

50 Practical Medication Tips at End of Life

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ABSTRACT

Patients with a life-limiting illness frequently experience pain and other symptoms. It is important to pay close attention when medication therapy is used to manage these symptoms. Occasionally, practitioners need to be creative in selecting, dosing, administering, and discontinuing medications at the end of life because of the patient's changing health care needs. This article offers practical end-of-life medication tips including, but not limited to, medication administration; guidance on how to increase and decrease doses; medication selection for difficult-to-treat patients; alternative dosage formulations; routes of medication administration; debridement medication regimens; and appropriate drug therapy selection.

The appropriate use of medications is critically important in the management of symptoms at the end of life. Given the increasing frailty and changing health care needs of patients with life-limiting illnesses, medication administration can be challenging and may require some creativity. This article, written by 3 palliative care pharmacists, provides 50 practical medication tips that will be useful when you care for patients at the end of their lives. After reading them, you'll probably think of 50 more on your own!



How do you deal with changing the goals of care for your dying patients and their families? Dr Kathryn Walker and Dr Lynn McPherson offer suggestions on how to integrate their end-of-life medication tips into your practice. Use your Smart-phone and scan here for the interview; or visit <http://www.oncologypractice.com/views/how-we-do-it/blog/50-practical-medication-tips-at-end-of-life/41fb22371f7cd6184232318c22e3e8a7.html>.

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1. Proper medication storage. Counsel patients regarding the importance of proper medication storage, as follows: (1) Avoid storing medications in the bathroom or kitchen, as heat and moisture can degrade medications. (2) Keep controlled substances in a location known only to the patient or caregiver. (3) If necessary for safekeeping, consider storing medications in a lock-box. However, patients should inform a trusted person on how to access their medications in case they are unable to do so themselves.

2. Proper disposal of medications. It is important to initiate a discussion with your patients and their families regarding the disposal of discontinued medications, or medications left behind at the time of the patient's death. The Drug Enforcement Administration has been working to sponsor national prescription drug take-back programs, and this is an excellent option if one is available locally.¹ For certain medications that carry a high degree of risk for harm if taken inappropriately (such as schedule II drugs, including most opioids), the Food and Drug Administration (FDA) recommends flushing them down the toilet as the safest method of medication disposal. If a medication take-back program is not available, and the medication is not on the "disposal by flushing" list, then the drug should be put in the trash after the following steps have been completed: (1) Take medications out of the container and mix them with an undesirable

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substance (eg, coffee grounds or kitty litter). (2) Place this mixture into a sealable bag or tight container to prevent the medication from leaking out of the garbage bag. (3) Remove all personal identifiers from labels before discarding medication containers.²

3. Medication reconciliation. Performing medication reconciliation at each transition in care is extremely important for palliative care patients. Pharmacists are uniquely qualified to perform this function and to collect accurate medication lists in these often-complicated patients. In one pilot study in which a pharmacist repeated a nurse-conducted medication history for 58 patients who had been admitted to 2 hospices, investigators found an average of 8.7 medication discrepancies per patient, 81% of which were omitted medications.³ They also identified 55 additional drug interactions that were rated mostly as moderate in severity. Reconciling medication lists can effectively reduce the potential for errors in these high-risk patients.

4. Order sets can be your friends. Palliative medicine is such an individualized form of care that it can seem counterintuitive to standardize orders. However, standardizing orders for medications ensures that medications are available to provide comfort for common end-of-life symptoms (eg, nausea, agitation, hallucinations, and pain). Because these symptoms can present suddenly, order sets can help to routinely provide available medications for symptoms that occur after regular work hours. Also, order sets help to validate to other providers what might seem like “strange” palliative medicine practices. For example, orders for haloperidol to treat nausea don’t seem rogue when they’re typed on a professional-looking order set (Tip No. 44). In addition, order sets can include triggers to clarify any orders that may seem confusing to other care providers if they are left in place after a change in care goals, such as whether or not to continue lab work, fingersticks, diet restrictions, scheduled turning/positioning, etc.^{4,5}

5. Don’t write “D/C all meds” to provide comfort care. It is appropriate to reevaluate the need for each medication as goals change at the end of life. But when comfort care is initiated, a provider might write orders to “discontinue all medications” and inadvertently discontinue medications that can provide comfort, such as opioids, anxiolytics, and antiemetics. Another complication with writing such a blanket order is that medications can be discontinued abruptly and precipitate a withdrawal syndrome. Any order for discontinuing medications on palliative care protocols should include the direction, “If a medication is still indicated or requires tapering, please continue.” This direction prompts the prescriber to carefully consider each medication in light of the established goals of care.⁴

6. Quantifying your teaspoon. In general, the dose measurement “one teaspoon” is considered to be 5 milliliters (mL), but there is tremendous variability among teaspoons. Researchers collected 71 teaspoons from 25 households in Greece and determined the volume of water when each spoon was filled.⁶ The results ranged from 2.5 to 7.3 mL. The study concluded that household teaspoons were not reliable mea-

suring devices when they were used for administering medication solutions, and a calibrated device should be used instead. This is particularly important when a controlled substance such as an opioid is administered. Always advise patients to use either the measuring device supplied with the medication or another calibrated device.

7. Flavoring bitter medication solutions. Patients frequently object to the bad taste of oral medication solutions, including a notoriously bitter-tasting oral opioid solution such as morphine. Pediatric or cognitively impaired patients may refuse to take medications that taste bad. Many community pharmacists offer a flavoring system (eg, FLAVORx) to make oral liquid medications more palatable. Children often prefer flavors such as grape bubble gum, or banana-orange. Some patients report good results when a bitter opioid is flavored with Tutti-frutti, crème de menthe, raspberry, or chocolate. Maybe Mary Poppins was right: A spoonful of sugar does help the medicine go down!

8. Use of liquid concentrates for medication administration. Because of frailty or complications, patients at the end of life often have difficulty swallowing. They may benefit from an oral “intensol” formulation of the most commonly used medications such as morphine, oxycodone, methadone, dexamethasone, lorazepam, and haloperidol. (An intensol formulation is a highly concentrated oral medication solution, such as morphine or oxycodone 20 mg/mL.) If the patient cannot swallow the oral solution, it is acceptable to place up to 1 mL of the oral solution in the buccal cavity. Prop the patient’s upper body up about 30 degrees to minimize risk of aspiration. Depending on the medication being administered, only a small percentage of the dose may actually be absorbed from the transmucosal tissue, but the buccal cavity serves as a holding area while the medication slowly trickles down the throat and is absorbed from the gastrointestinal tract. For patients who cannot swallow medications, this is an alternative way to administer frequently used medications at the end of life.⁷

9. Methadone is the only long-acting opioid available in solution. Let us say it again: Methadone is the only long-acting opioid that is available in solution form. Methadone is extremely useful in patients who require long-acting pain medications but who have difficulty swallowing, especially at the end of life. The solutions are available in 3 concentrations (5 mg/5 mL, 10 mg/5 mL, and 10 mg/mL). Caution should be used to ensure proper prescription and administration of doses when a methadone oral solution is started in any patient. The Institute for Safe Medication Practices recommends prescribing any opioid in milligrams (with or without specifying milliliters) and never in milliliters alone, because of the different concentration solutions available.⁸ Inaccurate dosing of methadone or other opioids can lead to serious adverse effects, including respiratory depression and death.^{8,9}

10. A whole lot of swishing going on. When patients use Nystatin swish-and-swallow oral suspension for oral candidiasis, it is imperative that they follow the appropriate directions for use.¹⁰ The prescribing information states that patients should “place half the dose in each side of the mouth and hold it here

or swish it throughout the mouth for several minutes before swallowing.” In other words, patients just can’t do “swish-swish” and swallow; the oral suspension must be retained for “several minutes.” Not all patients have the strength to do this. Instead, consider clotrimazole troches that are placed in the mouth and allowed to dissolve slowly. A bonus tip: Regardless of which antifungal agent is chosen for a patient who wears dentures, it’s a good idea to fill the denture cup (which holds about 3 ounces) with Nystatin swish-and-swallow suspension and soak the dentures for 24 hours. Rinse and repeat with another 3 ounces of Nystatin suspension for another 24 hours. Failure to do this will result in “reseeding” the fungal infection.

11. Fluconazole for oropharyngeal candidiasis. Two studies have shown the benefit of a single dose of fluconazole in the treatment of oropharyngeal candidiasis in HIV-positive patients. The first study compared a single dose of 150-mg fluconazole vs itraconazole 100 mg by mouth once daily for a week.¹¹ In all, 75% of fluconazole-treated patients were considered cured on day 8, compared with 24% of the itraconazole-treated patients. A second study of 220 HIV-infected patients compared the treatment of oropharyngeal candidiasis with one 750-mg dose of oral fluconazole vs 150-mg oral fluconazole daily for 2 weeks.¹² Results showed equivalent outcomes in achieving clinical (approximately 95% cure) and mycologic cure between the 2 interventions. A one-time dose of fluconazole may be an acceptable alternative for oropharyngeal candidiasis for some patients.

12. Rectal administration of oral medications? Really? In their zeal to get medications into their patients, hospice providers may want to use nontraditional routes of administration. A common example is the rectal administration of an oral medication. Aside from being pharmaceutically inelegant and undesirable to patients, not all medications have suitable chemical characteristics that allow an oral medication to be absorbed when administered rectally. The most important determining characteristics are the solubility and permeability of a medication. To consider rectal administration, both must be favorable—and unfortunately, data on this point are not available for the overwhelming majority of oral medications. Old data have shown that rectal administration of oral long-acting morphine tablets may give therapeutic results, showing equivalent bioavailability but a delayed time to peak effect.^{13,14} It would be more prudent to discuss having a pharmacist compound a rectal suppository if appropriate, or consider use of an alternative route, such as buccal administration of a concentrated oral solution.

13. Use of multidose inhalers. Studies have shown that many patients use their inhalers inappropriately and often revert back to poor technique if they are not given reinforcement. The following are the appropriate steps for inhaler use: (1) Breathe out fully through the mouth and expel as much air as possible from the lungs. (2) Position the inhaler and, as inhalation begins, press the inhaler once. (3) Continue to inhale deeply and slowly until the lungs are full, and hold the breath as long as possible, up to 10 seconds. If additional inhalations are needed, wait 1 minute before the next dose. If a steroid-type inhaler is used, the patient should rinse the

mouth, then gargle and expectorate. If a patient has difficulty using a multidose inhaler or has coordination problems, use of a spacer is extremely helpful.¹⁵

14. Use of Diskus inhalers (Advair/Flovent/Serevent). Diskus inhalers are dry-powder devices and require different administration instructions. It’s important not to shake the inhaler prior to use, because that will scatter the dry powder. Instructions for use are as follows: (1) Hold the Diskus in one hand as if it were a hamburger, and place the thumb from the other hand on the thumb grip. Push the thumb away until the mouthpiece appears and a click is heard. (2) While holding the Diskus horizontally, slide the lever until it clicks; this will load the dose. (3) Exhale fully with the mouth pointed away from the mouthpiece. (4) Place mouth securely around the mouthpiece and inhale quickly and deeply. Hold breath for at least 10 seconds, or as long as possible. (5) Close the Diskus; then rinse and gargle mouth afterwards, and expectorate.¹⁶

15. Oral ketamine? Increasingly, palliative care providers are using ketamine to treat difficult pain syndromes, including opioid-induced hyperalgesia. But many practitioners don’t realize that the parenteral formulation (the only formulation available in the United States) of 10-, 50-, and 100-mg/mL ketamine can also be administered orally. Draw up the desired dose, mix in a small amount of orange juice, and administer orally. When switching between oral and parenteral administration of ketamine, use a 1:1 ratio.¹⁷

16. Ketamine for localized pain. Ketamine has been shown to be effective in treating localized pain, such as pain from wound care or intractable mucositis. Before provision of care to the wound, ketamine may be given parenterally or orally, or compounded into a topical product. For intractable mucositis, ketamine has been used with success as an oral rinse.^{18,19}

17. Topical opioids for painful wound care. For patients with painful wound management who are not achieving satisfactory pain relief or who experience adverse effects from systemic opioid therapy, consider a trial of topical opioids. For instance, 1% topical methadone or morphine as a powder or gel (eg, 100 mg in 10 grams amorphous wound gel) has been shown to be beneficial, and may even necessitate reduction of systemic opioid therapy.²⁰

18. Make clinically significant dose increases. One of the most frustrating parts of providing pain management occurs when an opioid dose for a patient in pain is increased but is still ineffective. Many disgruntled providers have been haunted by thoughts like “Is this patient manipulating me?” or “Shouldn’t they feel better?” or “Are they selling these?” Instead, begin by thinking, “Was that dosage increase likely to be clinically significant?” (This means a dose increase of 25%-50% for mild to moderate pain, and an increase of 50%-100% for moderate to severe pain.) Often, clinicians increase the dose by a set milligram amount, which might be inadequate to produce a clinically significant analgesic effect.²¹

19. Quantify the use of short-acting opioids. When conducting a pain interview and discussing the patient’s use of breakthrough-pain medication at home, providers commonly ask, “How many tablets do you take at home?” This seems

innocuous, and fits criteria as an open-ended question, but many patients do not give accurate answers for fear that they will be caught “taking too much” or not taking them as prescribed. To get a more realistic answer, ask “How many tablets do you need per day to take to stay comfortable?” This question acknowledges that you believe they need the medication, and that you recognize they are trying to get comfortable, as opposed to using the drugs for nonmedical purposes. In our experience, this question has a better chance of receiving an honest answer from—and establishing a rapport with—the patient in pain.

20. Opioid conversion charts. Although equianalgesic opioid-dosing conversion charts are recommended for converting between opioids and routes of administration, they do have limitations. Most charts are based on data from single-dose crossover trials. Therefore, these charts may not be completely accurate in predicting responses in chronic pain patients who require repeated dosing and in whom the resulting accumulation would be expected. Data from crossover trials have also shown that the ratio can change depending on the direction of the conversion (eg, morphine to hydromorphone, compared with hydromorphone to morphine). Lastly, no chart could ever take into account all the patient-related characteristics (eg, age, weight, and comorbid conditions) that the provider would need to factor into an individualized dose for a pain patient. In spite of all this, we still use charts as a standard resource, but we also rely on clinical judgment to make conservative conversions and to adjust the opioid dose appropriately, understanding that our data are not perfect and that every patient must be vigilantly monitored.²¹

21. Transdermal fentanyl (TDF) patch conversion. Use caution when relying on the dosage conversion recommendations provided by the manufacturer of TDF patches. First, these conversion guidelines are unidimensional (converting to the TDF patch), not bidirectional. Second, the manufacturer’s guidelines are very conservative. Even when the patch is used as directed, about half of patients who converted to TDF will experience pain and require a dosage increase. A more clinically appropriate conversion for palliative care patients is to double the strength of the patch (in mcg) and use that number as the total daily dose of oral morphine in milligrams (eg, TDF 50 mcg/hour approximates oral morphine 100 mg/day, or morphine 45 mg by mouth twice daily).²¹

22. The skinny on TDF in cachectic patients. Although data are limited (as in 1 trial) and that trial was small (as in 10 patients), many clinicians support the notion that fentanyl patches don’t seem to have the same “bang for the buck” in cachectic patients. If a trial of TDF is warranted, it is wise to closely monitor cachectic patients for response; then, carefully reevaluate the appropriateness of continuing therapy, or increasing the dose. It is common in practice to see patch doses increased several times because of a lack of optimal analgesia in cachectic patients. The risky business really begins when a well-intentioned clinician carefully converts a titrated patient from TDF to another opioid without taking into account that the patient is cachectic. If that patient did not respond to recent

increases in the TDF dose, switching to a new opioid may result in overestimation and overdose from the new opioid. The tip here is to go back to the last TDF dose the patient did respond to and convert from there, or begin with opioid-naïve dosing and titrate. Be conservative!²²

23. Where is the TDF? When a patient reports being on a TDF, it is important to inspect the patch. Taking this step confirms that the patient is receiving the correct reported- and prescribed-dose strength of the medication. Checking also helps to prevent a duplicate placement of fentanyl patches, and the subsequent overdose complications. Also, check that the patch has been applied appropriately to the chest, back, flank, or upper arm in a dry, hairless area. In line with Tip No. 22, try to optimize the transdermal patch placement in “slim” patients by selecting an application site with sufficient tissue to optimize absorption (eg, definitely not over a bony prominence). One last consideration is to write the date of application on the patch to assure that the patch will be changed at the correct time (not too soon, not too late, just right).

24. Heat leads to increased fentanyl patch absorption. The use of transdermal fentanyl is one effective option to manage chronic pain. However, the exposure of the patch to heat causes more drug to be released and can lead to increased absorption of the medication. The heat source can be external (eg, a heating pad, hot bath water, or warming blankets) or internal (eg, increased body temperature resulting from high fever or exertion). Patients should be counseled on the importance of not applying heat to the patch, as this may lead to adverse side effects. Health care providers should also keep this fact in mind when patients have continuously high fevers; the patch might need to be removed or its strength decreased until the patient further stabilizes.²³

25. Opioid allergies. Patients will often report allergies to opioids. However, it is important to evaluate the specific reaction, because these “allergies” are commonly side effects (eg, nausea, vomiting, or constipation) from the medications. “Pseudoallergic” reactions will present as mild itching, hives, or hypotension. A true opioid allergy is one that is immune mediated; it usually manifests as severe hypotension, rash, angioedema, or anaphylaxis-type reactions. In the case of side effects that are reported as allergies, patients can often be managed by being switched to another opioid. If the patient has a true allergy, then nonopioids or opioids from a different pharmacologic class (with monitoring) should be considered. Classes of opioids include phenanthrenes (morphine, codeine, hydrocodone, oxycodone, oxymorphone, hydromorphone, levorphanol, and buprenorphine); phenylpiperadines (fentanyl, meperidine, sufentanil, and remifentanil); and diphenylheptanes (methadone).²⁴

26. Chronic pain management in opioid-agonist therapy (OAT) patients. Give special consideration to chronic pain patients who are receiving buprenorphine or methadone as opioid agonist therapy to treat a history of substance abuse, or who have grown too disabled to continue the procedures (eg, daily clinic visits) that are required for OAT. For patients on buprenorphine, there are 3 primary options: (1) If the pain is not severe, buprenorphine can be dosed every

4 hours as a short-acting opioid. (2) Opioids can be given along with buprenorphine, although higher doses might be needed to overcome buprenorphine's partial agonism of the mu receptor. (3) The buprenorphine can be discontinued, and the opioids can be titrated to analgesic effect; dose as needed if withdrawal symptoms are noted. Option 3 is the most commonly recommended approach for palliative care patients, as treating the pain becomes the primary goal. For patients who receive daily methadone as OAT, divide the total daily dose into 2 or 3 doses and titrate as needed to control pain.²⁵

27. Opioid continuous infusions. In acute pain settings (eg, postoperative, opioid-naïve patients), continuous-infusion opioids are not recommended because of their lack of proven benefit and their increased risk of overdose. In contrast, palliative care patients with chronic pain often require a continuous infusion to maintain baseline analgesia, which can be done effectively as long as opioids are dosed safely. An important tip: Resist the urge to titrate the continuous infusion dose more frequently than every 10 to 12 hours. Morphine and hydromorphone have a half-life of 2 hours, and it requires 5 half-lives for a drug to reach steady state (hence, the 10- to 12-hour guideline). "How quickly can I increase the bolus?" we hear you ask. Read on!²⁶

28. Patient-controlled analgesia (PCA) dosing. Here are a few quick tips on dosing PCAs that may come in handy. Bolus doses can be increased frequently (eg, every 30 to 60 minutes) and are the first line in titrating patients to comfort. To increase bolus dosing, the same principle applies as in Tip No. 18, and percentages should be used to escalate doses. When used with continuous infusions, bolus doses tend to be half of the hourly rate (eg, 1-mg bolus, 2-mg/hr continuous infusion with a lockout of 8 minutes). The lockout can be as long as desired, but should not be shorter than the onset of the opioid (ie, 5 minutes) to prevent overdose.²⁶

29. Terminal withdrawal of mechanical ventilation. This event can precipitate sudden and severe symptoms that require aggressive management. Typically, opioids and benzodiazepines are used to target symptoms of pain, shortness of breath (SOB), agitation, and anxiety. One tip to remember in the heat of the moment is that if the discomfort is perceived to be SOB and related anxiety, use the opioid first and then follow up with a benzodiazepine if needed. A benzodiazepine will not treat the symptom of dyspnea as effectively as an opioid will. If the SOB is palliated first, the benzodiazepine may not be necessary. One last tip: Don't forget to use a medication for secretions to avoid the need to suction these patients. (See Tip No. 38.)

30. Think before you jump: using naloxone in opioid-tolerant patients. If opioid overdose is suspected in a palliative care patient, do a careful assessment before administering naloxone. An actively dying patient can mimic the signs and symptoms of overdose, and it would be cruel to reverse opioids at this point. However, if a true overdose is suspected in an opioid-requiring patient, then administer only small increments of naloxone (0.04 mg) to step the patient out of an

un arousable state, which is preferable to fully reversing the opioid and leaving the patient in withdrawal and/or in pain for the next few hours. One 0.4-mg ampule can be diluted with 10-mL normal saline, and 1 mL (0.04 mg) can be given every minute until the patient is responsive. If no response is observed after 2 ampules of naloxone have been given, it is likely not related to the effects of the opioid.²⁷

31. Stopping medications abruptly vs tapering. Most medications can be stopped abruptly without any problems. However, there are certain medication classes that must be gradually stopped to prevent complications. As a general rule, this includes cardiovascular medications and those affecting the central nervous system. Beta-blockers and clonidine should be tapered, as an abrupt discontinuation can lead to rebound tachycardia and increased blood pressure. It is preferable to reduce the dose of a beta-blocker rather than to "hold" doses on some days and administer some days. Patients on moderate to high doses of antidepressants should also taper off these medications; if they stop these medications suddenly or taper too quickly, withdrawal symptoms (in the form of "flulike" symptoms, insomnia, anxiety, agitation, or sensory disturbances) commonly occur. It is also extremely important that benzodiazepines are not stopped abruptly, as this can lead to confusion, seizures, insomnia, sweating, tinnitus, and perception disturbances. Withdrawal symptoms are not always immediate and can occur anywhere between 1 day and up to 3 weeks after benzodiazepines are discontinued. The longer a patient has been receiving benzodiazepine therapy, the longer the taper should be to ensure a safe and comfortable discontinuation of the medications.²⁸

32. Should—or when should—corticosteroids be stopped? When a patient takes corticosteroids, a suppression of the hypothalamic-pituitary-adrenal (HPA) axis occurs after approximately 3 weeks of therapy, or earlier if high doses of steroids (> 40 mg of prednisone) are used. Although most health care practitioners are trained to use corticosteroids generally for short courses of therapy and then discontinue them, consider the possibility that the patient may continue receiving a corticosteroid until the time of death. If a decision is made to discontinue therapy, patients often need to be slowly tapered to allow the HPA axis to recover, which can take weeks to months. Taper by 2.5 to 5 mg every 3 to 7 days until a dosage of 5- to 10-mg prednisone is reached. Patients can be subsequently discontinued or tapered further, depending on their tolerance. Signs of corticosteroid withdrawal often present as flulike symptoms and include headache, dizziness, fatigue, muscle/joint pain, nausea, vomiting, weight loss, and fever. If patients present with any of these symptoms or are in a period of stress (eg, infection), they may need their dose to be temporarily increased or tapered more slowly. Patients who have been on steroids for a prolonged period of time (> 1 year) may need to be tapered more conservatively than the recommendation above.²⁹

33. Discussing the discontinuation of medications with patients. As patients near the end of life, it is common to reevaluate the benefits and burdens of maintenance medications and to focus primarily on palliative and supportive medications. It is important to discuss the role of medications with patients as

part of their current treatment plan and goals. The expected benefit of taking a medication must always outweigh the burden or risk of taking it. Patients and their caregivers should always feel comfortable with the decision to stop medications, a decision that is based not on abandonment of care, but rather on changing goals of care to ensure compliance, safety, and—most importantly—a supportive environment.

34. Toprol XL may be cut in half but not crushed. Most long-acting medications cannot be crushed or cut, as doing so damages the slow-release mechanism of the drug and can lead to dangerous adverse effects in patients. However, Toprol XL is an exception. This tablet is scored in the middle and can be cut in half, although it still cannot be crushed. Halving the tablet is a useful strategy when tapering metoprolol in this formulation.³⁰

35. Benefits of stopping bisphosphonates. As decisions are made at the patient's end of life regarding which maintenance medications should be continued or stopped, consider the discontinuation of bisphosphonates that are prescribed to prevent osteoporosis. These medications have an extremely long half-life and they remain in the bone for years, even after treatment has stopped. A study by Black et al.³¹ showed that discontinuation of alendronate after 5 years of use did not significantly increase fracture risk for up to 5 years after the medication was stopped. However, people at high risk of vertebral fractures may benefit with the continuation of this medication, as there was an increase in these fractures seen after alendronate was stopped.

36. Diabetes management at the end of life. Glucose intolerance is a frequent finding in patients with life-limiting illnesses, but the goals of care are modified at the end of life. The risk and consequences of hypoglycemia are greater than those associated with hyperglycemia at this point. One suggestion is to target blood glucose values between 140 and 250 mg/dL (or even 300 mg/dL), provided the patient does not experience symptoms of high or low blood glucose. Assure patients that tighter blood glucose control earlier in the disease process has long-lasting benefits, and looser control at this point is appropriate. Whatever you do, try to avoid sliding-scale insulin; poking the patient's finger 4 times a day is not very palliative.³²

37. Benzodiazepine equivalents. Given occasional medication shortages, and the need to change medications or dosage formulations based on the patient's ability to swallow, it is helpful to know the approximate equivalency of oral benzodiazepines. (See chart.)³³

MEDICATION	EQUIVALENT DOSES
Diazepam (Valium)	5.0 mg
Lorazepam (Ativan)	1.0 mg
Oxazepam (Serax)	30.0 mg
Temazepam (Restoril)	10.0 mg
Alprazolam (Xanax)	0.5 mg
Clonazepam (Klonopin)	0.5 mg
Chlordiazepoxide (Librium)	25.0 mg

38. Use the right drug for secretions. Several products are commonly used for treating secretions at the end of life. Tertiary amines (eg, scopolamine, atropine, and hyoscyamine) cross the blood-brain barrier and are more likely to cause side effects, such as sedation and delirium, than are quaternary amines (eg, glycopyrrolate). All are generally well tolerated for short durations and are equally effective for treating “death-rattle” secretions. Other factors should be considered when choosing the right medication for each patient. For example, the scopolamine patch has an onset of 12 hours and doesn't reach steady state until it's in place for 24 hours, so it is not appropriate for treating acute symptoms. Atropine can be administered sublingually using 1 or more drops of 1% ophthalmic solution and has an onset of 30 minutes.³⁴

39. Managing seizures. As patients approach the very end of life, the administration of antiepileptic medications by a nonparenteral route may be difficult. One strategy is to administer lorazepam oral concentrated solution in the buccal cavity on a scheduled basis if appropriate (eg, 0.5-1 mg in the buccal cavity every 6 hours). Additionally, for seizure activity, order lorazepam 1 mg in the buccal cavity every 5 minutes, up to 4 doses, or until the seizure activity stops.³⁵

40. Frozen petrolatum balls. For patients who experience a “high” fecal impaction, this home remedy may help. Petrolatum (petroleum jelly, sold under brand names like Vaseline) is simply a solid form of mineral oil. Roll petrolatum into pea-sized balls, then sugar-coat them and freeze them. Have the patient swallow 2 frozen petrolatum balls 1 to 3 times daily. As they go down the gut, the petrolatum balls will melt and lubricate the bowel, hopefully easing the impacted stool along the way.³⁶

41. It's a twofer! Lactulose has long been recognized as an effective laxative, and is used in the management of hepatic encephalopathy. If a patient has both indications, lactulose can handle the job. When lactulose is dosed for hepatic encephalopathy, the therapeutic end point is the production of 2 “pudding-soft” bowel movements per day.³⁷

42. Wrestling with dry skin. Hydrating the skin is best accomplished from the “inside out,” but practitioners frequently turn to topical agents as well. Oleaginous (or oily) products do a better job in occluding the skin and trapping moisture in the outer skin layers, but patients object to being lubed up with something that has the texture of petrolatum. One option is to use a 2-phase emulsion, either a “water-in-oil” lubricant or an “oil-in-water” lubricant. The patient feels whatever is in the outside layer, so a water-in-oil emulsion feels like petrolatum on the skin, while an oil-in-water emulsion is more soluble and feels like a water-based lotion. For optimal lubrication, consider using an oil-in-water emulsion during the day and a water-in-oil emulsion at bedtime. A pharmacist can suggest nonprescription lubricants to fit these needs.

43. Think nausea; think receptors. Many receptors are involved with the nausea/vomiting cascade, and agents that target different receptors all have their place. Antihistamines are great for motion-related nausea, such as vertigo, but are

not that great for treating other forms of nausea. Serotonergic drugs (eg, ondansetron or granisetron) are specifically helpful in postoperative and chemotherapy-induced nausea. When treating generalized nausea, consider dopamine receptor-blocking drugs, such as Haloperidol (Tip No. 44) and prochlorperazine (Compazine), both of which bind tightly to these receptors and are useful antiemetics. Promethazine, however, binds primarily to histaminic receptors, making it less useful as an antiemetic.³⁸

44. Haloperidol; a multipurpose drug! Haloperidol is a great utility drug in palliative medicine. It is available in a variety of dosage formulations (eg, tablets, oral concentrate, and IV) and is well tolerated when used in low doses. If you want to order haloperidol for nausea (as explained in Tip No. 43), do not assume that those reading your order will understand your rationale; haloperidol is routinely ordered in hospices and by palliative care teams, but it is not a familiar drug for nausea in general medical practice. To ensure that your patient will receive this medication “as needed,” be collegial and discuss your plan in person with those involved in their care (eg, nurses and pharmacists).

45. Bowel obstruction cocktail. Patients with bowel obstructions can benefit greatly from combining standing doses of dexamethasone (for inflammatory discomfort, edema, and nausea) and haloperidol (for nausea). This may be a good option before jumping to octreotide to palliate the associated symptoms, particularly with a partial bowel obstruction.³⁹

46. TCAs are not created equal. There is a big difference in the side effect profile of secondary amines (eg, nortriptyline or desipramine) and tertiary amines (eg, amitriptyline). Tertiary amines are more likely to cause side effects such as sedation, orthostatic hypotension, and anticholinergic effects, which can be very troublesome for an elderly palliative care patient. Avoid amitriptyline, especially in older adults.

47. Phenytoin serum levels. Phenytoin (Dilantin and other brands) is an antiepileptic medication with a dosage that is guided by therapeutic drug monitoring. Often we see a therapeutic range of 10-20 mcg/mL cited, but it is important to recognize that this is the total phenytoin concentration (ie, drug that is bound to albumin plus drug that is not bound to albumin). In healthy individuals, phenytoin is 90% bound to serum albumin; therefore, the true therapeutic range is 1 to 2 mcg/mL of unbound (or free) phenytoin. (It's the unbound or free portion of phenytoin that provides the therapeutic and toxic effect of the medication.) Therefore, it is imperative that practitioners order a “free” or “unbound” phenytoin level to guide therapeutic decision making about phenytoin dosing.⁴⁰

48. Drug-induced delirium. Patients with advanced illnesses frequently experience delirium, which can be challenging to diagnose and treat. Most importantly, practitioners need to be aware of medications that increase the risk for delirium. A meta-analysis of 14 studies found increased odds ratios for drug-induced delirium with the following medica-

tion classes: benzodiazepines (OR, 3.0), opioids (OR, 2.5), dihydropyridines (OR, 2.4), antihistamines (OR, 1.8), neuroleptics (OR, 0.9), and digoxin (OR, 0.5). Savvy practitioners should continually review the patient's medication regimen and carefully consider the benefits and burdens of all medications, particularly those shown to increase the risk of delirium.⁴¹

49. Use of antipsychotic agents in demented patients. The FDA has mandated the inclusion of a black box warning on antipsychotic agents regarding the increased risk of death from antipsychotic agents when they are used to treat elderly patients with dementia-related psychosis from cardiovascular, cerebrovascular, or infectious causes. The data show that antipsychotic agents increase the relative risk of death by 1.6 to 1.7, compared with placebo, in this patient population. However, the number needed to harm is about 10- to 15-fold higher than the number needed to treat. The bottom line is that practitioners must use good clinical judgment and common sense when deciding whether or not to use an antipsychotic agent. Practitioners must also educate families and other health care providers about the risks and benefits of treating vs not treating this distressing symptom.⁴²

50. Well, this is depressing news. A study conducted in the United Kingdom assessed the value of treating depression in patients with dementia.⁴³ A total of 326 patients with a diagnosis of depression for 4 or more weeks received either sertraline (titrated to a target dose of 150 mg/day), mirtazapine (45 mg a day), or placebo. The primary outcome was a reduction in depression at 13 weeks. The results showed that there was no difference between 111 controls and 107 drug-treated participants. Furthermore, 26% of the placebo-treated patients experienced an adverse effect, compared with 43% of the sertraline-treated patients and 41% of those who received mirtazapine. The researchers concluded that given the lack of benefit and the increased adverse effects, the treatment of depression in patients with Alzheimer's dementia should be carefully considered. Perhaps future research can investigate the role of stimulants such as methylphenidate in treating depression in this population.

51. BONUS TIP! If you enjoyed reading these 50 practical end-of-life medication tips, you will surely also enjoy reading “Fifty Reasons to Love Your Palliative Care Pharmacist.”⁴⁴ As a matter of fact, given the tremendous use of medications at the end of life and how critically important it is to use these medications with great care, every hospice and palliative care team should have a pharmacist on board. That's the best tip of all!

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