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February 2020 ~ Resource #360226

Giving Meds by Alternate Routes

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. Examples include administration of oral or injectable medications rectally, or injectables orally. 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, they aren't buffered for eye use, and they aren't always sterile.[11-13] **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 ophthalmic	Sublingual	Used to reduce oral secretions in end-of-life patients.[10,32,70] Regimens that have been used include three drops of the 1% solution 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] Many terminal patients may only need one or two doses.[10] For children with excessive drooling, consider one drop twice daily (e.g., morning and afternoon).[27]
Carbamazepine suspension	Rectal[a]	Dose as for oral. Dilute with an equal volume of water.[8] 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[11,13]	
Cortisporin ophthalmic (U.S.)	Ear[11]	

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Medication	**Alternative Route**	**Comments**
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] Oral suspensions of dexamethasone 0.5 mg/mL or 1 mg/mL can be prepared using injectable dexamethasone combined with a 1:1 mixture of *Ora-Sweet* (flavoring/sweetening agent) and *Ora-Plus* (a suspending agent). This mixture has been shown to be physically and chemically stable for up to 90 days, both with or without refrigeration. *Ora-Blend* (a sweetened oral suspending agent) can also be used in the place of *Ora-Plus* and *Ora-Sweet*.[14] For example, to make a 1 mg/mL suspension, place 50 mL of dexamethasone injection (4 mg/mL) in a graduated cylinder and qs with a 1:1 mixture of *Ora-Plus*/*Ora-Sweet* (approximately 150 mL) to make 200 mL. Add a "shake well" sticker.[46]
Dexmedetomidine injection	Nasal[b]	As a pre-procedure sedative, 1 to 2.5 mcg/kg has been used in children.[60,72] 3 mcg/kg has been used in children two to 36 months of age.[52] Preservative-free 100 mcg/mL solution was given undiluted via nasal atomizer (*MAD300*) or dripped slowly into the nose from a tuberculin syringe.[52] In adults, it was deemed effective as a pre-op **adjunct** to reduce sedative and analgesic requirements at a dose of 2 mcg/kg. The dose was diluted with normal saline to a final volume of 1.6 mL, and 0.8 mL was sprayed into each nostril (average weight in this study was <60 kg).[53] Volume may preclude use in adults.[60]
Dexmedetomidine injection	Oral	For use as a procedural sedative in pediatric dental patients, 2 to 5 mcg/kg in a mango-flavored drink or apple juice has been studied.[71,72] Onset may take >30 minutes.[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]
Divalproex tablet (*Depakote*)	Rectal[a,4]	See footnote "a" for general recommendations/guidance.
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 (U.S.)	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]

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Medication	**Alternative Route**	**Comments**
Esomeprazole injection	Do NOT give orally	Not acid-stable.[19]
Fentanyl injection	Nasal[b]	For acute pain or dyspnea. Most data are in patients ≥10 kg and age ≥1 year of age.[22,41,43,74] Doses are typically 1 to 2 mcg/kg.[22,41-44,74] Max single dose is 100 mcg, limited by volume.[60] Consider 50 mcg to palliate dyspnea in adults with heart failure.[5]
Gabapentin	Do NOT give rectally	Poorly absorbed rectally, in part because the rectum lacks the active transport mechanism necessary for its absorption.[15]
Haloperidol tablets	Rectal[a,4]	Dose as for oral.[4]
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	Mix with fruit juice or soft drink to mask bitter taste.[25,45] Another option is to dilute ketamine 50 mg/mL to 10 mg/mL with *OraSweet*.[48]
Ketamine injection	Nasal[b]	As an analgesic or pre-procedure sedative or analgesic in children, doses vary. Consider 0.5 to 2 mg/kg for children.[54,57,74] Higher doses (3 to 9 mg/kg) have been used for pre-procedural sedation (children).[60] A dose of 1 mg/kg has been used for adult emergency department patients with moderate to severe pain.[58] Volume may preclude use as a sedative in adults.[60] Administer using a 50 or 100 mg/mL solution with a nasal atomizer device and divide between nostrils.[54,57,58] May cause sore throat or bad taste.[60]
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]

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Medication	**Alternative Route**	**Comments**
Levothyroxine	Rectal[a,65]	See footnote "a" for general recommendations/guidance.
Lidocaine	Nasal[b]	To reduce nasal discomfort before administration of irritating intranasal medication (e.g., midazolam): 5 to 10 mg (or 0.5 mL of a 4% solution) via nasal atomizer.[55,56,60] Give lidocaine five minutes prior.[60] For migraine and cluster headache, a 4% solution has been used.[22,59] For migraine, 0.5 mL 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] For cluster headache, four sprays, followed by two sprays 15 min later, was used. Patients were premedicated with 0.5% phenylephrine to reduce nasal congestion. As with migraine, the patient's head was tilted back 45 degrees and turned toward the side of the pain.[22]
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]
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.[4,69] Start with lowest recommended dose for indication.[69] Advise patient not to swallow for at least 2 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	For surgical premedication. Dilute the 5 mg/mL injection 1:1 with a flavored, dye-free syrup such as *Syrpalta*. Stable for 56 days at 7, 20, and 40ºC (45, 68, and 104ºF).[22]

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Medication	**Alternative Route**	**Comments**
Midazolam injection	Nasal[b]	Pediatric dose for sedation is 0.1 to 0.5 mg/kg.[60] Pediatric dose for seizures is 0.2 mg/kg.[30] Most data are in children.[62] In adolescents and adults, a dose of 5 mg for patients <50 kg and 10 mg for patients over 50 kg has been used for seizures.[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 an atomization device to facilitate absorption.[30] May cause burning for 30 to 45 seconds, and bitter taste.[60,64] For acute seizures, use of commercially available nasal spray (U.S.) may be preferable.
Misoprostol tablets	Vaginal	For pre-procedure cervical softening, doses vary. 200 to 400 mcg 12 to 15 hours prior, or 400 mcg three hours before intervention has been used.[26,50] For cervical ripening and induction of labor: 25 mcg every three to six hours.[22] Moisten before insertion.[50]
Morphine injection	Rectal[a]	Dose as for oral.[33,45]
Morphine injection	Inhaled	For terminal dyspnea. Evidence mixed.[36] In adults, can try 5 mg of preservative-free injection diluted in 2 mL of normal saline every four hours, or "as needed." Titrate in increments of 5 to 10 mg.[37] Has also been used for acute pain at doses of 10 to 20 mg.[51]
MS Contin	Rectal[a]	Initially, dose as for oral. 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. However, the recommended conversion from oral to rectal controlled-release morphine is 1:1 at the same dosing interval (i.e., every eight or 12 hours).[3]
Morphine tablet or liquid	Sublingual or buccal	Reserve for patients who can't swallow when other routes aren't practical. Poorly absorbed. Tastes bad. Concentrated liquid may cause local reaction.[38]
Naloxone injection	Nasal[b]	Adult dose 2 to 8 mg. If using IV solution intranasally, max single dose is 2 mg (due to volume). For higher single doses, use commercial product (*Narcan* nasal spray). Consider 0.2 mg/kg for children.[60] Can be prepared and dispensed for home use. With permission from the Prescribe To Prevent group, prescription forms with tear-off patient instructions are being made available to subscribers of *Pharmacist's Letter/Prescriber's Letter: Naloxone for Overdose Prevention (Intranasal).*

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Medication	**Alternative Route**	**Comments**
Naproxen oral suspension	Rectal[a]	Dose as for oral.[6]
Ofloxacin ophthalmic	Ear[11,13]	
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,23]	No data for "new" formulation. With the original formulation, absorption was 40% higher when given rectally compared to oral administration.[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]
Pilocarpine ophthalmic	Oral	Cheaper than oral tablets as treatment for dry mouth.[21] Recommend four drops of the 2% solution. Swish and swallow (or spit to reduce systemic effects) three times daily.[21]
Tobramycin ophthalmic	Ear[11]	
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	An alternative to the commercial oral product for treatment of *C. difficile* pseudomembranous colitis or staphylococcal enterocolitis.[22] Vials of vancomycin should be reconstituted to a concentration of 50 mg/mL using sterile water. 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]

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Medication	**Alternative Route**	**Comments**
Vancomycin injection	Rectal[a]	Used for fulminant *C. difficile* pseudomembranous colitis complicated by ileus (usually with intravenous metronidazole).[39] Administer 500 mg in 100 to 500 mL normal saline every six hours as a 1-hr retention enema.[39,40]
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.[4] 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.[4] 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. Insert medications only finger-high for best absorption. Multiple tablets can be administered within a single "00" size gelatin capsule for convenience.[3,4] 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. 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 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]

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