**Supplemental Table 3. Recommendations for Analgesics, Sedatives, and Neuromuscular Blockers in the Setting of Medication ShortagesA**

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| --- | --- | --- | --- | --- | --- |
|  | **Analgesia** | | **Sedation** | | **Neuromuscular blockade** |
| **Goals** | **VAS10 ≤4;**  **(CPOT ≤3 or BPS ≤5)** | **CPOT ≤3 or BPS ≤5** | **Light sedation**  **RASS = -2 to 0;**  **SAS = 3 to 4** | **Deep sedation**  **RASS = -3 to -5;**  **SAS = 1 to 2** | **Always with deep sedation**  **RASS = -3 to -5;**  **SAS = 1 to 2** |
| **Light sedation goal**  **RASS = -2 to 0;**  **SAS = 3 to 4** | **Deep sedation goal**  **RASS = -3 to -5;**  **SAS = 1 to 2** |
| **First-line regimens** | -PRN fentanyl or hydromorphone IVP q15minA  -Scheduled acetaminophen  -Scheduled gabapentin or pregabalin if neuropathic pain | -Fentanyl or hydromorphone infusion  -Scheduled acetaminophen  -Scheduled gabapentin or pregabalin if neuropathic pain | -Dexmedetomidine infusion  -Propofol boluses | -Propofol infusion | -PRN Vecuronium bolus  -Cisatracurium infusion if PRN Vecuronium bolus not adequate |
| **Second-line regimens**  *(if first-line not available*) | -PRN oxycodone IR or hydromorphone IVP q4-6 hrB  -Fentanyl patch (when pain requirements consistent) | -Sufentanil infusion  -Scheduled oxycodone IR or hydromorphone IVP q 4-6 hours | -Midazolam boluses  -Scheduled clonidine or guanfacine | -Midazolam infusion | -Atracurium infusion |
| **Third-line regimens**  *(if second-line not available)* | -Remifentanil infusion  -Morphine IR  -Sufentanil SL | -Scheduled methadone oral or IV  -Ketamine infusion  -Morphine Infusion | -Lorazepam boluses  -PRN oral lorazepam or diazepam  -Haloperidol IV or oral  -Valproic acid IV or oral  -Quetiapine oral  -Olanzapine IM or oral | -Lorazepam infusion  -Scheduled lorazepam or diazepam (oral)C | -Vecuronium infusion or - -Rocuronium infusion |
| **Fourth-line regimens**  *(if third-line not available)* | -PRN meperidine oral or IV | -Scheduled methadone oral or IV  -Meperidine infusion | -PRN clonazepam or alprazolam  -Phenobarbital IV or oral  - Inhaled sedatives | -Chloral hydrate | -Pancuronium bolus or infusion |

BPS Behavioral Pain Scale; CPOT Critical Care Pain Observation Tool; IM Intramuscular; IR Immediate Release; IV Intravenous; SL Sublingual; PRN ‘as needed’; PT per enteral tube; Q every; SAS Sedation Agitation Scale; RASS Richmond Agitation Sedation Scale; VAS Visual Analog Scale.

AIf a specific route of medication is not indicated in table, it is oral. For each oral medication, if not available as an oral liquid, it can be crushed, mixed in water, and administered via a nasogastric or enteral tubes.

BIf greater than three doses administered in 1 hour, consider a continuous infusion.

CStart with prn and if require every PRN dose then change to a scheduled regimen.

DConsider using in addition to IV lorazepam to minimize the risk of propylene glycol toxicity.

**Table 4: Properties of Second, Third and Fourth-Line Analgesics, Sedatives and Neuromuscular Blockers.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Medication** | **Time to onset (mins)** | **Half-Life** | **Primary**  **metabolic**  **pathway** | **Active**  **Metabolite** | **Dosing** | **Adverse Effects** | **Other Notable Characteristics** |
| **Analgesics** | | | | | | | |
| Fentanyl transdermal  patch | 5-15 | 20-27 h | Hepatic via N-dealkylation (CYP 3A4/5 substrate) | None | 12-300 mcg applied q72h | -Serotonin syndrome  -Local irritation | -Takes 24-72h to take effect  -May stay in system for several h after removal  -Dose should be determined through PT or IV opioids prior to administration |
| Hydromorphone (oral) | 15-30 | 2-3 h | Hepatic via glucuronidation | None | 2-4 mg q4-6 h |  | -Safe to use in patients with renal dysfunction |
| Ketamine  (IV) | 0.5 | 2.5 h | Hepatic via N-dealkalation | Norketamine | 0.5 mg/kg IV push followed by 1-2 mcg/kg/min infusion | -Delirium  -Hallucinations  -Hypertension  -Hypotension  -Increased secretions | -Should be used an adjunct to opioids |
| Meperidine  (IV/Oral) | IV: 5  Oral: 10-15 | 2.5-4 h | Hepatic via hydrolysis | Normeperidine | Bolus: 25-100 mg q 2-3 h  Infusion: 15-35 mg/h  Oral: 50-150 mg q3-4 h | Seizures | -Accumulation normeperidine in renal failure causes seizures |
| Methadone  (IV/Oral) | IV: 10-20  Oral:  30-60 | 8-59 h | Hepatic via N-demethylation (CYP3A4 and 2B6 substrate) | None | IV:2.5-10 mg q8-12h  PT: 10-40 mg q8-12h | -QT prolongation  -Serotonin syndrome | -Use caution with hepatic and renal dysfunction |
| Morphine | IV: 5-10  Oral: 30 | 3-4 h | Hepatic via glucuronidation | 6-morphine glucuronide | Bolus: 1-10 mg  Infusion:1-2 mg/h  PT: 10-30 mg q4h | -Hypotension secondary to histamine release  -Cholecystitis | -Use caution with liver or renal dysfunction |
| Oxycodone  (Oral) | 10-15 | 3.2-4 h | Hepatic (CYP3A4 substrate) | Oxymorphone | 5-20 mg q4-6h |  | Easily crushed and administered via PT |
| Remifentanil | 1-3 | 3-10 min | Hydrolysis by plasma and tissue esterases | None | Loading Dose: 1.5 mcg/kg  Infusion:0.15-15 mcg/kg/h | Hyperammonemia | -High incidence of opioid associated tachyphylaxis  -High incidence of opioid associated hyperalgesia  -Accumulation in obese patients, use IBW to dose  -Chest wall rigidity  -Expensive |
| Sufentanil | IV: 1-3  SL: 30 | IV: 164 min  SL:2.5+0.85 min | -Hepatic and small intestine demethylation and dealkylation  -Renal elimination | None | Bolus: 0.5 mcg/kg  Infusion:0.5 mcg/kg/h  SL: 30 mcg q1h prn (no more than 12 doses per day) | -Headache  -Pruritis | -Expensive  -Use caution with renal and liver dysfunction |
| **Sedatives** | | | | | | | |
| Alprazolam | <60 | 6.3-26.9 h | Hepatic (CYP 3A4 substrate) | 4-hydroxyalprazolam, α-hydroxyalpraz-olam | PT: 0.5 to 2 mg tid | Delirium | -Very short acting, may need more frequent dosing |
| Chloral hydrate | 15-30 | 8-12 h | Hepatic via alcohol dehydrogenase | Trichloroethan-ol | 1000 mg PT q6h | -Delirium  -Hypotension | -May not be available in the United States |
| Clonazepam | 20-40 | 17 to 60 min | Hepatic via glucuronide and sulfate conjugation, (CYP 3A4 substrate) | None | PT: 0.25-1 mg bid | Delirium |  |
| Clonidine | 30-60 | 12-16 h | Hepatic | None | PT: 0.1-0.3 q6-8h | -Headache  -Dizziness  -Hypotension |  |
| Diazepam | IV:2-5  PT: 15 | 20-50 h | Hepatic via hydoxylation (CYP 3A4/5 Substrate) | Temazepam | Bolus:  0.03-0.1 mg/kg ever 0.5-6 h  PT:2-10 mg q3-6h | -Hypotension  -Phlebitis  -Delirium |  |
| Guanfacine | 60-240 | 10-30 h | Hepatic (CYP 3A4 substrate) | None | PT: 0.5-2 mg qday | -Hypotension  -Headache  -Dizziness  -Abdominal pain |  |
| Haloperidol | IV: 3-20  PT: 120 | IV:14-26 h | Hepatic via CYP 3A4 and 2D6 | None | IV or PT: 2-10 mg q6h | -Anticholinergic  -EPS  -NMS  -QT prolongation |  |
| Lorazepam | IV: 5-20  PT: 15-60 | 10-20 h | Hepatic via glucuronidation | None | Bolus: 0.02-0.06 mg/kg q 2-6 h  Infusion:  0.01-0.1 mg/kg/h (<10 mg/h)  PT: 0.5-2 mg q4-6h | -Delirium  -Propylene Glycol Toxicity with IV | -Use caution with renal dysfunction |
| Midazolam | IV:3-5  PT: 10-20 | 3-12 h | Hepatic via hydroxylation (CYP3A4/5 substrate) | α1-hydroxymidazolam | Bolus: 0.01-0.05 mg/kg  Infusion: 0.02-0.1 mg/kg/h | -Delirium  -Hypotension  -Respiratory Depression | -Use caution in renal and hepatic dysfunction  -Many drug interactions |
| Olanzapine | IM: 15  PT: 30 | 21-54 h | Hepatic via glucuronidation (CYP1A2 substrate) | None | IM: 5 to 10 mg, may repeat 2 and 4 h after initial dose, max 30 mg/day  PT: 5-20 mg qday | -Anticholinergic  -EPS  -NMS  -Neuromuscular Weakness |  |
| Phenobarbital | IV: 5  PO: 60 | 79 h | Hepatic via CYP 2C9, 2C19, 2E1 and N-glucosidation | None | IV/PO: 10-40 mg tid (max 400 mg/day) | -Bradycardia  -Hypotension  -Agranulocytosis  -Thrombocytopenia | -Many drug interactions  -IV is expensive |
| Quetiapine | PT:20-40 | 6 h | Hepatic via CYP 3A4 | N-desalkyl quetiapine | PT: 50-200 mg bid | -Anticholinergic  -NMS  -Orthostatic Hypotension |  |
| Valproic Acid | IV:15  PT: immediately | 9-19 h | Hepatic via glucuronide conjugation and mitochondrial beta-oxidation (substrate of CYP 2A6, 2B6, 2C19, 2C9, 2E1) | None | IV or PT:  500-1250 mg bid | -Headache  -Hyperammonemia  -Thrombocytopenia  -Pancreatitis | -Use caution with hepatic dysfunction  -Many drug interactions |
| **Neuromuscular Blockers** | | | | | | | |
| Atracurium | 2-3 | 20 min | Hoffman elimination | Laudanosine | Bolus: 0.4-0.5 mg/kg  Infusion: 4 to 20 mcg/kg/min | Prolonged weakness | Safe to use in hepatic and renal dysfunction |
| Cisatracurium | 2-3 | 22-29 min | Hoffman elimination | None | Bolus: 0.1-0.2 mg/kg  Infusion: 1-3 mcg/kg/min | Prolonged weakness | Safe to use in hepatic and renal dysfunction |
| Pancuronium | 3-5 | 89-161 min | -Hepatic  -Renal Elimination | 3-hydroxy pancuronium | Bolus:0.06-0.1 mg/kg  Infusion:1-2 mcg/kg/min | Tachycardia | -Use caution in renal and hepatic dysfunction  -Very long duration of action |
| Rocuronium | 1-2 | 1.4-2.4 h | -Hepatic  -Renal elimination | 17-desacetyl rocuronium | Bolus: 0.6-1 mg/kg  Infusion:8-12 mcg/kg/min | -Tachycardia  -Prolonged weakness | Use continuous infusion with caution in hepatic or renal dysfunction |
| Vecuronium | 2.5-3 | 65-75 min | -Hepatic  -Renal elimination | 3-desacetyl vecuronium | Bolus: 0.08-0.1 mg/kg  Infusion: 0.8 to 1.7 mcg/kg/min | -Prolonged weakness | Use continuous infusion with caution in hepatic or renal dysfunction |

Bid twice daily; CYP cytochrome; EPS extrapyramidal symptoms; h hours; IBW ideal body weight; IM intramuscular; IR immediate release; IV intravenous; kg kilograms; mcg micrograms; min minutes; NMS neuroleptic symptoms; PRN ‘as needed’; PT per enteral tube; Q every; SL sublingual; .