## ALTERNATIVE PARENTERAL AGENTS FOR ANALGESIA AND SEDATION

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<th>INCOMPATIBILITIES</th>
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<tr>
<td><strong>SEDATIVE INFUSIONS</strong></td>
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<tr>
<td>Clonidine</td>
<td>Onset: 30-60 min T1/2: 6-13 hr</td>
<td>3 to 5 mcg/kg IV⁶</td>
<td>Start: 1.5 mcg/kg/hr</td>
<td>Adjust dosage hourly by 0.75 mcg/kg/hr, titrating to effect. Max: 3 mcg/kg/hr.⁷</td>
<td>Continuous: BP and HR *monitor closely in renal impairment</td>
<td>COMPOUND/DILUENT: In NS; a typical dilution is 500 mcg/50 mL (0.1 mg/mL).⁸ Similar dilutions trialed in 50 mL of D5W.⁷</td>
<td>No incompatibilities have been recognized in NS.</td>
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<td><strong>OFF LABEL USE</strong></td>
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<tr>
<td>Standard conc: 500mcg/50mL NS</td>
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<td>Chlorpromazine</td>
<td>Onset: 15-30 min T1/2: 2-30 hr</td>
<td>12.5 to 50 mg IV¹</td>
<td>Start: 0.05 mg/kg/hr</td>
<td>Start low and titrate slowly. Do not exceed max rate.</td>
<td>Continuous: BP Baseline and as indicated: EKG</td>
<td>Stable in sodium chloride 0.9% (NS) and dextrose 5% (D5W). Dilute 25-50 mg in 500-1000 mL of NS.</td>
<td>Numerous Y-site incompatibilities have been demonstrated, particularly with chlorpromazine concentrations of 2 mg/mL or greater.⁴ Some examples include acyclovir, bumetanide, cefazolin, and cefepime.</td>
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<tr>
<td>Standard conc: 25mg/500mL NS</td>
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<tr>
<td>Haloperidol lactate</td>
<td>Onset: 0.5-1 hr t½ = 10-20 hrs</td>
<td>0.5 to 5 mg IV</td>
<td>Start: 10 mg/hr¹⁰</td>
<td>Adjust dose by 5 mg/hr every 30 minutes</td>
<td>Baseline EKG, repeated 2 to 3 times daily or</td>
<td>COMPOUND/DILUENT: D₃W is the preferred diluent. Stability is demonstrated with 100</td>
<td>Numerous Y-site incompatibilities, including acyclovir, bumetanide, and</td>
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<td><strong>USE</strong></td>
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<td>Standard conc:</td>
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updated 04.07.2020

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**CHEMICAL PROPERTIES**

**Clonidine**

- **Standard conc:** 500mcg/50mL NS
  - **Onset:** 30-60 min
  - **T1/2:** 6-13 hr
  - **Range:** 1 to 3 mcg/kg/hr⁶
  - **Start:** 1.5 mcg/kg/hr
  - **Adjust dosage hourly by 0.75 mcg/kg/hr, titrating to effect. Max: 3 mcg/kg/hr.⁷
  - **Continuous:** BP and HR *monitor closely in renal impairment
  - **ADRs:** hypotension, bradycardia, dry mouth, dry eyes, nausea, and otalgia.

**Chlorpromazine**

- **Standard conc:** 25mg/500mL NS
  - **Onset:** 15-30 min
  - **T1/2:** 2-30 hr
  - **Range:** 0.05 to 0.2 mg/kg/hr²
  - **Start:** 0.05 mg/kg/hr
  - **Administer at 1 mg/min**
  - ***maximum 60 mg/hr**
  - **Continuous:** BP Baseline and as indicated: EKG
  - **ADRs:** Dystonic movements have been reported. Incident arrhythmias have been seen at high doses, mostly among patients with concurrent electrolyte abnormalities.³

**Haloperidol lactate**

- **Onset:** 0.5-1 hr
  - **t½:** 10-20 hrs
- **Standard conc:** 500mcg/50mL NS
  - **Range:** 0.5 to 5 mg IV
  - **Start:** 10 mg/hr¹⁰
  - ***max 10 mg, administered**
  - **Continuous:** BP Baseline and as indicated: EKG
  - **ADRs:** Dystonic movements have been reported. Incident arrhythmias have been seen at high doses, mostly among patients with concurrent electrolyte abnormalities.³

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**PHARMACOKINETICS**

**Clonidine**

- **Onset:** 30-60 min
- **T1/2:** 6-13 hr
- **Range:** 1 to 3 mcg/kg/hr⁶
- **Start:** 1.5 mcg/kg/hr
- **Adjust dosage hourly by 0.75 mcg/kg/hr, titrating to effect. Max: 3 mcg/kg/hr.⁷

**Chlorpromazine**

- **Onset:** 15-30 min
- **T1/2:** 2-30 hr
- **Range:** 0.05 to 0.2 mg/kg/hr²
- **Start:** 0.05 mg/kg/hr
- **Administer at 1 mg/min**
- **Continuous:** BP Baseline and as indicated: EKG
- **ADRs:** Dystonic movements have been reported. Incident arrhythmias have been seen at high doses, mostly among patients with concurrent electrolyte abnormalities.³

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**COMPOUND/DILUENT**

- **Clonidine:** In NS; a typical dilution is 500 mcg/50 mL (0.1 mg/mL).⁸ Similar dilutions trialed in 50 mL of D5W.⁷
- **Chlorpromazine:** Stable in sodium chloride 0.9% (NS) and dextrose 5% (D5W). Dilute 25-50 mg in 500-1000 mL of NS. Literature review suggests max concentration of 0.25 mg/mL for D5W
- **Haloperidol lactate:** D₃W is the preferred diluent. Stability is demonstrated with 100 mg/mL in D₃W

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**DILUTIONS**

- **Clonidine:** 500mcg/50mL NS
- **Chlorpromazine:** 25mg/500mL NS
- **Haloperidol lactate:** 500mcg/50mL NS

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**ADRS**

- **Clonidine:** hypotension, bradycardia, dry mouth, dry eyes, nausea, and otalgia.
- **Chlorpromazine:** Dystonic movements have been reported. Incident arrhythmias have been seen at high doses, mostly among patients with concurrent electrolyte abnormalities.³

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**REFERENCES**

1. Provided courtesy of U of I Hospital Pharmacy

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**UPDATES**

- Updated 04.07.2020
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<tr>
<td><strong>OFF LABEL USE</strong></td>
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<tr>
<td>Standard conc:</td>
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<td>over 1 minute, for cases of severe</td>
<td>5 to 25 mg/hr IV(^{10})</td>
<td>until achieving desired effect.</td>
<td>monitor QTc via telemetry strips</td>
<td>mg haloperidol lactate in 100 mL D5W(^{14})</td>
<td>heparin.(^4) See Micromedex.</td>
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<tr>
<td>100mg/100mL D5W</td>
<td></td>
<td>agitation</td>
<td>Soft max: 15 mg/hr(^{11})</td>
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<tr>
<td><strong>ANALGESIC INFUSIONS</strong></td>
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<tr>
<td>Hydromorphone</td>
<td>Onset: 5-15 mins t(_{1/2}) = 2-3 hrs</td>
<td>1 to 2 mg IV(^{11})</td>
<td>Start: 0.5 to 1 mg/hr IV(^{11,15})</td>
<td>Start low; titrate by 0.2 mg/hr q1hr</td>
<td>Continuous: BP and RR.</td>
<td>Continuous: BP and RR.</td>
<td>For continuous infusions, dilute 100 mg hydromorphone in 100 mL of either NS or D5W.(^{17}) Protect from light</td>
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<tr>
<td>Standard conc:</td>
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<tr>
<td>50mg/50mL NS</td>
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*Caution, accumulation may occur with repeated dosing.

**Avoid initiation if baseline QTc is > 500 ms.**
Discontinue if QTc becomes > 500 ms or > 20% baseline. Dystonic movements may occur.

ADRs: QTc prolongation + arrhythmias have occurred and are associated with baseline QTc and high (>20 mg), intermittent doses.\(^{12,13}\)

Discontinue if baseline QTc is > 500 ms. Dystonic movements may occur.

**Maximum Concentration:**\(^4\)
3mg/mL in D5W, although stability may be limited to 24 hours. For NS, max: 0.75 mg/mL

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<tr>
<td>Lidocaine</td>
<td>Onset: 45-90sec $t_{1/2}$: 1.5-2hr</td>
<td>1.5 mg/kg IV bolus $^{18}$ <strong>USE IBW</strong></td>
<td><strong>USE IBW</strong></td>
<td><strong>USE IBW</strong></td>
<td><strong>USE IBW</strong></td>
<td>Continuous: BP and EKG</td>
<td>Stable in NS and D5W. Typical dilution is 2 g lidocaine in 250 mL D5W (0.8%) or 500 mL D5W (0.4%).</td>
</tr>
</tbody>
</table>

| Standard conc: 2000mg/500mL D5W | Start: 1-2mg/kg/hour $^{15}$ | Max: 200 mg/hr | Titration not needed. May start at target dose. $^{15}$ | Continuous: BP and EKG | Light-headedness is common, altered mentation may occur. Local thrombophlebitis has occurred. | Consider therapeutic drug monitoring with prolonged infusions (>24 hrs), with a range 1 to 5 mcg/mL. $^{21}$ | Neurologic toxicities appear at concentrations > 6 mcg/mL, which includes altered mental status |

**Weight-based dosing for pediatrics** $^{16}$

- blood pressure $^{15}$
- *Administered over 2-3 minutes.
- *50% dose-reduction in acute heart failure, acute liver or decompensated cirrhosis $^{15}$
- *Max: 200 mg/hr
- *Administered over 2-3 minutes.

**MAXIMUM CONCENTRATION:** 0.1% (1 mg/mL)

| MAXIMUM CONCENTRATION: | 0.1% (1 mg/mL) | **COMPOUND/DILUENT:** $^{15,20}$ |

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<tr>
<td>Remifentanil</td>
<td>Standard conc: 1000mcg/250mL NS</td>
<td>Onset: 1-3min, $t_{1/2}$: 3-10min</td>
<td>0.5 to 1 mcg/kg, $t_{1/2}$: 3-10min</td>
<td>Start: 0.05 mcg/kg/min</td>
<td>Titrate by 0.025 mcg/kg/min every 5 minutes, as needed.</td>
<td>Continuous: RR and SpO$_2$</td>
<td>May dilute sterile water for injection (SWFI), D5W, D5W-NS, NS, and 1/2NS, and LR-D5W.</td>
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- and both visual and auditory disturbances. Respiratory depression and seizure become a concern at levels > 10 mcg/mL$^2$

- **Reversal of Toxicity:** Lipid rescue is indicated for toxic presentations associated with local anesthetics. Benzodiazepines should be used for seizures and amiodarone for resultant arrhythmias.

- **Remifentanil**
  - Standard concentration: 1000mcg/250mL NS
  - Onset: 1-3min, $t_{1/2}$: 3-10min
  - Start: 0.05 mcg/kg/min
  - Range: 0.05 to 0.25 mcg/kg/min
  - *If patient weight is > 130% IBW, use IBW$^3$
  - *If patient weight is > 130% IBW, use IBW$^4$
  - *Doses > 0.2 mcg/kg/min are associated with Continuous: RR and SpO$_2$
  - Daily monitoring of bowel movements.
  - **Reversal:** Naloxone 0.4 mg IV/SC/ET initially,
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</table>
| Phenobarbital | **OFF LABEL USE** | Onset: 5-10min<br><br>\( t_{1/2} \): >48h | 7.5 mg/kg IV bolus<br><br>*administered at a maximum rate of 50 mg/min | **INTERMITTENT PARENTERAL THERAPIES**<br><br>**Intermittent:** 1 to 2 mg/kg/day IV\(^2\) divided q8-12hrs; consider dose of 60mg IV q12hr for patients < 90kg<br><br>*Max administration rate 50 mg/min.<br><br>**Range:** Up to 65-400 mg/day | Adjust dosage by 30-60 mg increments, titrating to desired sedation<br><br>*If frequent supplemental boluses are required, consider increasing scheduled dose.<br><br>*When weaning is | Continuous: BP and RR.<br><br>Daily monitoring of osmolar gap should be considered. If there is suspicion of toxicity and the osmolar gap is elevated, consider ordering a serum propylene glycol level to confirm.<br><br>Monitor liver function tests as phenobarbital | **Large veins preferred. Avoid administration into or adjacent to an artery, as gangrene is an undesired consequence, potentially requiring amputation.**<br><br>Enteral routes are preferred when available. Absorption of phenobarbital is rapid and efficient.<br><br>**COMPOUND/DILUENT:** Dilute in NS or D5W. Typical dilution is 0 to 100 mg in 50 mL NS, doses more than 100 mg in 100 mL NS. | mitomycin, and pantoprazole.<br><br>Parenteral phenobarbital solutions are highly alkaline - avoid infusing with acidic solutions.<br><br>Protect from light.<br><br>Some of the known Y-site incompatibilities include cefotaxime, cefoxitin, cefuroxime, cyclosporine, diazepam, doxycycline, epinephrine, midazolam, phenytoin sodium, and

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<tr>
<td>Valproic acid</td>
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<td>desired, reduce daily dose by 50%. At 65 mg daily, discontinue. *Accumulation risk in severe renal failure (CrCl &lt; 10 mL/min)</td>
<td>may be hepatotoxic and may cause more side effects in individuals with reduced liver function. Therapeutic drug monitoring is recommended to avoid toxic levels (&gt; 40 mcg/mL). Target concentrations for sedation are between 5-40 mcg/mL.</td>
<td></td>
<td>trimethoprim-sulfamethoxazole. Visit Micromedex for a full list.</td>
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**OFF LABEL USE**

- **Onset:** unknown
- **\( t_{1/2} \): 9-16 hr**
- **Max rate 20 mg/kg/min**
- **Administered IV, PO, or by enteral tube**
- **Titration not required.**
- **Baseline CBC and LFTs are recommended, with intermittent repeat draws.**
- **COMPOUND/DILUENT:** May dilute in NS, D5W or lactate ringers (LR). A total volume of 50 mL is typical.

**MAXIMUM CONCENTRATION:** Concentrations up to 10 mg/mL in NS have been found to be stable.

28 trimethoprim-sulfamethoxazole.
4 Visit Micromedex for a full list.

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<td>hepatic impairment. Dose-reduction is advised.¹⁵</td>
<td>ADRs: Nausea and vomiting is common. Trend serum ammonia if suspecting toxicity. Therapeutic drug monitoring for sedation is poorly defined. Targeting free serum concentrations of 5 to 13 mg/ML has been suggested.⁹</td>
<td>MAXIMUM CONCENTRATION: Not well-defined, but 500 mg in 50 mL (10 mg/mL) is frequently used.</td>
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