

Dosing Guidelines for Precedex[®]

Nonintubated Procedural Sedation
and
ICU Sedation



Precedex® Overview

- Precedex is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting and for sedation of nonintubated patients prior to and/or during surgical and other procedures.¹
- Precedex should be administered by continuous infusion not to exceed 24 hours.
- Precedex should be administered only by persons skilled in the management of patients in the intensive care or operating room setting.¹
- Due to the known pharmacologic effects of Precedex, patients should be continuously monitored.¹
- The most common adverse reactions with Precedex (incidence >2%) are hypotension, bradycardia and dry mouth.¹
- Due to the increased incidence of bradycardia and hypotension in the elderly, and the potential for reduced clearance in patients with impaired hepatic or renal function, dose reductions should be considered in these patient types.¹



Please see enclosed full Prescribing Information.

What to Expect

Cardiovascular Effects

- Clinically significant episodes of bradycardia have been associated with Precedex in young, healthy volunteers with high different routes of administration, such as infusion or bolus administration.¹
- Moderate heart rate and blood pressure be anticipated with Precedex.²
- If medical intervention is required for hypotension or bradycardia, treatment options include:
 - Decreasing or stopping the infusion
 - Increasing the rate of IV fluid administration
 - Elevation of lower extremities
 - Use of pressor agents, such as glycopyrrolate or atropine or ephedrine
- Because Precedex decreases sympathetic activity, hypotension and/or bradycardia to be more pronounced in hypovolemic patients with diabetes mellitus or chronic as well as in the elderly.¹
- Because Precedex has the potential to be induced by vagal stimuli, clinicians should be prepared to intervene with anticholinergic agents (e.g., glycopyrrolate or ephedrine) to modify the response.¹
- Caution should be exercised when administering Precedex to patients with advanced heart block or ventricular dysfunction.¹
- Use with caution when coadministering Precedex with vasodilators or negative chronotropic agents, as they may enhance the pharmacodynamic effects.¹
- Transient hypertension has been observed with the loading dose in association with vasoconstrictive effects of Precedex.¹

ICU Sedation

- In two pivotal Phase III clinical trials of ICU patients treated with Precedex®, the largest mean decrease in heart rate was approximately 7% and the largest mean decreases in systolic and diastolic blood pressures were 10% and 11%, respectively.²

Procedural Sedation

- Precedex has been studied in two pivotal Phase III clinical trials of nonintubated patients receiving monitored anesthesia care (MAC) sedation for a variety of surgical procedures as well as patients undergoing awake fiberoptic intubation.¹
- The table on page 5 shows the frequency at which Precedex-sedated patients undergoing MAC sedation may experience hypotension or bradycardia and the frequency at which certain types of interventions may be needed to manage these adverse events.

Incidence and Interventions for Hypotension in Patients Undergoing Procedural Sedation

Hypotension (n=318)	
Overall Incidence	173 (54%)
Intervention	(n=173)
No Intervention Required	113 (65%)
Intervention Required	60 (35%)
Type of Intervention When Required [#]	(n=173)
Ephedrine or Phenylephrine	55 (32%)
Glycopyrrolate	-
Atropine	-
Calcium Chloride	2 (1%)
Dopamine	1 (<1%)
IV Fluid Administration	16 (9%)
Precedex Dose Reduced	9 (5%)
Precedex Discontinued	1 (<1%)

^{*}Hypotension was defined in pivotal trial protocols in a patient as SBP <80 mm Hg, DBP <50 mm Hg or >30% decrease in systolic blood pressure values.

[†]Bradycardia was defined in pivotal trial protocols as a heart rate <50 bpm or >30% decrease from prestudy drug infusion values.

[‡]Other possible interventions included elevation of low infusion rates or other forms of intervention. Patients may have received multiple forms of intervention.

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Treatment Options for Drug-induced Bradycardia or Hypotension

In Precedex® clinical trials, atropine, glycopyrrolate and ephedrine were effective in the treatment of most episodes of Precedex-induced bradycardia. However, in some patients with significant cardiovascular dysfunction, more advanced resuscitative measures were required.^{1,3}

Glycopyrrolate Dosing for Drug-induced Bradycardia or Hypotension

Glycopyrrolate Injection may be used during surgery to counteract drug-induced or vagal reflexes and their associated arrhythmias (e.g., bradycardia). It should be administered intravenously as single doses of 0.1 mg (0.5 mL) and repeated, as needed, at intervals of 2 to 3 minutes.⁴

Atropine Dosing for Drug-induced Bradycardia or Hypotension

Initial single doses in adults vary from around 0.5 mg to 1 mg (5-10 mL of a 0.1 mg/mL solution). Administration of less than 0.5 mg can produce a paradoxical bradycardia because of the central or peripheral parasymphathomimetic effects of low doses in adults.⁵

When the recurrent use of atropine is essential in patients with coronary artery disease, the total dose should be restricted to 2 to 3 mg (maximum 0.03 to 0.04 mg/kg) to avoid the detrimental effects of atropine-induced tachycardia on myocardial oxygen

demand. For patients with bradycardic dose of atropine is administered intravenously every 3 to 5 minutes if asystole persists. (0.04 mg/kg) given IV is a fully vagolytic. The administration of this dose of atropine for patients with bradycardic cardiac arrest administration of atropine can be used in IV access. The recommended adult dose of endotracheal administration is 1 to 2 mg not to exceed 10 mL of sterile water or normal saline.

Ephedrine Dosing for Drug-induced Bradycardia or Hypotension

Ephedrine is indicated to counteract the effects of spinal or other types of nontopical anesthesia. Depending on the clinical circumstances, ephedrine injection may be given subcutaneously, intravenously. Usual adult dose: 25 to 50 mg injected subcutaneously or intravenously. 0.2 to 1 mL of 5% solution is usually administered to minimize hypotension secondary to spinal anesthesia. Doses should be governed by blood pressure. Absorption (onset of action) by the intravenous route is rapid (within 10 to 20 minutes) than by the intramuscular route. The intravenous route may be used if an effect is desired.⁶

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Titrate Precedex® and Concomitant Medications to Effect

Coadministration of Precedex with anesthetics, sedatives, hypnotics and opioids can enhance the pharmacodynamic effects of these agents. Specific studies have confirmed these effects with sevoflurane, isoflurane, propofol, alfentanil and midazolam. A decrease in the dosage of Precedex or the concomitant agent may be required.¹

These effects have been demonstrated in pharmacodynamic studies of healthy subjects and in patients undergoing sedation while taking the medications listed below.

Anesthetic Gases
• Sevoflurane ^{a,7} • Isoflurane ^{b,c,8,9}
IV Sedatives or Anxiolytics
• Midazolam ^{d,8} • Propofol ^{e,10}
Opioid-based Analgesics
• Morphine ^{f,11} • Alfentanil ^g

These clinical trials are of different designs in a variety of patient populations. Because clinical trials are conducted under widely varying conditions, rates observed may not be directly compared to other trials and may not always reflect the rates observed in practice.

^aSevoflurane. Dexmedetomidine 0.7 ng/ml of sevoflurane by 17% in patients under

^bIsoflurane. Low- and high-dose infusions decreased the end-tidal isoflurane concentration respectively, necessary to elicit the desired 50% of healthy subjects.⁸

^cIsoflurane. Dexmedetomidine decreased by 47% in patients who also received the as induction agents.⁹

^dMidazolam. In healthy subjects, the effect combination with dexmedetomidine on sedation with greater degrees of synergy occurred. At higher degrees of sedation, the effect of dexmedetomidine on midazolam

^ePropofol. In healthy subjects, dexmedetomidine concentrations required for sedation of motor response by approximately one required for sedation and induction of analgesia reduced in the presence of dexmedetomidine

^fMorphine. A single IV dose of 1 mcg/kg 10 minutes before induction reduced postoperative consumption by 28% at identical pain score control.¹¹

^gAlfentanil. In the presence of dexmedetomidine is needed to produce the same degree of impact on respiratory function can be less alfentanil when coadministered with Pre

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