# Intranasal Medication Administration – Adult/Pediatric – Inpatient/Ambulatory/Primary Care Clinical Practice Guideline

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## Executive Summary

### Guideline Overview

This clinical practice guideline is intended to guide clinicians in the use of medications intranasally for systemic effect which are not labelled for intranasal use.

### Key Revisions (2016 Periodic Review)

None

### Key Practice Recommendations

Refer to Table 1.

**Table 1. Intranasal medication administration for systemic absorption.**

| Drug | Appropriate Indications | Preferred Product | Dosing | Pharmacokinetics | Adverse Effects Related to Intranasal Administration |
|---|---|---|---|---|---|
| **Dexmedetomidine** | Premedication prior to general anesthesia and procedural sedation for minor surgeries and procedures[1-10] | Dexmedetomidine HCl 100 mcg/mL intranasal solution [785204] | **Adult:**<br>1-1.5 mcg/kg 45-60 minutes prior to surgery or procedure requiring sedation[15,17,23]<br><br>**Pediatric (≥10 kg and ≥1 year old):**<br>1-2 mcg/kg 45-60 minutes prior to surgery or procedure requiring sedation; use 1 mcg/kg for procedures of anticipated duration <45 minutes[1,3,5-9] | **Bioavailability:** 65% (range: 35-93%)[4]<br>**Onset:** 30-45 minutes (range: 25-68 minutes)[2,4,7-10]<br>**Peak effect:** 90-105 minutes (in adults)[10]<br>**Duration of action:**<br>▪ Adult: Easily arousable sedation with 1-1.5 mcg/kg dose for ≥180 minutes[10]<br>▪ Pediatric: Dose dependent; 1 mcg/kg dose 45 minutes (range: 40-100 minutes)[1,7,8] and 2 mcg/kg dose 95 minutes (range: 45-135 minutes)[7] | None specific to intranasal route of administration[1-10] |
| **Fentanyl** | Acute analgesia | Fentanyl citrate 50 mcg/mL intranasal solution [785209] | **Adult:**<br>0.9-2.2 mcg/kg (maximum of 100 mcg/2 mL) initial dose, may repeat with 60 mcg every 5 minutes thereafter[24,25]<br><br>**Pediatric (≥10 kg and ≥1 year old):**<br>1-1.5 mcg/kg/dose[11-17] | **Bioavailability:** 55-77%[18]<br>**Onset:** 5 to 10 minutes[15,16,18]<br>**Peak effect:** ~20 minutes[18]<br>**Duration of action:** ~50 minutes[18] | Self-resolving unpalatable taste, watery eyes, nasal congestion, or throat irritation in adult patients (information regarding pediatric adverse effects not available)[15,19] |
| **Flumazenil** | Initial route of administration for cases of suspected or actual benzodiazepine overdose when IV route is not available[96,97] | Flumazenil 100 mcg/mL intranasal solution [785205] | **Adult:**<br>Not recommended<br><br>**Pediatric:**<br>40 mcg/kg with a maximum dose of 200 mcg (100 mcg in each nostril)[20,21] | **Bioavailability:** Undetermined[21]<br>**Onset:** <2 minutes[21]<br>**Peak effect:** 2 minutes[21]<br>**Duration of action:** Undetermined[21] | None specific to intranasal route of administration[20,21] |
| **Glucagon** | **Not recommended for intranasal use**[22-33] | | | | |
| **Haloperidol** | **Not recommended for intranasal use** | | | | |

| Drug | Appropriate Indications | Preferred Product | Dosing | Pharmacokinetics | Adverse Effects Related to Intranasal Administration |
|---|---|---|---|---|---|
| **Hydromorphone** | Acute analgesia | Hydromorphone HCl 1 mg/mL intranasal solution [785206] | **Adult:**<br>1-2 mg per dose[34-36]<br><br>**Pediatric:**<br>Not recommended[34-36] | **Bioavailability:** ~55% (1 mg dose range 26-71%; 2 mg dose range 36-78%)[36]<br>**Onset:** 10-20 minutes[34,35]<br>**Peak effect:** 20-50 minutes[34,35]<br>**Duration of action:** 180 minutes[35] | Self-resolving unpalatable taste, nasal itching, nasal congestion, or nasal stinging[34,35] |
| **Ketamine** | Procedural sedation and premedication for reducing preoperative anxiety[37-49] | Ketamine HCl 100 mg/mL intranasal solution [785203] | **Adult:**<br>Not recommended[37-49]<br><br>**Pediatric (≥5 kg and ≥6 months old):**<br>▪ Procedural sedation: 6-9 mg/kg 4-8 minutes prior to procedures anticipated to last <30-40 minutes[37,38,48]<br>▪ Premedication: 0.5-10 mg/kg (preference of doses ≥3 mg/kg) 15-30 minutes prior to separation from parents[40-44,49,50] | **Bioavailability:** 50%[44]<br>**Onset:** ~5 minutes (range: 4-10 minutes)[37,38,48]<br>**Peak effect:** Not established[37-39,48,49]<br>**Duration of action:** 40 minutes (range: 22-69 minutes)[37-39,48,49] | None specific to intranasal route of administration[37-49] |
| **Lidocaine** | Treatment of moderate to severe migraines when alternatives are ineffective and for idiopathic second-division trigeminal neuralgia[51-55] | Lidocaine HCl 40 mg/mL (4%) intranasal solution [785202] | **Adult:**<br>▪ Migraines: 20 mg in nostril of affected side if unilateral, 20 mg in each nostril if bilateral; may repeat with second dose if lack of relief within 2-15 minutes[51-54]<br>▪ Idiopathic second-division trigeminal neuralgia: 8 mg in each nostril for a total dose of 16 mg[55]<br><br>**Pediatric:**<br>Not recommended[51-55] | **Bioavailability:** 26% (range: 5-48%)[56]<br>**Onset:** 5-15 minutes[51]<br>**Peak effect:** Undetermined<br>**Duration of action:** Undetermined | Self-resolving local irritation (burning, stinging, numbness), bitter taste, numbness of the throat, and nausea[51] |
| **Lorazepam** | Acute seizure treatment | Lorazepam 4 mg/mL injection solution | **Adult:**<br>0.1 mg/kg[55,57]<br><br>**Pediatric (≥2 months old):**<br>0.1 mg/kg (consider maximum of 4 mg dose)[57,58] | **Bioavailability:** ~78%[59]<br>**Onset:** ~5 minutes (range: 1-25 minutes)[57,58]<br>**Peak effect:** 30-105 minutes[59,60]<br>**Duration of action:** ~60 minutes[58] | Poor taste, cool feeling in nose and throat, burning nasal sensation[55,57] |

| Drug | Appropriate Indications | Preferred Product | Dosing | Pharmacokinetics | Adverse Effects Related to Intranasal Administration |
|---|---|---|---|---|---|
| **Midazolam** | Procedural sedation prior to minor procedures or imaging and pre-induction for general anesthesia and alternative therapy for pediatric seizures when the IV route is not available[61,62] | Midazolam HCl 5 mg/mL intranasal solution [785196] | **Adult:**<br>Not routinely recommended due to nasal volume limitations, but may consider 0.2-0.3 mg/kg if alternative routes unavailable (maximum of 10 mg due to volume administration limitations)[63]<br><br>**Pediatric:**<br>▪ Procedural sedation and pre-induction for general anesthesia: 0.2-0.5 mg/kg (consider maximum dose of 10 mg due to volume limitations)[50,61,62,64-82]<br>▪ Seizures: 0.2-0.5 mg/kg[63,83-89]; Reference Status Epilepticus - Pediatric - Emergency Department/Inpatient Clinical Practice Guideline for additional information | **Bioavailability:** 50-83%[64]<br>**Onset:** Average 3-15 minutes (range: 0.5 to 19 minutes)[64,67,68,73,83,86,88]<br>**Peak effect:** ~25 minutes (10-48 minutes)[90,91]<br>**Duration of action:** 21 to 60 minutes (dose-dependent)[61,64,67,73,79,92] | Self-limiting discomfort, irritation, or burning sensation in nasal passages[60,90] |
| **Morphine** | **Not recommended for intranasal use**[93-97] | | | | |
| **Naloxone** | Initial route of administration for cases of suspected or actual opioid overdose when the IV route is not available | Naloxone 1 mg/mL intranasal solution [785210] | **Adult:**<br>2 mg (1 mg in each nostril)[98-104]<br><br>**Pediatric:**<br>0.4 mg total dose (0.2 mg in each nostril) based upon a single case report[20] | **Bioavailability:** 4%[105]<br>**Onset:** Undetermined[105]<br>**Peak effect:** 6-9 minutes[105]<br>**Duration of action:** Undetermined[105] | None specific to intranasal route of administration[98-108] |

**Companion Documents**

- UWHC Clinical Policy 8.76: Pain Management
- UWHC Clinical Policy 8.38: Adult Sedation Policy
- UWHC Clinical Policy 8.56: Pediatric Sedation Policy
- UWHC Sedation Nursing Practice Guideline
- Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Pediatric
- Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Adult
- Status Epilepticus - Pediatric - Emergency Department/Inpatient Clinical Practice Guideline

## Scope

**Disease Condition:** Off-label intranasal medication administration

**Clinical Specialty:** All medical specialties

**Intended Users:** Physicians, Advanced Practice Providers, Nurses, and Pharmacists

**Objective**

The clinical practice guideline is intended to provide a standardized process for off-label intranasal administration of specific medications which are not commercially intended for administration via this route and which have demonstrated systemic absorption and effects.

For information regarding intranasal analgesia prior to insertion of nasogastric tubes, please see the following guidance documents: Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Pediatric and Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Adult.

**Target Population**

Adult and pediatric patients for whom off-label intranasal mediations are being considered.

**Interventions and Practices Considered**

This guideline recommends intranasal medication dosing, product selection, and other considerations for the use of medications given intranasally which are not labeled for intranasal use.

**Major Outcomes Considered**

- Utilization of intranasal medications as identified in guideline
- Adverse events associated with intranasal medication use

## Methodology

**Methods Used to Collect/Select the Evidence**

Electronic database searches (i.e. PUBMED) were conducted and workgroup members to collect evidence for review; for the 2016 revision, clinical evidence dating back to January 2014 was reviewed. Additionally, hand searches were performed within selected evidence for other relevant resources. Expert opinion, clinical experience, and regard for patient safety/experience were also considered during discussions of the evidence.

PubMed was used as the primary modality for identifying primary literature articles. The Boolean search string used for each drug was "[generic drug name without specifics about salts/chemical formulation] AND (nasal OR intranasal)". For example, the search string for fentanyl was "fentanyl AND (nasal OR intranasal)". All clinical and pharmacokinetic case reports and trials in human patients where the drug was used via the intranasal route were included, and all animal studies were excluded. A comprehensive

search was performed by reviewing the references of all included studies for more studies which should be considered in guideline development.

**Methods Used to Formulate the Recommendations**
All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees.

**Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:**
Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.[109]

**Rating Scheme for the Strength of the Evidence/Strength of the Recommendations:**
See Appendix A for the rating scheme used within this document.

**Recognition of Potential Health Care Disparities**
No potential disparities identified.

## Definitions

LMA MAD Nasal™: "mucosal atomization device" (MAD) made by the company LMA North America, Inc. which is attached to a standard syringe via Luer-Lock in order to turn an intravenous drug product into a fine mist for intranasal administration (See Figure 1).

**Figure 1. LMA MAD Nasal™**

## Introduction

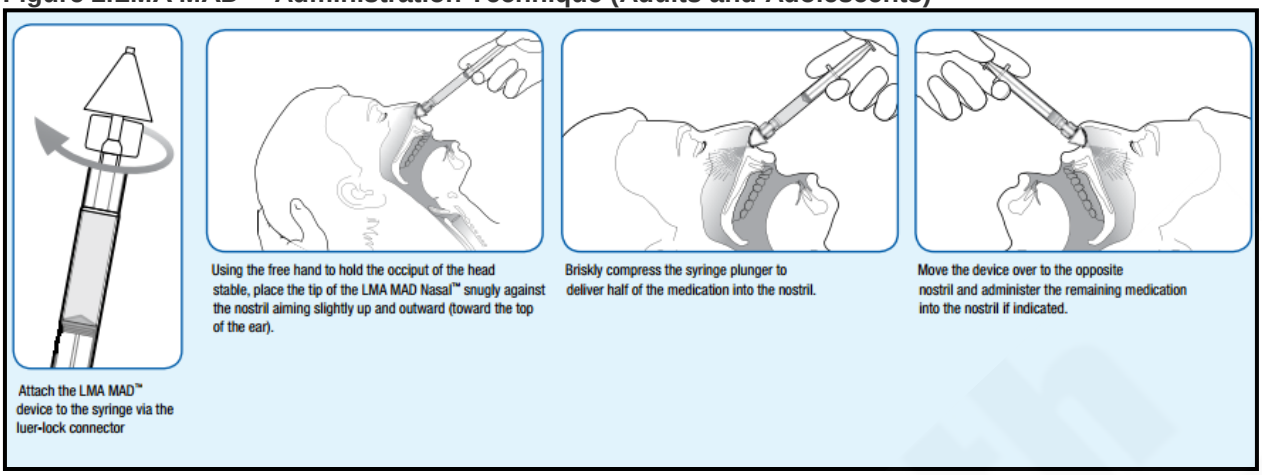
Intranasal (IN) administration of medications has previously demonstrated advantages in effectiveness, patient comfort, and workplace safety when compared to alternative routes such as intravenous (IV) and intramuscular (IM) for numerous medication classes including: opioid agonists, benzodiazepines (BZDs), anesthetics, sedatives, and antidotes.[110,111] Nasal administration is most commonly associated with local topical outcomes, but kinetic and clinical trials have previously confirmed bioavailability which approximates that of IV or IM administration for numerous systemic medications with IN administration. Therefore, the highly vascularized nasal mucosa can be considered an effective modality for parenteral administration which provides rapid absorption and bypasses first-pass metabolism.[112] IN administration may yield several advantages over other parenteral routes of administration, as it circumvents pain associated with IV line placement and IM delivery. Additionally, IV access can be difficult, may delay care, requires nursing time resources, and can be unnecessary in certain patient populations and conditions.[113]

## Recommendations

### *General Recommendations for Intranasal (IN) Administration*

1. Do not administer medications nasally if the patient's nasal passages demonstrate signs of local mucosal irritation, inflammation, bleeding, excoriation, or ulceration.[114] Consider an alternative route of administration.[115] *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
2. Administration volumes
   2.1. Administration volumes should be minimized, as mucosal surfaces may become saturated leading to runoff into the oropharynx and decreased absorption.[115] (*UWHealth Strong Recommendation, Moderate Quality of Evidence)*
   2.2. Optimal volume of administration per nostril is between 0.15 mL and 0.4 mL in order to prevent oral absorption, but up to 1 mL may be administered per nostril.[115-118] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
   2.3. Repeat dosing has not been studied for most medications administered via the IN route and is not recommended unless otherwise specified for a specific drug. *(UWHealth Strong Recommendation, Low Quality of Evidence)*
   2.4. Maximally concentrated drug products should be used whenever possible in order to reduce volume of administration.[115] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
3. Administration Technique (See Figure 2)
   3.1. If able, have the patient gently blow his or her nose prior to administration.[114] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   3.2. Draw appropriate volume of drug plus an additional 0.1 mL into a 1 mL or 3 mL syringe depending upon final volume of drug required. The volume drawn up should be 0.1 mL more than the volume to be administered in order to account for dead space in the LMA MAD Nasal.[11] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   3.3. Remove needle and discard securely. Attach the LMA MAD Nasal to the syringe via the Luer-lock connector on the syringe.
   3.4. Routine IN administration without the LMA MAD Nasal is not recommended, as the MAD increases consistent medication absorption.[115] *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
   3.5. IN Delivery Device Placement and Considerations
      3.5.1. Adults and adolescents: Use free hand to hold occiput of the patient's head stable. Place tip of LMA MAD Nasal snugly against the nostril and aim up and outward toward lateral nasal wall (the inferior and middle turbine mucosa).[114] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
      3.5.2. Young pediatric patients: Show patients the "squirter" (LMA MAD Nasal) and reassure that the device is not a "shot". Consider allowing the child to touch and feel the soft "pillow" of the device so they know it will not hurt them. It is encouraged for patients to sit on the parent or caregiver's lap with the parent or caregiver giving a hug over his or her arms (in a comfort hold) to prevent the child from covering his or her face. Patients can be told to "sniff like smelling a flower" as the medication is delivered. *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   3.6. Briskly compressing the syringe plunger, deliver half of the medication dose into each nostril to maximize dispersion and absorption surface area.[115] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
   3.7. Ideally, have the patient remain in a semirecumbent position with the head of the bed elevated 30-45 degrees for 10 minutes after administration in order to prevent runoff out of the nose, if able.[114] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   3.8. Instruct the patient to refrain from blowing his or her nose for at least 60 minutes after IN administration to maximize medication absorption.[114] *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
4. Adverse Effects
   4.1. The systemic adverse effects and patient monitoring associated with intravenous administration of the medications included in this guideline also apply to IN administration. (*UWHealth Strong Recommendation, Very Low Quality of Evidence)*
   4.2. Administration via the IN route has demonstrated self-limiting local adverse effects for several medications in addition to the systemic adverse effects associated with alternative routes of administration. See ***Drug-Specific Practice Recommendations*** for information regarding specific medication adverse effects. *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*

**Figure 2.LMA MAD™ Administration Technique (Adults and Adolescents)[119]**




## ***Drug-Specific Practice Recommendations***

**Dexmedetomidine**

1. Appropriate indications: Premedication prior to general anesthesia and procedural sedation for minor surgeries and procedures.[1-10] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
2. Dosing
   - 2.1. Adult: 1-1.5 mcg/kg 45 to 60 minutes prior to surgery or procedure requiring sedation.[2,4,10] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
     - 2.1.1. Use cautiously in patients over the age of 40 years due to limited evidence for IN administration in this patient population.[2,4,10] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
     - 2.1.2. Adjunct agents should be used to maintain adequate sedation for procedures lasting longer than 180 minutes.[2] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   - 2.2. Pediatric (patients ≥10 kg and ≥1 year of age): 1-2 mcg/kg 45 to 60 minutes prior to surgery or procedure requiring sedation.[1,3,5-9] *(UWHealth Strong Recommendation, High Quality of Evidence)*
     - 2.2.1. For procedures of anticipated duration fewer than 45 minutes, patients should receive 1 mcg/kg dexmedetomidine instead of 2 mcg/kg due to possible prolonged sedation and recovery time.[1,3,5,7] *(UWHealth Strong Recommendation, High Quality of Evidence)*
     - 2.2.2. Adjunct agents may be necessary to maintain adequate sedation for procedures lasting longer than 95 minutes in patients who receive 2 mcg/kg.[7] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
     - 2.2.3. Doses greater than 0.5 mcg/kg should be administered due to previously demonstrated inadequate levels of sedation.[9] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
3. Preferred product: dexmedetomidine HCl 100 mcg/mL intranasal solution
4. Pharmacokinetics
   - 4.1. Bioavailability: 65% (range: 35-93%)[4]
   - 4.2. Onset: 30-45 minutes (range: 20-68 minutes)[2,4,7-10]
   - 4.3. Peak effect: 90-105 minutes in adult patients (data on pediatric patients not available)[10]
   - 4.4. Duration of action: Dose dependent in pediatric patients - 1 mcg/kg dose 45 minutes (range: 40-100 minutes)[1,7,8] and 2 mcg/kg dose 95 minutes (range: 45-135 minutes)[7]; adult patients receiving 1-1.5 mcg/kg doses have previously demonstrated easily arousable sedation 180 minutes after administration.[10]
5. IN adverse effects: Previous studies have not demonstrated adverse effects specific to the IN route of administration.[1-10]

**Fentanyl**

1. Appropriate indications: Acute analgesia

2. Dosing
   2.1. Adult: 0.9-2.2 mcg/kg (maximum of 100 mcg/2 mL) initial dose; may repeat with 60 mcg doses every 5 minutes.[19,120,121] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
      2.1.1. Use cautiously in patients 70 years of age and older due to lack of data. *(UWHealth Strong Recommendation, Low Quality of Evidence)*
   2.2. Pediatric (patients ≥10 kg and ≥1 year of age): 1-1.5 mcg/kg/dose.[11-17,122] (*UWHealth Strong Recommendation, Moderate Quality of Evidence)*
3. Preferred product: fentanyl citrate 50 mcg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: 55-77%[18]
   4.2. Onset: 5 to 10 minutes[15,16,18]
   4.3. Peak effect: about 20 minutes[18]
   4.4. Duration of action: about 50 minutes[18]
5. IN adverse effects: Inform patients that IN fentanyl may cause self-resolving unpalatable taste, watery eyes, nasal congestion, or throat irritation in adult patients. Information regarding pediatric adverse effects with IN fentanyl is not available.[15,19]

**Flumazenil**

1. Appropriate indications: May be considered as initial route of administration for cases of suspected or actual benzodiazepine overdose when the intravenous route is not available.[20,21] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
2. Dosing
   2.1. Adult: Not recommended for administration as has not been studied in this patient population. *(UWHealth Strong Recommendation, Low Quality of Evidence)*
   2.2. Pediatric: 40 mcg/kg with a maximum dose of 200 mcg (100 mcg in each nostril).[20,21] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
3. Preferred product: flumazenil 100 mcg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: Undetermined[21]
   4.2. Onset: <2 minutes[21]
   4.3. Peak effect: 2 minutes[21]
   4.4. Duration of action: Undetermined[21]
5. IN adverse effects: No IN route-specific adverse effects have been identified.[20,21]

**Glucagon**

1. Not recommended for administration via the IN route, as has been previously demonstrated to have low absorption.[28] Previous studies have used absorption enhancers to increase the bioavailability of IN administration, and these are not available at UWHealth.[22-33] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

**Haloperidol**

1. Haloperidol: Not recommended for administration via the IN route. Previous studies have not been able to determine the optimal dose and the effect of repeat dosing using the IN route.[123,124]

**Hydromorphone**

1. Appropriate indications: Acute analgesia
2. Dosing
   2.1. Adult: 1-2 mg IN per dose is preferred.[34-36] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
      2.1.1. Redosing sooner than 20 minutes after the initial dose is not recommended.[34-36] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
   2.2. Pediatric: Not recommended, as has not been prospectively studied in this patient population.[34-36] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
3. Preferred product: hydromorphone HCl 1 mg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: about 55% (1 mg dose range 26-71%; 2 mg dose range 36-78%)[36]
   4.2. Onset: 10-20 minutes[34,35]

4.3. Peak effect: 20-50 minutes[34,35]
4.4. Duration of action: 180 minutes[35]
5. IN adverse effects: Inform patients that IN hydromorphone may cause self-resolving unpalatable taste, nasal itching, nasal congestion, or nasal stinging for a short period of time after administration.[34,35]

**Ketamine**
1. Appropriate indications: Procedural sedation and premedication for reducing preoperative anxiety.[37-49,125] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
2. Dosing
   2.1. Adult: Use is not recommended due to a lack of data evaluating the use of IN ketamine in this population and the suspected inability that therapeutic levels could be attained due to IN volume administration limits.[37-49] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*
   2.2. Pediatric (patients ≥5 kg and ≥6 months of age)
      2.2.1. Procedural sedation: 6-9 mg/kg 4 to 8 minutes prior to commencing for procedures anticipated to last fewer than 30 to 40 minutes.[37,38,48] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
      2.2.2. Premedication: 0.5-10 mg/kg between 15 to 30 minutes prior to procedure. Doses of at least 3 mg/kg are preferred due to more available data.[40-44,49,50] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
3. Preferred product: ketamine HCl 100 mg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: 50%[44]
   4.2. Onset: about 5 minutes (range: 4-10 minutes)[37,38,48]
   4.3. Peak effect: Not established[37-39,48,49]
   4.4. Duration of action: 40 minutes (range: 22-69 minutes)[37-39,48,49]
5. IN adverse effects: No IN route-specific adverse effects have been identified.[37-49]

**Lidocaine**
1. Appropriate indications: Treatment of moderate to severe migraines when alternatives are ineffective and for idiopathic second-division trigeminal neuralgia.[51-55] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
2. Dosing
   2.1. Moderate to severe migraines
      2.1.1. Adult: 20 mg in nostril of affected side if unilateral; 20 mg in each nostril if bilateral.[51-54] If moderate to severe pain persists after 2 to 15 minutes, may repeat initial lidocaine dose.[51,53] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
      2.1.2. Pediatric: Not recommended, as has not been studied in this patient population. *(UWHealth Strong Recommendation, Low Quality of Evidence)*[51-54]
   2.2. Idiopathic second-division trigeminal neuralgia
      2.2.1. Adult: 8 mg in each nostril for a 16 mg total dose.[55] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
      2.2.2. Pediatric: Not recommended, as has not been studied in this patient population.[55] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
3. Preferred product: lidocaine HCl 40 mg/mL (4%) intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: 26% (range: 5-48%)[56]
   4.2. Onset: 5-15 minutes[51]
   4.3. Peak effect: Undetermined
   4.4. Duration of action: Undetermined
5. IN adverse effects: Inform patients or caregivers about the potential for self-limiting local irritation (burning, stinging, numbness), bitter taste, numbness of the throat, and nausea.[51]

**Lorazepam**
1. Appropriate indications: Control of acute seizures.[57-60]
2. Dosing
   2.1. Adult: 0.1 mg/kg[59,60] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

2.2. Pediatric (patients ≥2 months of age): 0.1 mg/kg with consideration to a maximum dose of 4 mg.[57,58] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
3. Preferred product: lorazepam 4 mg/mL injection solution
4. Pharmacokinetics
   4.1. Bioavailability: about 78%[59]
   4.2. Onset: about 5 minutes (range:1-25 minutes)[57,58]
   4.3. Peak effect: 30-105 minutes[59,60]
   4.4. Duration of action: about 60 minutes[58]
5. IN adverse effects: Clinicians should inform patients or caregivers about the potential for poor taste, cool feeling in nose and throat, and burning nasal sensation which is self-limiting in nature.[59,60]

**Midazolam**

1. Appropriate indications: Procedural sedation prior to minor procedures or imaging and pre-induction for general anesthesia and alternative therapy for pediatric seizures when the IV route is not available.[61,62]
2. Dosing
   2.1. Adult: Not routinely recommended due to the inability to administer therapeutic doses secondary to nasal administration volume limitations, but may consider 0.2-0.3 mg/kg dose for patients (maximum of 10 mg due to volume administration limitations) with prolonged seizures if other routes of administration are unavailable.[63] *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
   2.2. Pediatric
      2.2.1. Procedural sedation and pre-induction for general anesthesia (patients ≥9 kg and ≥6 months of age): 0.2-0.5 mg/kg with consideration to a maximum dose of 10 mg due to volume administration limitations.[50,61,62,64-82] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
      2.2.2. Seizures (patients ≥1 month of age): 0.2-0.5 mg/kg[63,83-89] (*UWHealth Strong Recommendation, Moderate Quality of Evidence).* . Reference Status Epilepticus - Pediatric - Emergency Department/Inpatient Clinical Practice Guideline for additional information.
3. Preferred product: midazolam HCl 5 mg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: 50-83%[64]
   4.2. Onset: Average 3-15 minutes (range: 0.5-19 minutes)[64,67,68,73,83,86,88]
   4.3. Peak effect: about 25 minutes (10-48 minutes)[90,91]
   4.4. Duration of action: 21 to 60 minutes (dose-dependent)[61,64,67,73,79,92]
5. IN adverse effects: Clinicians should inform patients or caregivers about the potential for self-resolving discomfort, irritation, or burning sensation in the nasal passages after administration.[63,126]

**Morphine**

1. Not recommended for administration via the IN route. Previous studies have used a mucoadherant to increase bioavailability of IN administration which is not available at UWHealth.[93-97] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

**Naloxone**

1. Appropriate indications: May be considered as initial route of administration for cases of suspected or actual opioid overdose when the intravenous route is not available.
2. Dosing
   2.1. Adult: 2 mg administered as 1 mg/1 mL in each nostril.[98-104] *(UWHealth Strong Recommendation, High Quality of Evidence)*
   2.2. Pediatric: 0.2 mg in each nostril based upon limited data from a case report involving sedation reversal of a benzodiazepine and opioid.[20] *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
   2.3. The use of alternative routes of administration such as intravenous, intramuscular, and intraosseous should be considered if an adequate response is not achieved within 8 to 10 minutes after the first IN dose. This is due to the increased likelihood of orogastric absorption and reduced efficacy with subsequent IN administrations, as the oral bioavailability of naloxone is low and the nasal mucosa likely would not be dry and conducive for adequate absorption.
      2.3.1. Consider doses up to 2 mg of naloxone via the intravenous route for cases of non-response to IN naloxone in both pediatric patients and adults[99] *(UWHealth Strong Recommendation, Low Quality of Evidence)*

3. Product to be used: naloxone 1 mg/mL intranasal solution
4. Pharmacokinetics
   4.1. Bioavailability: 4%[105]
   4.2. Onset: Undetermined[105]
   4.3. Peak effect: 6-9 minutes[105]
   4.4. Duration of action: Undetermined[105]
5. IN adverse effects: No IN route-specific adverse events have been identified.[98-108]

## UW Health Implementation

### Potential Benefits

- Increased patient comfort, decreased administration pain compared to IV placement or IM administration, and faster administration time in situations where IV line access is challenging
- Increased workplace safety by potentially reducing healthcare employee needle sticks
- Decreased resources (e.g. nursing time for IV placement)

### Potential Harms

- Staff unfamiliarity with intranasal administration compared to other routes
- Dosage miscalculations or inappropriate use of other route of administration dosing for intranasal route

### Pertinent UWHealth Policies and Procedures

- UWHC Clinical Policy 8.76: Pain Management
- UWHC Clinical Policy 8.38: Adult Sedation Policy
- UWHC Clinical Policy 8.56: Pediatric Sedation Policy
- UWHC Sedation Nursing Practice Guideline
- Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Pediatric
- Pain Care Fast Facts: Intranasal Analgesia Prior to Insertion of Nasogastric Tube – Adult

### Patient Resources

None

### Guideline Metrics

1. Utilization rate of intranasal medications in guideline
2. Adverse event rate of intranasal medications in guideline

### Implementation Plan/Clinical Tools

1. Guideline will be posted on UConnect in a dedicated location for Clinical Practice Guidelines.
2. Release of the guideline will be advertised in the Physician/APP Briefing newsletter.
3. Content and hyperlinks within clinical tools, documents, or Health Link related to the guideline recommendations will be reviewed for consistency and modified as appropriate.

### ERX

- Dexmedetomidine HCl 100 mcg/mL intranasal solution [785204]
- Fentanyl citrate 50 mcg/mL intranasal solution [785209]
- Flumazenil 100 mcg/mL intranasal solution [785205]
- Hydromorphone HCl 1 mg/mL intranasal solution [785206]
- Ketamine HCl 100 mg/mL intranasal solution [785203]
- Lidocaine HCl 40 mg/mL (4%) intranasal solution [785202]
- Midazolam HCl 5 mg/mL intranasal solution [785196]
- Naloxone 1 mg/mL intranasal solution [785210]

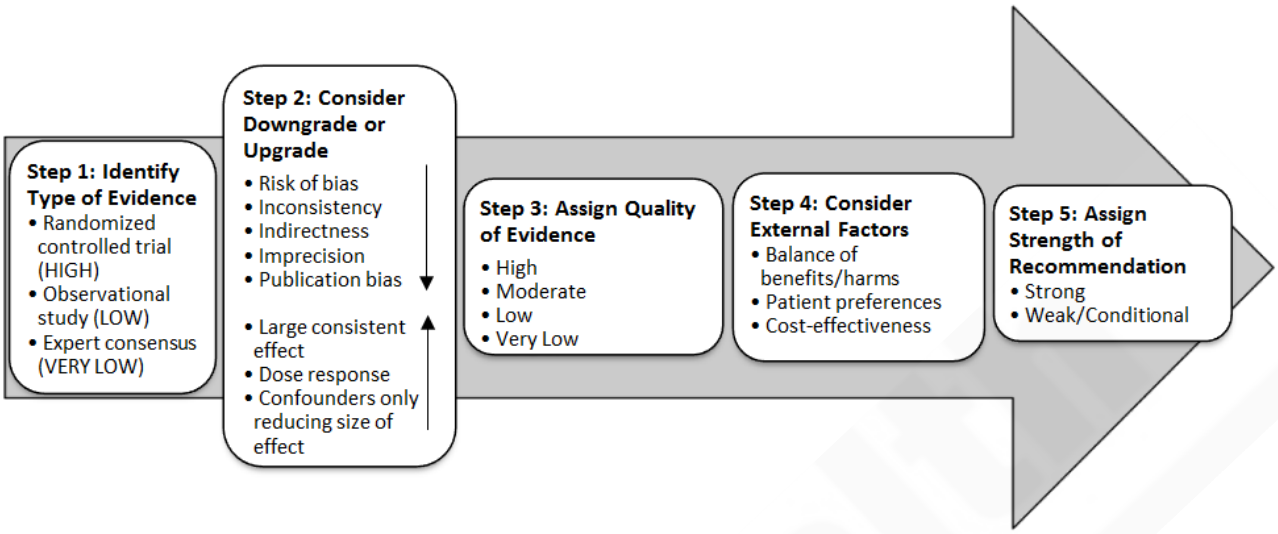
### Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or

to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

## Appendix A. Evidence Grading Scheme

Figure 1. GRADE Methodology adapted by UWHealth[109]




**GRADE Ranking of Evidence**

| | |
|---|---|
| **High** | We are confident that the effect in the study reflects the actual effect. |
| **Moderate** | We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different. |
| **Low** | The true effect may differ significantly from the estimate. |
| **Very Low** | The true effect is likely to be substantially different from the estimated effect. |

**GRADE Ratings for Recommendations For or Against Practice**

| | |
|---|---|
| **Strong** | The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision. |
| **Weak/conditional** | Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. |

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