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

Algorithm 1 – IV with PO Analgesia
All patients receiving continuous analgesia and/or sedation should receive daily SATs/SBTs per institution-specific policies.

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)

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

Negative for pain

Assess for need for sedation

*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

• 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

• 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

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**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

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)

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)

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)

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

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

• 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)
    - Persistent agitation despite adequate pain control
      - Diazepam 5-10 mg PO Q 8 hr OR Lorazepam 4 mg PO Q 4 hr around the clock (up to 10 mg PO Q 4 hr)
      - 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
<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate Parenteral Equianalgesic Dose (mg)</th>
<th>Onset</th>
<th>Half-Life</th>
<th>Initial Intermittent Dosing</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>Loading: N/A, Initial Infusion Rate: 25 mcg/hr (0.7 mcg/kg/hr)</td>
<td>Adjust by 25 mcg/hr every 15 min + 50 mcg Q 30 min; give bolus dose prior to increasing drip rate based on PRN frequency</td>
<td>Muscle rigidity when administered in high doses; Less hypotension than with morphine; accumulation with hepatic impairment</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>IV: 5-10 min, Enteral: 15-30 min</td>
<td>2-3 hr</td>
<td>IV: 0.2-0.6 mg every 1-2 hr</td>
<td>N/A, Initial Infusion Rate: 0.5 mg/hr</td>
<td>Adjust by 0.2 mg/hr every 20 min + 0.5 mg Q2H PRN; give bolus dose prior to increasing drip rate based on PRN frequency</td>
<td>Potential for potency-related dosing errors; May work in patients tolerant to morphine/fentanyl; accumulation with hepatic/renal impairment</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
<td>IV: 5-10 min, Enteral: 30 min</td>
<td>3-4 hr</td>
<td>IV: 2-4 mg every 1-2 hr</td>
<td>N/A, Initial Infusion Rate: 1 mg/hr</td>
<td>Adjust by 1 mg/hr every 30 min; give bolus dose prior to increasing drip rate based on PRN frequency</td>
<td>Hypotension, bronchospasm; Accumulation with hepatic/renal impairment</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>Loading: 0.5-1 mg/kg/hr, Initial Infusion Rate: 1 mg/kg/hr</td>
<td>Adjust by 0.5 mg/kg/hr every 15 minutes</td>
<td>May cause hallucinations and other psychological disturbances; consider administration of benzodiazepines to attenuate psychological disturbances; Attenuates the development of acute tolerance to opioids; potential for neurotoxicity with prolonged use</td>
</tr>
<tr>
<td>Drug</td>
<td>Onset</td>
<td>Half-Life</td>
<td>Initial IV Dosing (Intermittent)</td>
<td>Continuous Infusion</td>
<td>Side Effects and Considerations</td>
<td>Special Comments</td>
<td></td>
</tr>
<tr>
<td>------------</td>
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</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>Loading Dose: 2.5 mg, Initial Rate of Infusion: 1 mg/hr (0.02mg/kg/hr) every 10 min; GIVE BOLUS DOSE WITH EACH RATE INCREASE</td>
<td>Respiratory depression</td>
<td>Intermittent dosing preferred; active metabolite prolongs sedation, especially in patients with renal failure</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>2-5 min</td>
<td>2-12 hr</td>
<td>2.5-10 mg every 4-6 hr</td>
<td>N/A</td>
<td>N/A</td>
<td>Intermitent dosing preferred; consider enteral administration</td>
<td></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>Loading Dose: 1 mg/hr, Initial Rate of Infusion: 1 mg/hr (0.02mg/kg/hr) every 15 min; GIVE BOLUS DOSE WITH EACH RATE INCREASE</td>
<td>Respiratory depression; propylene glycol-related acidosis; renal failure</td>
<td>Intermittent dosing preferred; no active metabolites</td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>1-2 min</td>
<td>1.5-12.4 hr</td>
<td>N/A</td>
<td>Loading Dose: 5 mcg/kg/min, Initial Rate of Infusion: 5 mcg/kg/min every 5 min</td>
<td>Hypotension, respiratory depression, hypertriglyceridemia, pain on injection when administered through peripheral vein, pancreatitis, propofol-related infusion syndrome</td>
<td>Use caution when hypotension is likely to occur (e.g. patients with compromised myocardial function, intravascular volume depletion, or abnormally low vascular tone [sepsis])</td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>5-10 min</td>
<td>1.8-3.1 hr</td>
<td>N/A</td>
<td>Loading Dose: 0.2 mcg/kg/hr, Initial Rate of Infusion: 0.2 mcg/kg/hr every 15 min</td>
<td>Bradycardia, hypotension</td>
<td>No active metabolites</td>
<td></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>Loading Dose: 0.5-1 mg/kg, Initial Rate of Infusion: 1 mg/kg every 15 min; Adjust by 0.5 mg/kg/day every 15 min</td>
<td>May cause hallucinations and other psychological disturbances; consider administration of benzodiazepines to attenuate psychological disturbances</td>
<td>Attenuates the development of acute tolerance to opioids; potential for neurotoxicity with prolonged use</td>
<td></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>N/A</td>
<td>Respiratory depression, potential for drug interaction due to hepatic enzyme induction</td>
<td>May supplement with 65 mg every 1 hr as needed and consider increasing scheduled dose if frequent supplemental doses are required; do not exceed administration rate of 60mg/min</td>
<td></td>
</tr>
</tbody>
</table>
COVID-19 Neuromuscular Blocker Treatment Algorithm

PaO₂/FiO₂ ≤ 150 on PEEP
≥ 15 cm H₂O at 24 hours of mechanical ventilation

Rocuronium 0.6-1 mg/kg Intermittent Bolus Dosing (round to nearest 50 mg) IV push PRN

If rocuronium not available

Vecuronium 0.2 mg/kg Intermittent Bolus Dosing (round to nearest 10 mg) IV push PRN

If requiring >5 doses in any 24-hour period

Atracurium IV push load dose followed by titratable infusion
OR
Rocuronium IV push load dose followed by titratable infusion
OR
Cisatracurium IV push load dose followed by titratable infusion

Titrated to ventilator compliance

If atracurium, rocuronium, cisatracurium not available

Vecuronium titratable infusion

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

Refer to attached table for details on dosing, side effects, and monitoring

- All patients receiving paralysis should have the following orders in place:
  o Continuous adequate sedation and pain management (BIS 40-60, RASS -4 to -5)
  o 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.
### 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>ED₉₅ (mg/kg)</th>
<th>Initial Intubation Adult Dose (mg/kg)</th>
<th>Intermittent Bolus Dosing</th>
<th>Continuous Infusion</th>
<th>Elimination (Renal, Hepatic, Biliary, Plasma)</th>
<th>OTHER COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultra-Short Duration</strong></td>
<td></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>n/a</td>
<td>Plasma, &lt;10% Renal, Histamine release (hypotension)</td>
</tr>
<tr>
<td><strong>Intermediate Duration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></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>4-12</td>
<td>Hofmann elimination, ester hydrolysis, &lt;5% Renal, Minimal/no change in renal/hepatic failure, Histamine release (hypotension)</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>2.5-3</td>
<td>Hofmann elimination, ester hydrolysis &lt;20% Renal/Hepatic, Minimal/no change in renal/hepatic failure, Reserve for patients experiencing tachyphylaxis or Neuro</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>10-12</td>
<td>30% Renal, 50% Biliary, 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>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>0.8-1.2</td>
<td>10-20% Renal, 20-30% Hepatic, 40-75% Biliary, 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>Atracurium (Tracrium®)</td>
<td>↓</td>
<td>↔</td>
<td>↔ or ↑</td>
<td>↔</td>
</tr>
<tr>
<td>Cisatracurium (Nimbex®)</td>
<td>↓</td>
<td>↑</td>
<td>↔ or ↑</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></td>
</tr>
<tr>
<td>Cations: calcium, magnesium</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressants: cyclophosphamide, cyclosporine</td>
<td></td>
</tr>
<tr>
<td>Inhaled anesthetics: desflurane, sevoflurane, isoflurane, halothane</td>
<td></td>
</tr>
<tr>
<td>Local anesthetics</td>
<td></td>
</tr>
<tr>
<td>Other: dantrolene, diuretics, lithium</td>
<td></td>
</tr>
</tbody>
</table>