

**Adjunctive PO/NG Agents:**
- APAP** 650 mg PO/NG Q4H SCH (if not already receiving)
- Gabapentin^^ 300 mg PO/NG Q8H SCH (if pt has historical use, resume previous regimen at prior-to-admission dose)

**Max daily dose of Acetaminophen from all sources is 4000 mg/day. For patient with hepatic failure, doses up to 2000 mg/day are considered safe.

^^For patient with renal dysfunction, dose adjustments will be done per Renal Dosing Guidelines
### Algorithm 2 – IV with PO Sedation

The following recommendations are in order of preference and are subject to availability.

1. **Pt with continuous IV analgesia requiring sedation**
   - **Paralyzed** (Ensure adequate pain and sedation)
   - **Not paralyzed**

   **Propofol infusion + Midazolam/Lorazepam IVP PRN option**
   - OR **Midazolam infusion + Midazolam/Lorazepam IVP PRN option**
     - (If not available, alternate therapies include ketamine and/or phenobarbital)

2. **Midazolam 5mg IV x 1 PLUS Diazepam 5mg PO Q6hr PLUS**
   - Midazolam 2-5mg IV Push Q 30 min PRN
   - OR **Lorazepam 4mg IV x 1 PLUS Lorazepam 2mg PO Q6hr PLUS**
     - Lorazepam 2 mg IV Push Q 30 min PRN

   Dose escalation of scheduled and/or PRN regimen should be performed for patients requiring 2 PRN doses per hour (e.g. Consider up to Diazepam 10mg, Lorazepam 4mg)

3. **If requiring >3 PRN doses in any 2-hour period**
   - **Continue PO/NG scheduled Diazepam/Lorazepam regimen above PLUS**
     - Propofol infusion (preferred)
   - **Check baseline TG and Q 48 hr**
   - **If TG ≥ 400 or Propofol dose ≥ 40 mcg/kg/min, re-check TG Q 24 hr**
     - Notify physician if TG ≥ 700
     - (Recommend D/C therapy if TG > 1000)

4. **If propofol unavailable or patient refractory**
   - **Continue PO/NG scheduled Diazepam/Lorazepam regimen above PLUS**
     - Midazolam infusion PLUS Midazolam IV bolus PRN per standard protocol

5. **If additional adjunctive therapy needed OR propofol and midazolam unavailable**
   - Phenobarbital 65 mg IV/PO/NG x1 followed by 30 mg IV/PO/NG Q 4 hr PRN RASS > 0 (maximum 400 mg/day)
     - OR **Dexmedetomidine infusion* (see text box) per standard protocol**
     - OR **Ketamine infusion per standard protocol**

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- All patients receiving continuous analgesia and/or sedation should receive **DAILY** SATs/SBTs per institution-specific policies. If pain/sedation goals are met, attempt to decrease by 10-25% when resuming infusion after assessment – titrate up/down based on response.
- Refer to attached table for further information on dosing, side effects and monitoring.
- * Dexmedetomidine should be reserved for patients with agitation to avoid intubation or weaning mechanical ventilation in patients who cannot tolerate being off sedation.
- In the case of a severe IV sedation shortage, Algorithm 3 (all PO therapy) is to be implemented.
Algorithm 3 – All PO Analgesia & Sedation Protocol

**IV analgesia/sedation agents are critically low or not available**

- **Paralyzed**
  - Oxycodone 5 mg PO Q 6 hr (up to 10 mg PO q6h), OR
  - Norco 5/325 Q 6 hr (if LFTs ok), OR
  - Hydromorphone 2-4 mg PO Q 4 hr
  - PLUS
    - Diazepam 5-10 mg PO Q 8 hr OR
    - Lorazepam 6 mg PO Q 4 hr (up to 10 mg PO Q 4 hr)
  - Titrate up until RASS -4 to -5 prior to paralysis

  If RASS remains greater than -4 on diazepam 10mg PO Q 8 hr OR lorazepam 10 mg PO Q 4 hr

  Add:
  - Phenobarbital 65 mg PO q12h (titrate to maximum of 400 mg PO/day)

- **Not paralyzed**
  - Assess pain scale (Wong-Baker, CPOT, or BPS)
  - Positive for pain
    - Oxycodone 5 mg PO Q 6 hr + 5 mg PO Q 4 hr PRN, OR
    - Norco 5/325 Q 6 hr (if LFTs ok), OR
    - Hydromorphone 2-4 mg PO Q 4 hr
    - (increase dosing if pain is not under control)
    - Diazepam 5-10 mg Q 8 hr OR
    - Lorazepam 4 mg PO Q 4 hr around the clock (up to 10 mg PO Q 4 hr)
    - Persistent agitation despite adequate pain control
    - If RASS remains greater than -4 on diazepam 10mg PO Q 8 hr OR lorazepam 10 mg PO Q 4 hr
    - Add:
      - Phenobarbital 65 mg PO q12h (titrate to maximum of 400 mg PO/day)
  - Negative for pain
### Analgesics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate Parenteral Equianalgesic Dose (mg)</th>
<th>Onset</th>
<th>Half-Life</th>
<th>Continuous Infusion</th>
<th>Side Effects and Considerations</th>
<th>Special Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>IV: 1-2 min</td>
<td>2-4 hr</td>
<td>IV: 25-50 mcg every 0.5-1 hr</td>
<td>N/A</td>
<td>Adjust by 25 mcg/hr (0.5 mcg/kg/hr) every 15 min + 50 mcg Q 30 min; give bolus dose prior to increasing drip rate based on PRN frequency</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>IV: 5-10 min</td>
<td>2-3 hr</td>
<td>IV: 0.2-0.6 mg every 1-2 hr Enteral: 2-4 mg every 4-6 hr</td>
<td>0.5 mg</td>
<td>Adjust by 0.2 mg/hr every 30 min + 0.5 mg Q2H PRN; give bolus dose prior to increasing drip rate based on PRN frequency</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
<td>IV: 5-10 min</td>
<td>3-4 hr</td>
<td>IV: 2-4 mg every 1-2 hr Enteral: 10-30 mg</td>
<td>N/A</td>
<td>Adjust by 1 mg/hr every 30 min; give bolus dose prior to increasing drip rate based on PRN frequency</td>
</tr>
<tr>
<td>Ketamine</td>
<td>N/A</td>
<td>IV: 30-40 sec</td>
<td>2-3 hr</td>
<td>IV: 0.1-0.5 mg/kg; may repeat as needed</td>
<td>0.5-1 mg/kg</td>
<td>Adjust by 0.5 mg/kg/hr every 15 minutes</td>
</tr>
<tr>
<td>Drug</td>
<td>Onset</td>
<td>Half-Life</td>
<td>Initial IV Dosing (Intermittent)</td>
<td>Continuous Infusion</td>
<td>Loading Dose</td>
<td>Initial Rate of Infusion</td>
</tr>
<tr>
<td>------------</td>
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<td>-----------</td>
<td>----------------------------------</td>
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<td>--------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Midazolam</td>
<td>2-5 min</td>
<td>3-11 hr</td>
<td>2-4 mg every 0.5-2 hr</td>
<td>Continuous Infusion</td>
<td>2.5 mg</td>
<td>1 mg/hr (0.02mg/kg/hr)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2-5 min</td>
<td>20-120 hr</td>
<td>2.5-10 mg every 4-6 hr</td>
<td>Continuous Infusion</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>15-20 min</td>
<td>8-15 hr</td>
<td>1-2 mg every 2-6 hr</td>
<td>Continuous Infusion</td>
<td>2 mg</td>
<td>1 mg/hr</td>
</tr>
<tr>
<td>Propofol</td>
<td>1-2 min</td>
<td>1.5-12.4 hr</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>5 mcg/kg/min</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>5-10 min</td>
<td>1.8-3.1 hr</td>
<td>N/A</td>
<td>N/A</td>
<td>0.2 mcg/kg/min</td>
<td>Adjust by 0.1 mcg/kg/hr every 15 min</td>
</tr>
<tr>
<td>Ketamine</td>
<td>30-40 sec</td>
<td>2-3 hr</td>
<td>0.1-0.5 mg/kg IV; may repeat as needed</td>
<td>Continuous Infusion</td>
<td>0.5-1 mg/kg</td>
<td>1 mg/kg/hr</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>5 min</td>
<td>53-140 hr</td>
<td>Bolus with 7.5 mg/kg IV over 1-2 hr then 1-2mg/kg/day divided every 12 hr; for adults less than 90 kg, initiate at 65mg every 12 hr</td>
<td>Continuous Infusion</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
- All patients receiving paralysis should have the following orders in place:
  - Continuous adequate sedation and pain management (BIS 40-60, RASS -4 to -5)
  - Artificial tears ointment should be applied daily (at a minimum) as well as q1h PRN dry eyes
    - Place in order comments: Please apply to both eyes every time room is entered.
    - KEEP TUBE AT BEDSIDE, SHOULD NOT RE-ENTER Pyxis.

**PLEASE NOTE:**
Product selection will be driven by local Pharmacy inventory

Refer to attached table for details on dosing, side effects, and monitoring
**Pharmacokinetics/Pharmacodynamics & Dosing**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Onset of Action (min)</th>
<th>Clinical Duration of Initial Dose (min)</th>
<th>Half-life (min)</th>
<th>ED₉₀ Adult Dose (mg/kg)</th>
<th>Initial Intubation Bolus Dosing</th>
<th>Continuous Infusion</th>
<th>Elimination (Renal, Hepatic, Biliary, Plasma)</th>
<th>OTHER COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra-Short Duration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinylcholine (Quelicin*)</td>
<td>0.5-1</td>
<td>4-8</td>
<td>Unknown</td>
<td>0.2</td>
<td>1-1.5</td>
<td>n/a</td>
<td>n/a</td>
<td>Plasma, &lt;10% Renal, No active metabolites</td>
</tr>
<tr>
<td>Atracurium (Tracrium*)</td>
<td>2-3</td>
<td>20-45</td>
<td>20</td>
<td>0.2</td>
<td>0.4-0.5</td>
<td>0.08-0.1 mg/kg Q 30 min</td>
<td>0.4-0.5</td>
<td>Hofmann elimination, ester hydrolysis, &lt;5% Renal</td>
</tr>
<tr>
<td>Cisatracurium (Nimbex*)</td>
<td>2-3</td>
<td>40-60</td>
<td>22-29</td>
<td>0.05</td>
<td>0.15-0.2</td>
<td>0.03 mg/kg Q 30-60 min</td>
<td>0.1-0.2</td>
<td>Hofmann elimination, ester hydrolysis &lt;20% Renal/Hepatic</td>
</tr>
<tr>
<td>Rocuronium (Zemuron*)</td>
<td>1-2</td>
<td>31-67</td>
<td>60-70</td>
<td>0.3</td>
<td>0.6-1.2</td>
<td>0.1-0.225 mg/kg Q 30 min PRN</td>
<td>0.6-1</td>
<td>30% Renal, 50% Biliary, No active metabolites</td>
</tr>
<tr>
<td>Vecuronium (Norcuron*)</td>
<td>2-3</td>
<td>20-40</td>
<td>51-80</td>
<td>0.05</td>
<td>0.08-0.1</td>
<td>0.1-0.2 mg/kg Q 30-60 min</td>
<td>0.08-0.1</td>
<td>10-20% Renal, 20-30% Hepatic, 40-75% Biliary, No active metabolites</td>
</tr>
<tr>
<td>Intermediate Duration</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Atracurium (Tracrium*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active metabolites, Minimal/no change in renal/hepatic failure, Histamine release (hypotension)</td>
</tr>
<tr>
<td>Cisatracurium (Nimbex*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active metabolites, Minimal/no change in renal/hepatic failure, Reserve for patients experiencing tachyphylaxis or Neuro</td>
</tr>
<tr>
<td>Rocuronium (Zemuron*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increased duration in renal failure, moderate increased effect in hepatic failure, Can cause vagal block (tachycardia) at higher doses</td>
</tr>
<tr>
<td>Vecuronium (Norcuron*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active metabolites, Increased effect in renal failure, mild increased effect in hepatic failure, Has prolonged ICU block</td>
</tr>
</tbody>
</table>

**Alteration in Duration of Action in Various Patient Groups**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Children</th>
<th>Elderly</th>
<th>Renal Failure</th>
<th>Hepatic Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultra-Short Duration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinylcholine (Quelicin*)</td>
<td>↓?</td>
<td>↔ or ↑?</td>
<td>↔</td>
<td>↑</td>
</tr>
<tr>
<td><strong>Intermediate Duration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium (Tracrium*)</td>
<td>↓</td>
<td>↔</td>
<td>↔ or ↑</td>
<td>↔</td>
</tr>
<tr>
<td>Cisatracurium (Nimbex*)</td>
<td>↓</td>
<td>↑</td>
<td>↔</td>
<td>↑</td>
</tr>
<tr>
<td>Rocuronium (Zemuron*)</td>
<td>↓</td>
<td>↑</td>
<td>↔</td>
<td>↑</td>
</tr>
<tr>
<td>Vecuronium (Norcuron*)</td>
<td>↓</td>
<td>↑</td>
<td>↔ or ↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

? = possible effect or insufficient data

**Medications Affecting Neuromuscular Blocker Activity**

<table>
<thead>
<tr>
<th>Potentiate</th>
<th>Antagonize</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics: procainamide, quinidine, verapamil</td>
<td>Antiepileptics: carbamazepine, phenytoin</td>
</tr>
<tr>
<td>Antibiotics: aminoglycosides, tetracyclines, clindamycin</td>
<td>Other: ranitidine, theophylline</td>
</tr>
<tr>
<td>Cardiovascular medications: Beta-blockers, Calcium channel blockers</td>
<td>Cations: calcium, magnesium</td>
</tr>
<tr>
<td>Immunosuppressants: cyclophosphamide, cyclosporine</td>
<td>Immunosuppressants: cyclophosphamide, cyclosporine</td>
</tr>
<tr>
<td>Inhaled anesthetics: desflurane, sevoflurane, isoflurane, halothane</td>
<td>Local anesthetics</td>
</tr>
<tr>
<td>Other: dantrolene, diuretics, lithium</td>
<td>Other: dantrolene, diuretics, lithium</td>
</tr>
</tbody>
</table>