Intranasal (IN) Medication Administration
MBED Clinical Practice Guideline

**Purpose and Indications:** Intranasal administration of medications to achieve rapid sedation/anxiolysis, pain control, and/or control of seizure activity when IV access is not available, desirable, or indicated.

**Contraindications:** Nasal trauma or obstruction (copious mucous, bleeding, anatomic obstruction, or foreign body) or a known allergy to the medication being considered for IN administration.

**General Points About IN Medication Use:**
- Medications most commonly administered via the IN route are: fentanyl for pain and midazolam (Versed) for anxiolysis/mild sedation. Additionally, other medications may be administered by this route (see Dosing Guideline Chart below). Dosing is ordered in mg/kg, except for fentanyl and Precedex which is dosed in mcg/kg.
- The maximum volume to be delivered is 1 mL per nostril. Greater volumes are not effective as they cannot be further absorbed by the nasal mucosa.
- Time of onset of action is rapid and similar to that with IV administration of the same medication. Therefore, the medication should only be administered once all supplies are assembled and the physician is ready to begin the procedure (or the patient is ready to go for imaging, etc).
- **Monitoring and documentation is the same as would be done for IV administration of the same medications.** For example, children receiving medication via this route for pain, anxiolysis (mild sedation), or seizures should have continuous pulse oximetry and periodic blood pressure measurements recorded, as well as frequent pain reassessments.
- **In general, IN medications alone are usually not sufficient to achieve moderate/deep levels of sedation.** However, the exceptions to this are the use of IN Ketamine (in the sedation dosing range of 6-9 mg/kg) and IN Dexmedetomidine. Even IN Fentanyl and IN Midazolam can achieve a moderate/deep level of sedation by using them in combination or by repeated dosing. **In any of these situations, following the MHS moderate/deep sedation pathway is required.**

**Practical Considerations When Preparing for Administering of IN Medications**

1. Items needed: 1 ml or 3 ml luer-lock syringe, needle to draw up the medication, mucosal atomization device (MAD), and medication vial
2. Utilize the patient’s developmental level to provide procedural education prior to administration and allow the parent to participate in patient positioning/swaddling. Remember that this route of administration is desirable to reduce anxiety, pain, fear, and trauma, so we should not be causing these things when we administer them!
3. IN medications can cause a mild burning sensation for up to 30 seconds (usually with midazolam and it lasts 30-45 seconds) so forewarn the parents that the child will initially cry (but nothing like they will cry with a shot).
4. **Volume and Concentration:**
   - 0.25 – 0.5 mL is the ideal volume per nostril
   - 1 mL is the maximum volume per nostril
   - For best absorption, the dose should always be divided with half of the dose administered in each nostril. The divided doses may be administered simultaneously by 2 providers or one at a time by the same provider.
   - If a higher volume (more than 1 ml per nostril) of medication is required, apply it in two separate doses allowing a few minutes (5-15 minutes) for the former dose to be absorbed.
   - Always use the MOST concentrated form of the medication available – dilute forms are less effective (example – use midazolam 5 mg per ml, not 1 mg per ml).
Intranasal Medication Administration Technique Using the Mucosal Atomizing Device (MAD)\textsuperscript{1-3}

1. Draw up the full medication dose in luer-lock syringe (remember to draw up an extra 0.1 mL of medication into the syringe to account for dead space in the MAD device.)
2. Remove needle (or vial adapter if used) and attach the MAD to the syringe via the luer-lock connector
3. Using a free hand to hold the head stable, place the tip of the MAD gently but firmly against the nostril aiming slightly up and outward (toward the top of the ear).
4. Rapidly compress the syringe plunger to deliver half of the medication into the nostril (If the plunger is not pushed fast enough, the atomized misting of the medication will not be achieved and which will likely cause the medication to be swallowed).
5. Repeat this technique with the second half of the dose in the other nostril. Alternatively, the total dose may be administered to both nostrils at the same time.
6. After administration, it is best to step back and allow the patient to be comforted by family and allow the medication to take effect.
Medication-specific information:

- **Midazolam (Versed):** onset of mild sedation/anxiolysis occurs within 5-10 minutes of administration and lasts for about 30-50 minutes. The IN Midazolam Kits (prepared by MHS pharmacy), and the associated EPIC order for the kit, come with an optional dose of IN lidocaine that can be given several minutes before giving the IN Midazolam to decrease the mild burning sensation that is sometimes experienced by patients. Of course doing this means having to give 2 medications via the IN route. Therefore, it is recommended to ask the parents (or the child if it is developmentally appropriate to do so) whether or not they would like to have the IN lidocaine given.

- **Fentanyl (Sublimaze):** onset of analgesia occurs within 1-2 minutes and it lasts for about 15-30 minutes. Therefore, it would be ideal to give the patient an oral analgesic medication (if no contraindications exist to taking PO medications) at about 15-20 minutes after the IN Fentanyl administration so that oral medication will kick in at about the time that the IN Fentanyl is wearing off. Another option is to simply repeat the IN Fentanyl dose.

- **Ketamine (Ketalar):** IN Ketamine can provide some mild sedation/anxiolysis and pain control, not unlike IN Midazolam and IN Fentanyl respectively, but it does not consistently achieve a moderate/procedural sedation level (as is needed for laceration repair, fracture reduction, I&D of complex skin abscesses, etc). There is some limited evidence that using higher doses of IN Ketamine, up to 9mg/kg/dose, can achieve a moderate/procedural sedation level but our experience thus far is that this is inconsistent (that is in contrast to intramuscular, IM, ketamine at 5mg/kg which is quite effective and its use for procedural sedation has been well studied.) Following our MHS moderate/deep sedation pathway is required when using sedation range dosing of IN Ketamine (6-9 mg/kg) since a moderate/procedural sedation level may be achieved.

- **Dexmedetomidine (Precedex):** Use of IN Dexmedetomidine often leads to a moderate to deep level of sedation, therefore, following our MHS moderate/deep sedation pathway is required when using IN Dexmedetomidine. Current data does not clearly support that IN Dexmedetomidine is more effective than IN Midazolam or IN Ketamine for procedural sedation. Also, compared to IN Midazolam and IN Ketamine, IN Dexmedetomidine has a slower onset (25-30 min), a longer sedation duration (60-90 minutes) and is much more expensive.

DUE TO THESE ISSUES, IN Dexmedetomidine IS APPROVED FOR USE AT MHS ON A RESTRICTED BASIS (SEE APPENDIX A BELOW FOR THE MHS PHARMACY AND THERAPEUTICS COMMITTEE DOCUMENT) AND SHOULD ONLY BE USED IF THE FOLLOWING APPLY:

1) Other non-IV sedation medications (rectal Brevital, oral or intranasal Versed, etc.) are not appropriate options. For example, allergies or the volume for an intranasal dose exceeds 1 mL per nostril.

AND

2) One of the indications listed below apply:
   - Procedure for which the child requires sedation and does not require administration of an IV medication or blood draw (so an IV is only required for administering sedation medications)
   - A lack of an IV during sedation does not expose the child to undue risk
   - The child has had several failed attempts at IV start (or is known to be or expected to be a very difficult IV start with the expectation of multiple failed IV attempts)
**Intranasal Medication Dosing Guideline:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Dose</th>
<th>Maximum Dose</th>
<th>Concentration</th>
<th>Mean Onset (minutes)</th>
<th>Mean Duration (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>Pain</td>
<td>1.5 – 2.0 mcg/kg</td>
<td>100 mcg</td>
<td>50 mcg/mL</td>
<td>1-2</td>
<td>15-30</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Seizures</td>
<td>0.2-0.3 mg/kg</td>
<td>10 mg</td>
<td>5 mg/mL</td>
<td>5-10</td>
<td>30-50</td>
</tr>
<tr>
<td></td>
<td>Anxiolysis</td>
<td>0.4 – 0.5 mg/kg</td>
<td>10 mg</td>
<td>5 mg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Seizures</td>
<td>0.1 mg/kg</td>
<td>4 mg</td>
<td>2 mg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anxiolysis</td>
<td>0.4 – 0.5 mg/kg</td>
<td>10 mg</td>
<td>5 mg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
<td>0.5 – 2 mcg/kg</td>
<td>100 mcg</td>
<td>50 mcg/mL</td>
<td>25-30</td>
<td>60-90</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Sedation</td>
<td>6 – 9 mg/kg</td>
<td>200 mg</td>
<td>100 mcg/mL</td>
<td>5-15</td>
<td>40-70</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>0.5-1 mg/kg</td>
<td>100 mcg</td>
<td>100 mcg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naloxone</td>
<td>Opioid reversal</td>
<td>0.1 mg/kg</td>
<td>2 mg</td>
<td>1 mg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Benzodiazepine reversal</td>
<td>0.01 mg/kg</td>
<td>1 mg</td>
<td>0.2 mg single dose, 1mg or cumulative dose</td>
<td>0.1 mg/mL</td>
<td>0.5-1mg/kg</td>
</tr>
</tbody>
</table>

*Studies using IN Dex as sedation for imaging studies or for pre-procedural sedation in the OR setting prior to general anesthesia.
**Adult data from studies in pre-hospital settings.

**References:**

3. [www.intranasal.net](http://www.intranasal.net)

This guideline is endorsed by Mary Bridge Emergency Department but it is not intended as a substitute for clinical judgment. It should be used as an adjunct to sound clinical decision making which accounts for individual patient considerations.

Updated 7.1.2014
GENERIC NAME: DEXMEDETOMIDINE HCl Injection

Proprietary Name: PRECEDEX™ (Abbott Laboratories)

Therapeutic Class: Sedative/Analgesic

Indications: Dexmedetomidine is indicated for short-term (≤ 24 hrs) sedation of intubated and mechanically ventilated patients in the intensive care setting.

*Currently looking into its off-label use for procedural sedation in pediatrics when used intranasally.

Clinical Pharmacology: Dexmedetomidine is a selective α₂-adrenergic receptor agonist that has sedative, analgesic, anesthetic and sympatholytic properties. Its effects are thought to be linked to the activation of G-proteins by the alpha₂a receptors in the brainstem, which results in the inhibition of norepinephrine release. In IV studies, it was shown to be 8 to 10 times more selective for the α₂-adrenergic receptor than clonidine. ICU data supports the fact that in contrast to other agents, the sedation and analgesia produced by dexmedetomidine are achieved without significant respiratory or hemodynamic compromise.

Pharmacokinetics: Dexmedetomidine pharmacokinetic parameters are well established for IV use and are as follows. The drug undergoes rapid distribution following intravenous administration with a distribution half-life of 6 minutes. Dexmedetomidine is metabolized by direct glucuronidation and metabolism by the cytochrome 2A6 isozyme of the liver. None of the drug is excreted unchanged in the urine. The elimination half-life of dexmedetomidine is 2 hours. Dexmedetomidine’s steady-state volume of distribution is 118 liters. Protein binding is 94%, and systemic clearance is 39 L/h. Gender does not affect the pharmacokinetic parameters of dexmedetomidine, nor is there a difference in the pharmacokinetic parameters between young (18 to 40 years), middle-aged (41 to 65 years), and elderly (>65 years) subjects. Severe renal dysfunction has no effect on the elimination of dexmedetomidine, but its impact on the metabolites has not been evaluated. Hepatic dysfunction (Child-Pugh Class A, B, or C) decreases the systemic clearance of dexmedetomidine. The mean clearance is decreased by 26% with mild hepatic impairment, 36% with moderate hepatic impairment, and 47% with severe hepatic impairment.

Dexmedetomidine’s off label use intranasally is not nearly as common as its IV use, but certain parameters and estimates have been established. Bioavailability during a buccal study was 82% and it is hypothesized that the intranasal bioavailability would be similar due to both routes using the mucous membrane for absorption.

Comparative Efficacy: Dexmedetomidine for intranasal use has been featured in numerous studies over the past few years. One study focused on using intranasal dexmedetomidine for sedation for diagnostic magnetic resonance imaging (MRI) studies. This particular study was open label and featured 28 children all under the age of 10. Patients were given a 2 mcg/kg dose of intranasal dexmedetomidine 30 minutes prior to a MRI. The children were then assessed using the University of Michigan Sedation Scale (UMSS).
Sedation scores at 15 and 30 min were 1.17±1.6 and 2.60±0.9. Also, 11 of the 28 children had to be supplemented with IV midazolam, yielding a 60% success rate. No adverse events were noted and important aspects like separation from parents went well. This study showed that dexmedetomidine had the potential to be used as a safe and effective procedural sedation agent.

A second study in Hong Kong sought to determine which doses of dexmedetomidine would be more effective for intranasal sedation as premedication prior to anesthesia. 116 children ages 1-8 were randomized to get either dexmedetomidine at a 1 mcg/kg dose or a 2 mcg/kg dose intranasally 45 min before anesthesia induction. Anesthesiologists determined if the child was adequately sedated at the time of induction and 53% of the patients doses at 1 mcg/kg were satisfactory, while 66% of the patients doses at 2 mcg/kg were deemed acceptable. Neither group noted having any adverse effects. The study showed that both doses could be effective for helping sedate a child intranasally, but that the 2 mcg/kg dose appeared slightly more effective. The results showed this to be especially true for the slightly older children in the study.

The *British Journal of Anaesthesia* published a study that looked at the analgesic and sedative effects of intranasal dexmedetomidine used in third molar surgery under local anesthesia. This randomized trial compared a 1 mcg/kg dose of dexmedetomidine to an intranasal saline dose. The study assessed perioperative sedation, postoperative pain, analgesic use, vitals, and adverse reactions. Pain scores during hours 1-12, at rest, and with mouth opening were all lower in the dexmedetomidine group with P=0.003 and P=0.009 respectively. Propofol was available as a rescue sedative and the dexmedetomidine group used less propofol intra-operatively. Sedation scores were lower with the dexmedetomidine group in recovery. In terms of safety, dexmedetomidine had significantly lower heart rate in recovery and lower systolic blood pressure at times, but nothing that required treatment. The placebo/saline group did experience more dizziness (P= 0.026). Overall, patients in the dexmedetomidine group were more sedate perioperatively and had better pain relief.

Intranasal dexmedetomidine began to be compared to other sedative agents, and one study compared dexmedetomidine and intranasal midazolam in pediatric patients undergoing anesthesia. This study featured 90 children ages 2-9 who were undergoing an elective adeno-tonsillectomy. Both groups of patients were dosed with their randomized double-blinded medication 45-60 minutes before the anesthesia and the primary endpoint was satisfactory mask induction deemed by the anesthesiologist. The midazolam group (dosed at 0.2 mg/kg) achieved the primary endpoint in 82.2%, while the dexmedetomidine group (dosed at 1 mcg/kg) was only deemed to have achieved a satisfactory sedation for mask induction 60% of the time (P=0.01). There were no differences in the sedation scores or anxiety scores upon parental separation. No safety concerns were noted in either group, but post-op analgesia use was significantly higher in the midazolam group (P=0.045).

A final study looked at the effectiveness of intranasal dexmedetomidine compared to intranasal ketamine for procedural sedation in children preparing to undergo a MRI. This double-blind randomized trial had 150 patients ages 1-10 and separated them into three groups: saline (placebo), dexmedetomidine at 1 mcg/kg, and ketamine at 5 mg/kg. The patients were assessed in terms of their response, ease of IV, anesthesiologist satisfaction, awakening times, and total propofol dose. The results showed that dexmedetomidine and ketamine were equally effective and that the anesthesiologists were satisfied with dexmedetomidine 90.4% of the time and ketamine 82.7%. Both drugs needed less propofol than the saline group, and featured earlier awakenings. No adverse reactions were noted, with the exception of mild discomfort with intranasal administration.
CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS: The following has been established for dexmedetomidine use intravenously. Parts below, can be applied to intranasal use.

Cardiovascular effects: Clinically significant episodes of bradycardia and sinus arrest have been reported in young adults with high vagal tone or with different routes of administration, including rapid IV or bolus administration. Reports of hypotension and bradycardia have been associated with dexmedetomidine. If medical intervention is required, treatment may include decreasing or stopping the infusion of dexmedetomidine, increasing the rate of IV fluid administration, elevating the lower extremities, and using pressor agents. Because dexmedetomidine has the potential to augment bradycardia induced by vagal stimuli, be prepared to intervene. In clinical trials, atropine and glycopyrrolate were effective in the treatment of most episodes of dexmedetomidine-induced bradycardia. However, in some patients with significant cardiovascular dysfunction, more advanced resuscitative measures were required. Transient hypertension has been observed primarily during the loading dose in association with the initial peripheral vasoconstrictive effects of dexmedetomidine. Treatment of transient hypertension has generally not been necessary, although reduction of the loading infusion rate may be desirable. Exercise caution when administering dexmedetomidine to patients with advanced heart block or severe ventricular dysfunction. Because dexmedetomidine decreases sympathetic nervous system activity, hypotension and/or bradycardia may be expected to be more pronounced in patients with hypovolemia, diabetes mellitus, or chronic hypertension, and in elderly patients.

Alertness: Some patients receiving dexmedetomidine have been observed to be arousable and alert when stimulated. Do not consider this alone as evidence of lack of efficacy in the absence of other clinical signs and symptoms.

Withdrawal:

Intensive care unit sedation: With administration up to 7 days, regardless of dose, 5% of dexmedetomidine-treated adults experienced at least 1 event related to withdrawal within the first 24 hours after discontinuing study drug and 3% of dexmedetomidine adults experienced at least 1 event 24 to 48 hours after the end of study drug. The most common events were nausea, vomiting, and agitation. Tachycardia and hypertension requiring intervention in 48 hours following study drug discontinuation occurred at frequencies of less than 5%. If tachycardia and/or hypertension occurs after discontinuation of dexmedetomidine, supportive therapy is indicated.

Procedural sedation: Withdrawal symptoms were not seen after discontinuation of short-term infusions of dexmedetomidine (less than 6 hours).

Tolerance and Tachyphylaxis: Use beyond 24 hours has been associated with tolerance tachyphylaxis and dose-related increase in adverse reactions.

Hepatic function impairment: Consider dose reduction in patients with impaired hepatic function. Long-term use may result in decreased ACTH-stimulated cortisol release. Single-dose administration has no effect on ACTH-stimulated cortisol release. Subcutaneous infusion over 1 week in dogs resulted in a 40% decrease in ACTH-stimulated cortisol release.

PREGNANCY AND LACTATION: Dexmedetomidine has been classified as Pregnancy Category C. High-dose administration in pregnant rats resulted in post-implantation losses, reduced live pups, decreased pup weight, and delayed motor development. No adequate and well controlled studies have been conducted in pregnant women. Dexmedetomidine is not recommended during labor and delivery, including cesarean section deliveries. Dexmedetomidine is excreted in the milk of lactating rats. It is unknown if it is excreted in human milk.

SPECIAL POPULATIONS: The elimination of dexmedetomidine is unaltered in the geriatric population, but the dose should be decreased to minimize the risk of bradycardia and hypotension. No safety and efficacy studies had been conducted in pediatric patients below 18 years of age for IV use at the time of FDA approval. As touched on in the comparative efficacy section, there is some data showing the benefits of this medication in a pediatric population when used intranasally.
ADVERSE REACTIONS: The following has been established for dexmedetomidine use intravenously. Parts below can be applied to intranasal use. Through the minimal amount of research done with intranasal use in pediatrics, no adverse reactions were noted. One study comparing dexmedetomidine with a saline showed that the dexmedetomidine group did have significantly lower heart rate during recovery and lower systolic blood pressure at times. The dexmedetomidine group did have significantly less dizziness than the placebo group. Another study reported that children only experienced minimal discomfort during administration.

The most common adverse effects associated with dexmedetomidine therapy are hypotension, nausea, bradycardia, atrial fibrillation, hypoxia, anemia, pain, and pleural effusion. Other adverse effects have included vomiting, fever, tachycardia, infection, leukocytosis, oliguria, pulmonary edema, and thirst. A complete list of the adverse effects can be found in the product labeling.

<table>
<thead>
<tr>
<th>IV Dexmedetomidine Adverse Reactions in Procedural Sedation (&gt;2%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reactions</td>
<td>Dexmedetomidine (n = 318)</td>
<td>Placebo (n = 113)</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>14%</td>
<td>4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13%</td>
<td>24%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>54%</td>
<td>30%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>5%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradypnea</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Respiratory Depression</td>
<td>37%</td>
<td>32%</td>
</tr>
</tbody>
</table>

**Bradycardia-** < 40 bpm or ≤ 30% lower than prestudy drug infusion value

**Hypertension-** was defined in absolute and relative terms as systolic blood pressure > 180 mm Hg or ≥ 30% higher than prestudy drug infusion value or diastolic blood pressure > 100 mmHg

**Hypotension-systolic blood pressure < 80 mm Hg or ≤ 30% lower than prestudy drug infusion value or diastolic blood pressure < 50 mmHg**

**Tachycardia-** > 120 bpm or ≥ 30% greater than prestudy drug infusion value

**Hypoxia-** SpO2 < 90% or 10% decrease from baseline

**Respiratory Depression-** respiratory rate < 8 breaths or > 25% decrease from baseline.

Overdose can result in first degree AV block, second degree AV block, cardiac arrest, bradycardia, and hypotension. Most of these patients recovered spontaneously.

Prolonged sedation, tachyphylaxis, paradoxical and psychotic reactions (midazolam), polyethylene glycol toxicity (lorazepam), hyperlipidemia, hallucinations and prolonged delusional state (propofol) are not observed with dexmedetomidine.
**DRUG INTERACTIONS:** Beta blockers have their AV-blocking effect enhanced by alpha2-agonists and sinus node dysfunction may also be increased. This information was gathered from IV studies, and one intranasal dose would not likely be as strong of interactions. IV data also suggested that beta-blockers may enhance the rebound hypertensive effect of alpha2-agonist class as well. Dexmedetomidine was shown in original studies to decrease the metabolism of CYP2A6 substrates, and CYP2A6 strong inhibitors should be avoided with coadministration of continuous dexmedetomidine. However, because the plasma concentrations of dexmedetomidine are low, the chances of a clinically significant drug interaction developing with drugs metabolized by the CYP2D6 and CYP3A enzymes are also low. Dexmedetomidine requires vigilant monitoring and extra caution should be used if other hypotensive agents or sedative agents are used concurrently. Lastly, past studies showed that serotonin/norepinephrine reuptake inhibitors and tricyclic antidepressants can both decrease the antihypertensive effect of dexmedetomidine and should be monitored carefully.

**DOsing:** Intranasal dexmedetomidine has been experimentally tested in numerous studies in pediatrics. Most reports suggest that the appropriate dosing range for dexmedetomidine is between 1 mcg/kg/dose and 2 mcg/kg/dose. One study indicated that the 2 mcg/kg dose was especially appropriate in slightly older children (ages 5-8). Multiple studies have reported data regarding onset of effect and duration with intranasal dexmedetomidine. When dosed at 1 mcg/kg the median onset time of sedation was 25-30 min, with a duration an average duration of 85 minutes (55-100 min). A separate study showed that the 2 mcg/kg dose had an onset of 15 minutes.

Intranasal dosing does come with its volume limitations. Volumes of 0.2-0.3 are in the ideal range and doses should not exceed 0.5-1 mL of medication in each nostril. If higher doses and volumes are needed, make sure to separate the dose and apply it in two smaller doses a few minutes apart.

**PRODUCT AVAILABILITY AND COST:** Dexmedetomidine HCl is available as a sterile, nonpyrogenic, preservative-free solution in 2 ml glass vials and 2 ml glass ampules. Each milliliter contains dexmedetomidine HCl 118 mcg (equivalent to dexmedetomidine base 100 mcg) and sodium chloride 9 mg in water. The product should be stored at controlled room temperature (25 degrees C); excursions are allowed from 15 to 30 degrees C.

<table>
<thead>
<tr>
<th>Drug and Strength</th>
<th>Acquisition Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precedex 100 mcg/mL 2 mL vials</td>
<td>$77.09 per vial</td>
</tr>
<tr>
<td><em>Single-use vials</em></td>
<td></td>
</tr>
<tr>
<td>Midazolam 5mg/mL 2 ml vial</td>
<td>$1.25 per vial</td>
</tr>
<tr>
<td>Midazolam 5mg/mL 10 ml vial</td>
<td>$3.66 per vial</td>
</tr>
<tr>
<td>MAD300 intranasal mucosal atomization device</td>
<td>$3.19 per device</td>
</tr>
</tbody>
</table>

**MEDICATION ERROR POTENTIAL:** Administration of dexmedetomidine with anesthetics, sedatives, hypnotics, and opioids should enhance their pharmacodynamic effects; this may require a reduction in dexmedetomidine dose when used concomitantly with an anesthetic, sedative, hypnotic, and/or opioid. Dexmedetomidine may not alter the magnitude or neuromuscular blockade induced by rocuronium and other neuromuscular blockers.

Intranasal use of dexmedetomidine will necessitate education to all interdisciplinary team members on appropriate indications for use, dosing, and administration with the use of the MAD300 intranasal mucosal atomization device. Due to the fact that this medication is intended for use in high risk situations, orders will be placed and the medication will be prepared and double checked in the pharmacy IV room. Having the IV room handle preparation will also help with any potential medication errors that might be from incorrect dosing mcg/kg. Please see the attached *Failure Mode and Effects* Analysis table for a complete overview.

**MSDS REQUIRED?** No
CONCLUSION: Dexmedetomidine is an FDA approved intravenous medication used for sedation of intubated and mechanically ventilated patients in the intensive care unit (ICU) setting. It is a selective $\alpha_2$-adrenergic receptor agonist that has sedative, analgesic, anesthetic and sympatholytic properties. Alternative routes of drug administration are often desired and explored in pediatric patients to overcome varying barriers to administration. The intranasal route is an alternative choice to more standard options like oral and intravenous routes. Intranasal drug administration offers a quick, painless, noninvasive way to give medications, with onset of action generally comparable to that of IV administration where the central nervous system is the site of action\(^9\). Intranasal use of dexmedetomidine is being explored as sedative, and is desirable in the setting of procedural sedation, prior to anesthesia, and overcoming complications like getting venous access. There is a lot of strong data supporting the use of dexmedetomidine for its intravenous use, but the information and for intranasal use is still developing.

Intranasal dosing allows for absorption through the mucous membranes, similar to the buccal route. Bioavailability during a buccal study approximated to be at 82% and it is hypothesized that the intranasal bioavailability would be similar. Multiple studies have come forward showing the benefits of dexmedetomidine as a sedative when given intranasally. Studies have indicated that dexmedetomidine should be given between a dose of 1-2 mcg/kg/dose and that the onset of action is typically between 15-30 minutes. The effects of the drug last on average between 55-100 minutes\(^9\). It terms of dosing intranasally, it is important to keep in mind the volume of the medication. Volumes of 0.2-0.3 mL are in the ideal range for intranasal dosing and doses should not exceed 0.5-1 mL of medication in each nostril. Various studies have shown the sedative benefits of using dexmedetomidine. One study showed that using dexmedetomidine will result in less propofol used and lower pain scores when compared to placebo (saline). In comparison to other drugs, midazolam and dexmedetomidine were assessed as pre-sedation medications prior to anesthesia. Midazolam ultimately was determined to have done a better job at preparing patients for mask induction, but both drugs were equally effective in decreasing the separation anxiety associated when leaving a parent. Midazolam did require more pain medication use post-operatively. Another study showed that ketamine and dexmedetomidine were both equally effective in terms of sedation and that the anesthesiologists were satisfied with dexmedetomidine 90.4% of the time and ketamine 82.7% of the time. Both medications showed a decrease in the need of other sedating agents like Propofol compared to placebo.

The studies completed so far for intranasal dexmedetomidine have indicated a very clean safety profile with minimal adverse reactions. Many of the considerations and warnings for continuous sedation in the ICU are not present or common at all with this one time intranasal dose. Minimal nasal discomfort has been noted with intranasal dosing and patients in placebo groups reported more dizziness than in the dexmedetomidine group. This sedating drug should only be used by clinically trained staff experienced in monitoring sedation as lower heart rate and systolic blood pressure can present during times of sedation.

Dexmedetomidine is still featured under its brand name, Precedex, and remains rather expensive compared to other sedatives that could be used intranasally like midazolam. Precedex vials are single-use and can be over sixty times the price of a midazolam vial. Intranasal administration is done through the use of MAD300 intranasal mucosal atomization device and costs just over three dollars.

RECOMMENDATION: Add intranasal dexmedetomidine to the formulary on a restricted basis

Only to be used if the following apply:

- Other non-IV sedation medications (rectal Brevital, oral or intranasal Versed, etc.) are not appropriate options. For example, allergies or the volume for an intranasal dose exceeds 1 mL per nostril.

AND it is for one of the indications listed below:

- Procedure for which the child requires sedation and does not require administration of an IV medication or blood draw (so an IV is only required for administering sedation medications)
- A lack of an IV during sedation does not expose the child to undue risk
- The child has had several failed attempts at IV start (or is known to be or expected to be a very difficult IV start with the expectation of multiple failed IV attempts)

Respectfully Submitted by Brent Dammeier, PharmD

References available upon request.