

UNIVERSITY OF VIRGINIA HEALTH SYSTEM  
**ADULT AND GERIATRIC SEDATION/ANALGESIA FOR DIAGNOSTIC AND THERAPEUTIC PROCEDURES**

DRUG	CLASS & MECHANISM OF ACTION	DOSING GUIDELINES (IV ADMINISTRATION)	ONSET, PEAK EFFECT, AND DURATION OF ACTION	ADVERSE DRUG REACTIONS	COMMENTS	REVERSAL
<b>Midazolam</b> (Versed)	Benzodiazepine  (Binds to GABA receptor resulting in CNS depression)	<i>Adults 18 - 64 years of age:</i> 0.05 mg/kg repeated every 2 - 3 minutes to adequate sedation up to a max dose of 0.2mg/kg. (Small incremental doses of 1 - 3mg every 2-3 minutes up to an average total dose of 5mg)  <i>Elderly (&gt; 65) and those with COPD, congestive heart failure, or chronic debilitation:</i> 0.02mg/kg repeated every 2 - 3 minutes to adequate sedation up to a max dose of 0.2mg/kg (Small incremental doses of 0.5 - 1mg every 2-3 min)	Onset: 1- 3 min  Peak Effect: 5 -7 min  Duration of Action: 20 - 30 min	Respiratory and cardiovascular depression may occur. May also cause ataxia, dizziness, hypotension, bradycardia, blurred vision, and paradoxical agitation.	Advantages include quick onset and short duration of action. Due to quick onset and rapid clearance, is often the most satisfactory benzodiazepine for peri-procedure sedation. Combine with an opioid for painful procedures but reduce dose by 25 -50%. Cautions: (1,3)	Flumazenil (0.2mg over 15 seconds, may repeat at 1 min as needed)
<b>Lorazepam</b> (Ativan)	Benzodiazepine  (Binds to GABA receptor resulting in CNS depression)	<i>Adults 18 - 64 years of age:</i> 0.02 - 0.05 mg/kg repeated every 3-4 minutes up to a max dose of 4mg. (Small incremental doses of 1 -2 mg every 3-4 minutes up to a max dose of 4mg)  <i>Elderly (&gt; 65) and those with COPD, congestive heart failure, or chronic debilitation:</i> 0.02mg/kg repeated every 3-4 minutes up to a max dose of 4mg. (Small incremental doses of 0.5 - 1mg repeated every 3-4 minutes up to a max dose of 4mg)	Onset: 3 - 7 min  Peak Effect: 10-20 min  Duration of Action: 6-8 hours	Respiratory and cardiovascular depression may occur. May also cause ataxia, dizziness, hypotension, bradycardia, blurred vision, and paradoxical agitation.	Compared to midazolam, has slower onset and longer duration of action. In upper end of dosing range listed, may cause dysphoria and confusion. Due to slower onset and longer duration of action, has limited utility for procedural sedation. Combine with an opioid for painful procedures but reduce dose by 25 -50%. Cautions: (1,3)	Flumazenil (0.2mg over 15 seconds, may repeat at 1 min as needed)
<b>Diazepam</b> (Valium)	Benzodiazepine  (Binds to GABA receptor resulting in CNS depression)	<i>Adults 18 - 64 years of age:</i> 5mg which may be repeated every 5 minutes to a max dose of 20mg  <i>Elderly (&gt; 65) and those with COPD:</i> 2.5 mg which may be repeated every 5 minutes to a max of 10mg	Onset: 1 - 5 min  Duration of Action: 1 - 8 hours	Respiratory and cardiovascular depression may occur. May also cause ataxia, dizziness, hypotension, bradycardia, blurred vision, and paradoxical agitation.	Has a longer half-life and several long-acting active metabolites compared to midazolam and lorazepam. Due to longer and highly variable duration of action, has limited utility for procedural sedation. May be useful for longer procedures such as HBO treatment. Use with caution in the elderly due to unpredictable duration of action. Combine with an opioid for painful procedures but reduce the dose by 25 -50%. Caution: (1)	Flumazenil (0.2mg over 15 seconds, may repeat at 1 min as needed)
<b>Fentanyl</b> (Sublimaze)	Opioid narcotic  (Binds to opioid receptor in the CNS)	<i>Adults 18 - 64 years of age:</i> 0.5 -1 mcg/kg given in small incremental doses of 25 - 50 mcg up to a max dose of 250mcg  <i>Elderly (&gt; 65):</i> 0.5 - 1 mcg/kg given in small incremental doses of 25 mcg up to a max dose of 100mcg. The elderly are more susceptible to CNS depression.	Onset: 1 - 2 min  Peak Effect: 10-15 min  Duration of Action: 30 - 60 min	Hypotension, bradycardia, respiratory depression, nausea, vomiting, constipation, biliary spasm, and skin rash	Advantages include quick onset and short duration of action. Due to quick onset and rapid clearance, is often the most satisfactory opioid narcotic for peri-procedure sedation. Adverse effects are more common in the elderly. When combined with benzodiazepines, use reduced initial doses of each. Causes less histamine release and is associated with less hypotension and skin rash compared with morphine. Cautions: (1,2)	Naloxone (0.4mg initially followed by 0.1 - 0.2 mg every 2-3 min as needed) Caution: (4)

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<b>Meperidine</b> (Demerol)	Opioid narcotic  (Binds to opioid receptors in the CNS)	<i>Adults 18 - 64 years of age:</i> 25 - 50mg incremental doses to a max dose of 150mg  <i>Elderly (&gt; 65):</i> 25mg incremental doses to a max dose of 75mg. The elderly are more susceptible to CNS depression. The elderly are also more susceptible to seizures from nor-meperidine accumulation, a metabolite of meperidine, as a result of reduced renal function in the elderly.	Onset: 5 min  Peak Effect: 1 hour  Duration of Action: 2 - 4 hours	Hypotension, bradycardia, respiratory depression, nausea, vomiting, constipation, biliary spasm, and skin rash. Seizures as a result of nor-meperidine accumulation in patients with renal failure may also occur.	Has no major advantages over other opioids such as fentanyl and morphine, and is associated with a risk of seizures in patients with renal dysfunction. Use is not recommended in the elderly due to increased risk of adverse effects including seizures. When combined with benzodiazepines, use reduced initial doses of each. Cautions: (1,2)	Naloxone (0.4mg initially followed by 0.1 – 0.2 mg every 2-3 mins as needed) Caution: (4)
<b>Morphine</b>	Opioid narcotic  (Binds to opioid receptors in the CNS)	<i>Adults 18 - 64 years of age:</i> 2 - 4mg incremental doses every 5 minutes up to a max dose of 10 - 20mg  <i>Elderly (&gt; 65):</i> 1 - 2mg incremental doses every 5 minutes up to a max dose of 10mg. The elderly are more susceptible to CNS depression with opioid narcotic drugs.	Onset: 2 - 3 min  Peak Effect: 20 min  Duration of Action: 2 - 4 hours	Hypotension, bradycardia, respiratory depression, nausea, vomiting, constipation, biliary spasm, and skin rash	Slower onset and longer duration of activity compared to fentanyl. More histamine release associated with hypotension and itching compared to fentanyl. Adverse effects are more common in the elderly. When combined with benzodiazepines, use reduced initial doses of each. Cautions: (1,2)	Naloxone (0.4mg initially followed by 0.1 – 0.2 mg every 2-3 mins as needed) Caution: (4)
<b>Propofol</b> (Diprivan)	Hypnotic/anesthetic hindered phenolic compound  (General anesthetic and sedative properties; Structurally unrelated to opioid, barbiturate, and benzodiazepine drugs)	<i>Adults 18 - 64 years of age:</i> 10 - 20mg incremental doses every 5 minutes as needed to a max dose of 100mg. Give slow IV push to avoid hypotension.  <i>Elderly (&gt; 65):</i> 10mg incremental doses every 5 minutes as needed to a max dose of 50mg. Give slow IV push to avoid hypotension which is more common in the elderly and in hypovolemic patients.	Onset: 30 sec  Duration of Action: 10 - 15 min	Hypotension, heart block, asystole, and other arrhythmias, bradycardia, and possible infection from lipid based vehicle. Allergic reactions in patients with a history of an egg allergy.	Due to risk of hypotension, and bradycardia with bolus doses, use is restricted to monitored ICU/ED patients and/or use by anesthesia personnel. Has advantages of rapid onset and very short duration of action. Patients who are debilitated, cardio-vascularly compromised, hypovolemic, elderly, or on concomitant beta blockers are at greatest risk of hypotension. Has minimal to no analgesic effects; combine with an analgesic agent for painful procedures. Caution: Combinations of propofol and opioid narcotics may produce profound respiratory depression.	
<b>Ketamine</b> (Ketalar)	Dissociative general anesthetic arylcyclohexylamine agent  (Produces a cataleptic-like state in which the patient is dissociated from the surrounding environment; Produces intense analgesia and sedation without causing hypotension)	<i>Adults 18 - 64 years of age:</i> 0.2 - 1.0 mg/kg May repeat as necessary up to a maximum dose of 2mg/kg.  <i>Elderly (&gt; 65):</i> 0.2 - 0.75 mg/kg May repeat as necessary up to a maximum dose of 2mg/kg.	Onset: 1 - 2 min  Duration of Action: 15 - 30 min	Emergence CNS reactions including vivid dreams, hallucinations, and delirium; hypertension, tachycardia; increased ICP; tonic clonic movements; respiratory depression. Wide dose range effects, with analgesic action at low doses ( $\leq 0.2$ mg/kg).	In contrast to other sedative/analgesics, can cause hypertension and tachycardia and should be avoided in patients with aneurysms, elevated ICP, or hypertension. Adverse psychotic reactions may be avoided by pre-treatment with benzodiazepines. Many adult patients do not tolerate the negative CNS side-effects. Unlike other agents, produces both sedation and analgesia. Emergence psychotic reactions may last longer than sedative/analgesic effects. Caution: Combinations of ketamine and opioid narcotics may produce profound respiratory depression.	

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<b>Thiopental</b> (Pentothal)	Barbiturate hypnotic/ anesthetic  (Depresses CNS activity by binding to the barbiturate site on GABA-receptor complex, enhancing GABA activity)	<i>Adults 18 - 64 years of age:</i> Incremental doses of 50 - 100mg up to a maximum of 3mg/kg  <i>Elderly (&gt; 65):</i> 25 - 50mg incremental doses up to a maximum of 2mg/kg. The elderly are more susceptible to excessive sedation and smaller initial doses should be utilized.	Onset: 1- 2 min  Duration of Action: 10 - 30 min	Hypotension, myocardial depression, CNS and respiratory depression, nausea, vomiting, diarrhea, cramping, laryngospasm	Short-acting barbiturate useful for intubation. No analgesic effects. Inactive, debilitated, and elderly may be more susceptible to adverse effects. Increased toxicity with other CNS depressants.	
<b>Pentobarbital</b> (Nembutal)	Barbiturate  (Sedative, hypnotic, and anticonvulsant properties; Increases GABA activity in the CNS)	<i>Adults 18 - 64 years of age:</i> 100mg every 1- 3 minutes up to a maximum dose of 500mg.  <i>Elderly (&gt; 65):</i> 50mg every 1 - 3 minutes up to a maximum dose of 250mg. The elderly are more susceptible to adverse effects of barbiturates. Also, duration of action is unpredictable due to variable kinetics in this population.	Onset: Within 1 minute  Duration of Action: 15 min	Hypotension, cardiovascular depression, respiratory depression, nausea, vomiting, laryngospasm	Short-acting barbiturate useful for pre-procedure sedation. No analgesic effects. Inactive, debilitated, and elderly may be more susceptible to adverse effects. Increased toxicity with other CNS depressants.	
<b>Methohexital</b> (Brevital)	Barbiturate anesthetic  (Depresses CNS activity by binding to the barbiturate site on GABA-receptor complex, enhancing GABA activity)	<i>Adults 18 - 64 years of age:</i> 1mg/kg to a maximum of 2mg/kg  <i>Elderly (&gt; 65):</i> 0.5 - 1mg/kg up to a maximum of 2mg/kg. The elderly are more susceptible to adverse effects of barbiturates.	Onset: 1 - 3 min  Duration of Action: 10 - 15 min	Hypotension, myocardial depression, CNS and respiratory depression, nausea, vomiting, diarrhea, cramping, laryngospasm	Ultra-short acting barbiturate useful for short procedures. No analgesic effects. Inactive, debilitated, and elderly may be more susceptible to adverse effects. Increased toxicity with other CNS depressants.	
<b>Nitrous Oxide</b>	General CNS depressant  (May act similarly as inhalant general anesthetics by mildly stabilizing axonal membranes; May also act on opioid receptors to cause mild analgesia)	<i>Adults:</i>  For sedation and analgesia, concentrations of 25% - 50% nitrous oxide with oxygen, inhaled through the nose via a nasal mask.  Avoid in pregnant patients, especially during the first two trimesters, due to increased risk of spontaneous abortion and teratogenicity.	Onset: 2 - 5 minutes	Prolonged use may produce bone-marrow suppression and/or neurologic dysfunction. The developing fetus and patients with vitamin B12 and other nutritional deficiencies are at increased risk of developing neurologic disease with exposure to nitrous oxide.	Inhaled gas used for dental and other short procedures which induces sedation and mild analgesia. Should not be administered without oxygen. Should not be administered to patients after eating a meal.	

*Guidelines are general and cannot take into account all of the circumstances of a particular patient. Judgment regarding the propriety of using any specific procedure or guideline with a particular patient remains with that patient's physician, nurse, or other health care professional, taking into account the individual circumstances presented by the patient.*

- Cautions:
- (1) There is an increased risk of respiratory and cardiovascular depression with combinations of benzodiazepines and opioid narcotics.
  - (2) Respiratory depression effects may last longer than analgesia; monitor for respiratory depression and apnea.
  - (3) Use smaller incremental doses in the elderly, patients with COPD, and in chronically debilitated patients.
  - (4) Use of Narcan (at 0.4 mg dose) to reverse narcotic respiratory depression, especially if mild, can result in a surge in sympathetic tone, hypertension, and ultimately pulmonary edema, in some cases.
- References:
1. Lacy CF, Armstrong LL, Goldman MP, Lance LL. Drug Information Handbook. 11<sup>th</sup> Edition; American Pharmaceutical Association and Lexi-Comp Inc. Hudson, Ohio, 2003-2004.
  2. McArdle P. Intravenous analgesia. Crit Care Clin 1999;15(1):89-104.
  3. Horn E, Nesbit SA. Pharmacology and pharmacokinetics of sedatives and analgesics. Gastrointestinal Clinics of North America 2004; 14(2):247-268.

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