Giving Meds By Alternate Routes

(full update June 2024)

Off-label routes of drug administration are considered when patients can't take a medication by the usual route. Other reasons for using an alternative administration route include minimization of side effects, dosing accuracy, improved efficacy, or cost savings. Consider injectables orally when an oral solution is needed, but isn't available or is unsuitable. Rectal administration of tablets, capsules, oral liquids, or injectables may be the best route at the end of life. Ophthalmic drops can generally be used in the ear to save money.[11] But ear drops cannot be used in the eye; their preservatives may harm the eye.[12] Furthermore, eye drops are sterile and buffered specifically for eye use.[13] **Evidence supporting off-label administration routes is often anecdotal and from experience in end-of-life patients.** Use your knowledge of physiology, pharmacokinetics, pharmacodynamics, and pharmaceutics to avoid mishaps. Avoid oral use of injectable meds if the drug isn't stable in the GI tract or is poorly absorbed orally. Ensure patients or caregivers know how to administer the drug by the alternative route, and give specific instructions for the label instead of writing "as directed." The table below provides information on alternative routes for certain medications. For important information specific to **rectal administration, see footnote "a."** For important information specific to **intranasal** administration see footnote "b."

Medication	Alternative Route	Comments
Acetylcysteine injection solution	Oral	• Dilute the 20% solution with three-parts diet soda to one-part acetylcysteine injection. May use water if giving via nasogastric tube.[24]
Atropine 1% ophthalmic	Sublingual	• Used for death rattle in **end-of-life patients**, although it is probably ineffective.[76,77] Regimens that have been used include three drops three times daily, plus "rescue" doses, or two drops every two hours, as needed, or one to four drops every four hours or as needed.[10,32,70] • For children with **excessive drooling**, consider one drop twice daily (morning and afternoon).[27]
Carbamazepine suspension	Rectal[a]	• Dose as for oral.[78] Dilute with an equal volume of water to prevent a laxative effect.[8,74] Monitor levels.[3]
Carbamazepine tablets	Rectal[a]	• Crush and administer in a gelatin capsule. Use the same total daily dose rectally as orally, but the dose may have to be divided six or eight times daily to reduce volume. Monitor levels due to variable absorption.[3]
Ciprofloxacin ophthalmic	Ear[12]	---

Medication	**Alternative Route**	**Comments**
Cortisporin ophthalmic (US; generic only)	Ear[12]	---
Dexamethasone injection	Oral	• Alternative to dexamethasone oral solution, which contains alcohol.[16] • Mix with wild cherry-flavored syrup, or "chase" with juice or a popsicle.[16,17]
Dexmedetomidine injection	Nasal[b]	• Used as a sedative/analgesic pre-procedure (e.g., 2 to 3 mcg/kg) or pre-op (e.g., 1 to 2 mcg/kg).[46] • Volume may preclude use in adults.[60] • Can give diluted or undiluted, with a syringe or atomizer (examples): o Dilute dose with normal saline to a final volume of 1.6 mL, and spray half (0.8 mL) in each nostril.[52] **or** o Give undiluted dose via an intranasal mucosal atomization device, or drip slowly into the nose from a tuberculin syringe.[53] **or** o Make a more dilute solution before drawing up the dose if the dose is very small. See https://www.health.qld.gov.au/__data/assets/pdf_file/0029/1225487/nmq-dexmedetomidine.pdf.
Dexmedetomidine injection	Oral	• Used as a pre-op sedative/analgesic pre-op in children (often 2 to 4 mcg/kg).[56,71,72] • Has been diluted in apple juice or honey.[56,71,72]
Diazepam injection	Rectal[a]	• Most data are for acute use in children. • May cause burning sensation, perhaps due to the presence of propylene glycol.[47] • For acute seizures, use of **commercially available rectal gel** may be preferable.[15]
Docusate liquid (not syrup)	Ear	• To soften ear wax. Instill 1 mL into the affected ear, wait 15 minutes, then allow the solution to drain out. Any remaining wax may be removed with gentle, lukewarm water irrigation using an ear syringe.[35]
Doxepin capsules	Rectal[a]	• Doses of 25 mg once daily to 50 mg three times daily have been reported to be effective for pain, but a dose of 50 mg twice daily may be needed to achieve "therapeutic" levels.[73]
Droperidol injection (US)	Rectal[a]	• Extent of absorption unknown. Effects may last only two to four hours.[6]
Enalaprilat injection	Do NOT give orally	• Poorly absorbed orally.[18]

Medication	**Alternative Route**	**Comments**
Esomeprazole injection	Do NOT give orally	• Not acid-stable.[19]
Fentanyl injection (50 mcg/mL)	Nasal[b]	• Used for acute pain or end-of life dyspnea.[4,5,41] • Doses are typically 1 to 2 mcg/kg for acute pain.[41,55] Consider 50 mcg to palliate dyspnea in adults.[5] • Most data are in patients ≥3 years of age.[55] • Administer intranasally with a mucosal atomizer device or dripped into the nose with a needless syringe.[22] Patient should sit in a semi-reclined position for several minutes after administration.[22] Max volume 0.5 to 1 mL per nostril.[22] For larger doses, give in divided doses a few minutes apart.[22]
Gabapentin	Do NOT give rectally	• Poorly absorbed rectally, in part because the rectum lacks the active transport mechanism necessary for its absorption.[15]
Haloperidol oral solution 2 mg/mL	Rectal[a,40]	• No data.[44] • Consider dosing as for oral.[40]
Ibuprofen oral suspension	Rectal[a,6]	• Can use same dose as oral, but consider volume with higher doses may be too high to be retained (e.g., 600 to 800 mg = 30 to 40 mL).[6]
Ketamine injection	Oral	• Used for preanesthesia sedation in children (e.g., 6 to 8 mg/kg [3 mg/kg with midazolam]), or refractory chronic pain in adults (e.g., 10 to 25 mg three to four times daily, initially [usual max 400 mg/day]).[22] • Mix with sour cherry juice, cola, or other beverage immediately before administration to mask bitter taste.[22]
Ketamine injection	Nasal[b]	• Used for procedural sedation/analgesia in children (e.g., 3 to 9 mg/kg [monotherapy]; 0.5 to 2 mg/kg with midazolam),[23,60] or acute pain in the emergency department in adults and children (e.g., ~1 mg/kg [avoid in children <3 months of age]).[7,14,60] • Volume may preclude use as a sedative in adults.[60] • Use a 50 or 100 mg/mL solution, undiluted or diluted with normal saline to make a final volume of 0.5 to 2 mL. Administer with a mucosal atomizer device and divide between nostrils if needed (max 0.5 mL per nostril).[22] • May cause sore throat or bad taste.[60]

Medication	**Alternative Route**	**Comments**
Lamotrigine tablet or chewable tablet	Rectal[a]	• Lamotrigine suspension for rectal administration via a small catheter has been prepared by crushing a 100 mg tablet or a 100 mg chewable tablet in 6 mL of room temperature tap water followed by two 2 mL syringe-tubing rinses. Bioavailability was 63% for the tablets and 52% for the chewable tablets, with wide intersubject variability.[28,29] Clinical response and lamotrigine levels should be monitored if lamotrigine is administered rectally.[29]
Levothyroxine	Rectal[a,65]	• See footnote "a" for general recommendations/guidance.
Lidocaine injection or topical	Nasal[b]	• Used to reduce nasal discomfort due to irritating intranasal medication (e.g., midazolam or other acidic solutions).[48] It is unclear whether pre-administration with lidocaine is more effective than co-administration in the same mucosal atomizer device as midazolam.[25,48] Options: o Administer 0.5 mL of preservative-free 4% lidocaine (0.25 mL per nostril) via mucosal atomizer device five minutes prior to irritating medication.[25,48,60] Keep in mind that some patients might not tolerate receiving multiple intranasal medications.[60] o Alternatively, 0.5 mL of 4% lidocaine can be mixed with the intranasal midazolam dose, but this will require multiple administrations due to volume limitation (1 mL per nostril).[48] • For migraine and cluster headache, lidocaine has been used intranasally.[54.,59] o For migraine, 0.5 mL of lidocaine 4% topical solution was dripped over 30 seconds into the nostril on the side of the headache, with the patient's head tilted back 45 degrees and rotated 30 degrees to the side of the headache. This was repeated on the other side for bilateral headache. The dose could be repeated after two minutes.[59] o A simplified dosing method for cluster headache has been suggested: a cotton-tipped applicator saturated with lidocaine 4% could be applied to the area of the sphenopalatine fossa (lateral posterior nasal cavity wall).[57] Another option is application of 0.5 to 1 mL with a dropper.[54] • Nasal lidocaine has an unpleasant taste, and its administration can be painful or distressing to children.[48,54]
Lorazepam injection	Rectal[a]	• Lorazepam parenteral solution given rectally has a slow absorption rate and low peak, so initial doses may need to be high, increasing the risk of toxicity.[3,15] In addition, repeated dosing is irritating due to the presence of propylene glycol as a solubilizing agent.[6] For acute seizures, use of commercially available rectal diazepam gel may be preferable.[15] In a case report, lorazepam 2 mg administered to an adult for alcohol withdrawal via *Macy Catheter* (Hospi Corporation) provided noticeable effects on agitation, disorientation, and tachycardia within one minute.[49]

Medication	**Alternative Route**	**Comments**
Lorazepam injection	Nasal[b]	• Dose as for parenteral (e.g., 0.1 mg/kg). Max single dose 8 mg using 4 mg/mL solution. May cause nasal irritation, bad taste, lacrimation, and cool feeling in nose and throat.[62]
Lorazepam tablets	Sublingual	• Dissolution may be manufacturer-specific.[69] Start with lowest recommended dose for indication.[69] Advise patient not to swallow for at least two minutes to allow time for absorption.[69] (Lorazepam sublingual tablets are available in Canada.)
Metoclopramide tablets	Rectal[a,3]	• See footnote "a" for general recommendations/guidance.
Midazolam injection	Oral	• Used for surgical premedication. Dilute the 5 mg/mL injection 1:1 with a flavored, dye-free syrup such as *Syrpalta*. Stable for 56 days in an amber glass bottle at 7, 20, and 40ºC (45, 68, and 104ºF).[22]
Midazolam injection	Nasal[b]	• Most data are in children.[62] Consider 0.1 to 0.5 mg/kg for pediatric sedation.[60] Consider 0.2 to 0.3 mg/kg (max 10 mg) for pediatric seizures.[30,64] • For acute seizures, use of commercially available nasal spray (US) may be preferable. Dose for seizures in patients ≥12 years is 5 mg, repeated in the opposite nostril in 10 minutes if needed.[63] • Max dose is 10 mg due to volume, and also to limit respiratory depression.[60,62] • Use 5 mg/mL concentration for fast onset.[60] Consider administration with a mucosal atomization device to facilitate absorption.[30] May cause burning for 30 to 45 seconds, and bitter taste.[60,64]
Misoprostol tablets	Vaginal	• Individual doses vary from 25 mcg to 800 mcg depending on the indication.[22] • Moisten with a few drops of water before insertion.[22]
Morphine injection	Rectal[a]	• Dose as for oral.[33]
Morphine injection	Inhaled	• Used for terminal dyspnea. The most common dose studied is 20 mg every four hours, but some patients may respond to as little as 3 mg.[50,51] • Has also been used for acute pain at doses of 10 to 20 mg.[58] • Dilute dose in 5 mL normal saline and nebulize.[22] • Monitor for bronchospasm, especially in patients with uncontrolled asthma.[50]

Medication	**Alternative Route**	**Comments**
MS Contin	Rectal[a]	• Initially, dose as for oral.[34] Some patients may require a dose reduction.[20] ○ The pharmacokinetics of rectally administered controlled-release morphine are more variable than when the controlled-release formulation is given orally, perhaps due to movement of the tablet within the rectum or differences in hydration status.[3,34] Also, it takes longer to reach peak morphine concentrations than with the oral route, but morphine levels are higher. Active metabolite levels are lower when morphine is given rectally compared to orally due to partial avoidance of first-pass metabolism.[3]
Morphine immediate-release tablet or liquid	Sublingual or buccal	• Generally avoid.[33] ○ Poorly absorbed.[71] ○ Bitter taste.[38] ○ Local reaction possible.[38]
Morphine immediate-release tablet	Rectal[a]	• Dose as for oral.[33]
Naloxone injection	Nasal[b]	• See our FAQ, *Meds for Opioid Overdose*.
Naproxen oral suspension	Rectal[a]	• Dose as for oral.[6]
Ofloxacin ophthalmic	Ear[12]	---
Ondansetron injection	Rectal[a]	• Based on bioavailability, consider dosing as for tablets given orally.[67,68]
Ondansetron tablets	Rectal[a]	• Administer tablets with a water-based lubricant.[66]
OxyContin	Rectal[a]	• There is limited information on dose equivalency between oral and rectal routes for the 2010 reformulation.[31]
Pantoprazole injection	Do NOT give orally	• Not acid-stable.[19]
Phenytoin injection	Rectal[a]	• Avoid if possible. Poorly absorbed. Consider alternatives, such as intramuscular fosphenytoin, instead.[15]

Medication	Alternative Route	Comments
Pilocarpine ophthalmic	Oral	• For treatment of dry mouth: four drops of the 2% solution, swish and swallow three times daily.[21]
Tobramycin ophthalmic	Ear[12]	---
Valproic acid capsule	Rectal[a,6,43]	---
Valproic acid syrup	Rectal[a]	• Valproic acid syrup can be given rectally without dose adjustment, but must be diluted with an equal volume of tap water. Empty the rectum prior to administration. After administration, press the buttocks together for 15 minutes, or leave the tube in place, clamped, for 15 minutes. Monitor levels.[15]
Vancomycin injection	Oral	• Used an alternative to the commercially available oral product. • Vials of vancomycin should be reconstituted to a concentration of 50 mg/mL using sterile water for injection. The resulting solution should be refrigerated and given a 14-day expiration. Subsequently, the appropriate volume/dose may be diluted (at time of administration) in one ounce (30 mL) of water for the patient to drink. Common flavoring syrups may be added to the solution to improve the taste.[22]
Vancomycin injection	Rectal[a]	• Used for fulminant *C. difficile* pseudomembranous colitis complicated by ileus (usually with intravenous metronidazole).[26] • Administer 500 mg in 100 mL normal saline every six hours as a one- or two-hour retention enema.[22,26,36]
Vitamin K injection	Oral[9]	• Useful for doses smaller than commercially available tablet strength. Can mix with orange juice to improve taste.[9]

a. Rectal administration may provide rapid absorption and partial avoidance of hepatic first-pass metabolism. However, the absorption of drugs by this route may also be delayed/prolonged or unpredictable.[1,2] Several factors may affect the extent of rectal drug absorption: drug characteristics (e.g., lipophilicity); formulation pH, volume, and concentration; rectal pH, temperature, and contents; rectal retention; and placement of drug (i.e., high vs low in the rectum).[1,3] The dosage must be individualized. The rectal drug dose may need to be higher or lower than the dose administered intravenously or orally to achieve the same effect.[1] In the absence of better information, **a rule of thumb when changing from the oral to rectal route** is to begin with the same dosage that had been given orally, then titrate as needed.[39] Due to the **potential** for rapid and almost complete absorption, patients should be monitored closely after rectal administration.[1] Some tablets do not dissolve well when given rectally, and this may vary depending on brand.[39] Alternatively, crushed tablets or capsule contents (assuming crushing/opening is appropriate) can be mixed with water; this might improve absorption.[45] Prior to rectal drug administration, the rectum should be emptied to improve absorption.[37] Insert medications only

finger-high for best absorption.[37] Multiple tablets can be administered within a single "00" size gelatin capsule for convenience.[37] Liquids can be administered with a small lubricated syringe.[5] For lubrication, use a water-soluble lubricant, not petroleum jelly; it inhibits absorption.[4] A catheter tip syringe can be useful. A #14 nasogastric tube cut to 5 cm and attached to a syringe can facilitate correct placement of the medication within the rectum.[5] Other options for administering liquids include an enema bulb, urinary catheter, or nasal prong oxygen tubing cut to six inches and attached to a syringe.[75] For absorption, drugs in solid dosage forms must dissolve in rectal fluid. Instill about 10 mL of warm water in the rectum after inserting tablets or capsules to improve absorption, especially in dehydrated patients.[3,6] Up to 25 mL of liquid is usually easily retained.[3] If patients expel an unmeasurable amount of the drug, it is difficult to determine how much more of the drug to administer to achieve therapeutic effect. Syrups may need to be diluted with water; a high sorbitol concentration may cause bowel evacuation.[1] For repeated administration (e.g., hospice patients), consider placement of a Macy Catheter (Hospi Corporation) to prevent leaking, and to reduce discomfort/distress associated with accessing the rectum.[45] Rectal administration may not be appropriate for patients with diarrhea, anal/rectal lesions, mucositis, thrombocytopenia, neutropenia, or immunosuppression.[1,7] It may not be practical for patients who have fractures, or who are very obese. Some patients may refuse this route of administration.[7] Drugs that require active transport for absorption are generally not appropriate for rectal administration because they are not well absorbed; rectal absorption occurs via passive diffusion.[3]

b. **Nasal administration**. Compared to nasal delivery via syringe, a nasal atomizer improves absorption by distributing the medication over a large surface area, and its use does not require patient cooperation in regard to head position.[60] If using a nasal atomizer for administration, draw up 0.1 mL extra (or per manufacturer recommendation) for the first dose to account for the dead space within the device, when feasible.[42,60] Do not draw up extra if a repeat dose is given with the same device.[42] Max volume 1 mL per nostril (ideally 0.2 to 0.5 mL) to avoid loss down the throat.[60] If the atomizer does not have an attached syringe, use a Luer lock syringe.[60] Avoid the nasal route if there is nasal trauma, excessive nasal blood or mucus, or recent vasoconstrictor use (e.g., cocaine).[60,61]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Cite this document as follows: **Clinical Resource,** ***Giving Meds By Alternate Routes. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights.*** **June 2024. [400664]**