Criteria for Use
Dexmedetomidine (Precedex®) in the Intensive Care Unit (ICU) Setting
VHA Pharmacy Benefits Management Services and the Medical Advisory Panel
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The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient. Individual cases that are outside the recommendations should be adjudicated at the local facility according to the policy and procedures of its P&T Committee and Pharmacy Services.

EXCLUSION CRITERIA (If one is selected, patient is NOT eligible)

- ☐ Advanced heart block
- ☐ Baseline bradycardia (e.g., <50 bpm)
- ☐ Known hypersensitivity
- ☐ Concurrent use of or anticipated need for neuromuscular blockade where dexmedetomidine would be the sole sedative agent used
- ☐ Active myocardial ischemia
- ☐ Severe hypotension (e.g., systolic blood pressure <90 mmHg with the use of 2 or more vasopressors)

INCLUSION CRITERIA

*The following **must** be selected for the patient to be eligible*

- ☐ Patient is receiving continuous respiratory monitoring and cardiac monitoring while receiving dexmedetomidine

***One** of the following must be checked for the patient to be eligible*
Dexmedetomidine may be considered in patients in the following situations:

- ☐ When short term sedation is anticipated (<24 hours) as an alternative to propofol
- ☐ For intermediate-term sedation (e.g., 24-72 hours) as an alternative to propofol or benzodiazepines (e.g., intermittent bolus dosing or continuous infusions) where avoidance is desired (See Issues for Consideration)
- ☐ When transitioning from another sedative agent is desired to facilitate the process of ventilator weaning (dexmedetomidine may be continued during and post-extubation (e.g., typically 24-48 hours)

DOSAGE AND ADMINISTRATION

- FDA approved dosing: Optional loading dose of 1 mcg/kg over 10 min (commonly omitted in ICU setting due to potential for hypotension and/or bradycardia) followed by a continuous infusion of 0.4 mcg/kg/hr, titrated to desired level of sedation (usual range 0.2-0.7 mcg/kg/hr), for up to 24 hours
- Additional dosing information: Omission, reduction, or slower infusions of the loading dose (which may be associated with transient hypertension or hypotension) have been studied and observed commonly in clinical practice. Lower and higher maintenance doses (up to 1.4 mcg/kg/hour, with most patients requiring ≤1 mcg/kg/hr), and longer infusion durations (approximately 3-5 days) have been used in clinical trials. Use of dexmedetomidine beyond 24 hours has been associated with withdrawal symptoms (see Issues for Consideration), tolerance, tachyphylaxis, and dose-related increase in adverse reactions.
- Special Populations: dose reductions should be considered in the elderly and in patients with hepatic impairment.

RECOMMENDED MONITORING

- Dexmedetomidine should only be administered by persons privileged and able to provide care in the management of patients in the intensive care (and intensive-care level), procedural, or operating room setting; continuous respiratory and cardiac monitoring is recommended (e.g., heart rate, pulse oximetry, etc.).
  - Although dexmedetomidine typically does not cause significant respiratory depression in most patients, it can cause loss of oropharyngeal muscle tone resulting in airway obstruction in nonintubated patients. Continuous respiratory monitoring is recommended when dexmedetomidine is used in nonintubated patients (e.g., post-extubation).
  - Dexmedetomidine administration may be associated with clinically significant bradycardia, hypotension and sinus arrest requiring intervention which may include: dose reduction, discontinuation, administration of fluids, pressors, or anticholinergic agents (e.g., atropine, glycopyrrolate). Monitor blood pressure and heart rate.
  - Patient's level of and need for sedation should be routinely evaluated using a validated assessment tool.
  - Although dexmedetomidine possesses some analgesic properties, this is not primary use, and patients should be routinely assessed for pain and treated when needed.

ISSUES FOR CONSIDERATION

- **Withdrawal:** Dexmedetomidine may potentially be associated with a withdrawal syndrome similar to that observed with clonidine (another alpha-2 adrenergic agent) if administered for greater than 24 hours. When administered for up to 7 days, 5% of dexmedetomidine patients experienced withdrawal symptoms within 24 hours of discontinuation. Most commonly reported symptoms were nausea, vomiting, and agitation; hypertension and tachycardia have also been reported.
- **Hypotension, Bradycardia, and Sinus Arrest:** Dexmedetomidine reduces sympathetic nervous system activity and should be used with caution in states where the risk of bradycardia and hypotension may be more pronounced (e.g., severe ventricular dysfunction, hypovolemia, advanced age, diabetes, chronic hypertension, significant aortic stenosis or left ventricular outflow tract obstruction, etc.).
- **Serious central nervous system pathology:** Limited data are available on the use of dexmedetomidine in patients with serious central nervous system pathology (e.g., trauma, acute stroke, active seizures, etc.). Dexmedetomidine has not been shown to possess anti-seizure activity. In situations where maintenance of arterial blood pressure is critical, consider the potential for dexmedetomidine to cause hypotension (which may impact cerebral hemodynamics as well).
- **Drug Interactions:** Additive effects may occur with co-administration of anesthetics, sedatives, hypnotics, opioids, negative chronotropic agents, and vasodilators.
- **Targeted sedation goals in ICU sedation:** Patients should have a targeted sedation goal measurable with the use of a validated assessment tool. Reassessment should occur regularly, with adjustments in therapy made as needed.

- **Adjunctive treatment of alcohol withdrawal:** Benzodiazepines remain the standard of treatment for alcohol withdrawal syndrome. There is some interest in the use of dexmedetomidine as adjunctive treatment with its desirable sedative effects as well as blood pressure and heart rate lowering effects. However, evidence is limited to 2 small, randomized controlled trials and several observational, retrospective studies. In total, dexmedetomidine may be associated with some benzodiazepine sparing properties, but the effect of dexmedetomidine on other outcomes such as rates and duration of intubation and hospital and ICU lengths of stay remain unclear. Dexmedetomidine should not be used alone in the management of alcohol withdrawal, as dexmedetomidine has not been shown to possess antiseizure activity or be effective in the management of delirium tremens. Requests for dexmedetomidine as an adjunct for alcohol withdrawal should be considered on a case by case basis.
- **ICU Delirium:** Delirium is associated with an increased risk of adverse outcomes. Optimal strategies to prevent and treat delirium in the ICU have not been definitively established. There is interest in using dexmedetomidine for ICU sedation, rather than benzodiazepines, for its potential to reduce the risk of developing delirium. Evidence on the effectiveness of dexmedetomidine in minimizing delirium in the ICU is limited and has not consistently shown improvement in outcomes, although current guidelines endorse its use to shorten the duration of delirium. Dexmedetomidine produces a state of lighter sedation and appears to reduce requirements of additional agents such as benzodiazepines, known to increase delirium risk. Dexmedetomidine may be a reasonable therapeutic option for ICU sedation in appropriately selected patients according to the CFU.
- **Hepatic impairment:** Dexmedetomidine clearance decreases with increasing severity of hepatic impairment. Even though doses are titrated to effect, consider dose reduction in patients with impaired hepatic function.
- **Pregnancy:** There are no adequate, well controlled studies of the use of dexmedetomidine in pregnant women. In vitro and animal studies and human case reports suggest that dexmedetomidine does cross the placenta. Teratogenic effects have not been observed, though some adverse effects in rats have been found. Dexmedetomidine should be used during pregnancy only if the benefit outweighs potential risks.
- **Perioperative and periprocedural use of dexmedetomidine:** Perioperative use of dexmedetomidine will be addressed in a separate guidance document (see PBM website). Operational details on the periprocedural use of dexmedetomidine (e.g., qualified staff, approved locations for administration, etc.) should be determined at the facility level.