Appropriate Use of Oral Benzodiazepines

modified December 2024

Questions often arise regarding the safe prescribing of benzodiazepines. The charts below provide information to help you choose the most appropriate agent and dose based on indication, age, hepatic function, and drug interactions. Prescribing and deprescribing tips are included, as well as patient counseling points. **Information in the charts may differ from product labeling**. See our chart, *Outpatient Alcohol Withdrawal Treatment and Management of Alcohol Use Disorder*, for benzodiazepine use in this disorder.

Benzodiazepine Oral Dosing and Pharmacokinetics

Drug	**Approximate Equivalent Oral Dose**	**Adult Dosing** (oral) (also see **footnote a**)	**Metabolism** (also see **footnote c**)
Alprazolam (*Xanax*, etc., generics)	0.5 mg[3]	**Anxiety, Panic** *Immediate release*: • Initial: 0.25 to 0.5 mg three times daily (anxiety), or 0.5 mg three times daily (panic).[1] Elderly: 0.25 mg two to three times daily.[1] • Usual: 0.25 to 0.5 mg three times daily(anxiety) or 0.5 mg three times daily (panic).[2] Elderly: usual dose is 0.25 mg two or three times daily (anxiety).[1] • Max total daily dose: 4 mg (anxiety) or 10 mg (panic), divided.[1] *Extended release* (US) (**panic**): • Initial: 0.5 mg to 1 mg once daily[1] Elderly: 0.5 mg once daily.[1] • Usual: 3 to 6 mg once daily[1] • Max total daily dose: 10 mg[1]	CYP3A4 to metabolites with little to no clinically significant activity[1] **Half-life**: 12 to 15 hours[2]
Bromazepam (Canada)	3 mg[2]	**Anxiety** • Initial: 6 to 18 mg/day, divided.[2] Elderly: 3 mg/day, divided.[5] • Usual: 6 to 30 mg/day, divided[2] • Max total daily dose: 60 mg, divided[5]	Conjugation[2] **Half-life**: 8 to 30 hours[2]
Chlordiazepoxide (*Librium* [US], generics	10 to 25 mg[2,3]	**Anxiety** • Initial: 5 to 10 mg three to four times daily, or 20 to 25 mg three to four times daily for severe symptoms.[1] Elderly: 5 mg twice daily.[1] • Usual (elderly): 5 mg two to four times daily.[1] • Max total daily dose: 100 mg, divided.[1]	CYP1A2 to desmethyldiazepam,[b] then to oxazepam by CYP3A4 and CYP2C19 (minor)[1,2,4.] **Half-life**: 100 hours[2,d]

Drug	**Approximate Equivalent Oral Dose**	**Adult Dosing** (oral) (also see **footnote a**)	**Metabolism** (also see **footnote c**)
Clobazam (*Onfi*, *Sympazan* [US], generics	10 mg[2]	**Seizures (adjunct)** • Initial: 5 mg twice daily (once daily in poor CYP2C19 metabolizers, and in the elderly)[1] • Max total daily dose: 40 mg, divided[1]	CYP3A4 (major), CYP2C19, and CYP2B6 to active metabolites[1] **Half-life**: 71 to 82 hours[1,d]
Clonazepam (*Klonopin* [US], *Rivotril* [Canada], generics)	0.25 mg[2]	**Seizures** • Initial: 0.5 mg three times daily[1] • Usual: 2 to 8 mg/day, divided[1] • Max total daily dose: 20 mg, divided[1] **Anxiety**: 0.25 to 0.5 mg twice daily[2] **Panic** • Initial: 0.25 mg twice daily[1] • Usual: 1 mg/day, divided.[1] • Max total daily dose: 4 mg, divided.[1]	CYP3A4 to inactive metabolites[1] **Half-life**: 20 to 60 hours[2]
Clorazepate (*Tranxene* [US], generics)	7.5 mg[2]	**Anxiety** • Initial: 7.5 mg to 15 mg twice daily, or 15 mg once daily at bedtime. Elderly: reduce dose by 50%.[1] • Usual: 15 mg twice daily[1] • Max total daily dose: 60 mg, divided.[1] **Seizures, adjunct (US)** • Initial: 7.5 mg two or three times daily[1] • Max total daily dose: 90 mg, divided[1]	Decarboxylated in gastrointestinal tract to desmethyldiazepam[b] (active moiety), then to oxazepam by CYP3A4 and CYP2C19 (minor).[1] **Half-life**: 100 hours[2,d]
Diazepam (*Valium*, generics)	5 mg[2]	**Anxiety, seizures (adjunct), muscle spasms**: 2 to 10 mg two to four times daily (elderly: 2 to 2.5 mg once or twice daily). Max total daily dose: 40 mg, divided.[1]	CYP3A4, CYP2C9, CYP2C19, and CYP1A2 to desmethyldiazepam[b] (major), temazepam (minor), and oxazepam (minor)[1,2] **Half-life**: 100 hours[2,d]

Drug	**Approximate Equivalent Oral Dose**	**Adult Dosing** (oral) (also see **footnote a**)	**Metabolism** (also see **footnote c**)
Estazolam (US)	1 mg[3]	**Insomnia** • Initial: 1 mg at bedtime.[1] Elderly: 0.5 mg at bedtime.[1] • Max total daily dose: 2 mg at bedtime.[1]	CYP3A4 to active metabolites with little clinically significant activity[1] **Half-life**: 10 to 24 hours[1]
Flurazepam	15 mg[2]	**Insomnia**: • Initial: 15 to 30 mg at bedtime (15 mg in females or the elderly).[1] • Max total daily dose: 30 mg at bedtime. Elderly: 15 mg at bedtime.[1]	CYP3A4 and CYP2C9 to active metabolites.[1,2] **Half-life**: 47 to 100 hours[1,d]
Lorazepam (*Ativan*, generics)	1 mg[2]	**Anxiety** • Initial: 2 to 3 mg/day (elderly: 1 to 2 mg/day), divided two or three times daily[1] • Usual dose: 2 to 6 mg/day, divided[1] • Max total daily dose: 10 mg, divided.[1] I**nsomnia due to anxiety or situational stress**: 2 to 4 mg at bedtime as needed.[1] Elderly: 1 to 2 mg at bedtime as needed.[1]	Glucuronidation to inactive metabolite[1] **Half-life**: 12 hours[1]
Nitrazepam (Canada) (*Mogadon*)	5 mg[2]	**Insomnia** • Initial: 5 to 10 mg at bedtime. Elderly: 2.5 mg at bedtime.[8] • Max total daily dose: 10 mg at bedtime. Elderly: 5 mg at bedtime.[8]	CYP2E1 to inactive metabolite.[2] **Half-life**: 16 to 55 hours[2]
Oxazepam	15 mg[2]	**Anxiety** • Initial: 10 mg to 15 mg three to four times daily. Elderly: 10 mg three times daily.[1] • Max total daily dose: 120 mg, divided. Elderly: 60 mg, divided.[1]	Glucuronidation to inactive metaboltes[1] **Half-life**: 5 to 15 hours[1]

Drug	**Approximate Equivalent Oral Dose**	**Adult Dosing** (oral) (also see **footnote a**)	**Metabolism** (also see **footnote c**)
Quazepam (US) (*Doral*)	7.5 mg[3]	**Insomnia** • Initial: 7.5 mg at bedtime.[1] • Max total daily dose: 15 mg at bedtime.[1]	CYP3A4 (major) and CYP2C9 and CYP2C19 to active metabolites[1] **Half-life**: 73 hours[1,d]
Temazepam (*Restoril*, generics)	15 mg[3]	**Insomnia** • Initial: 7.5 mg to 15 mg at bedtime[1]. Elderly: 7.5 mg at bedtime.[1] • Max total daily dose: 30 mg at bedtime. Elderly: 15 mg at bedtime.[1]	Glucuronidation to inactive metabolites[1] **Half-life**: 8 to 15 hours[1]
Triazolam (*Halcion*, generics)	0.25 mg[2]	**Insomnia** • Initial: 0.125 to 0.25 mg at bedtime.[1] Elderly: 0.125 mg at bedtime.[1] • Max total daily dose: 0.5 mg at bedtime. Elderly: 0.25 mg at bedtime.[1]	CYP3A4 to inactive metabolites[1,2] **Half-life**: 1.5 to 5.5 hours[1]

a. In general, start with the lowest dose in elderly or debilitated patients, and in patients with liver or kidney impairment, and increase slowly; pharmacokinetics and/or pharmacodynamics may be altered in these patints.[1,2]
b. Desmethyldiazepam: long-acting metabolite responsible at least in part for therapeutic and toxic effects of diazepam, clorazepate, and chlordiazepoxide.[3]
c. For the **elderly**, and for patients with **liver disease**, benzos that undergo glucuronidation (lorazepam, oxazepam, temazepam) are preferred over those that undergo oxidative metabolism (e.g., CYP450), especially those with long-acting metabolites: flurazepam, chlordiazepoxide, clorazepate, quazepam, and diazepam.[1-3] See our chart, *Drug Interactions: Cytochrome P450 (CYP), P-glycoprotein, and More*, for help identifying potential drug interactions based on metabolic pathway.
d. Includes active metabolite(s).

Preferred Oral Benzodiazepine per Condition

Benzodiazepines are among the treatment options for several conditions but are not usually the drugs of first choice for chronic use. The chart below addresses preferred benzodiazepines for given conditions when a benzodiazepine might be appropriate.

Condition	Preferred Benzodiazepine	Comments
Alcohol withdrawal	• Chlordiazepoxide, diazepam, lorazepam, or oxazepam.[9] • See our chart, *Outpatient Alcohol Withdrawal Treatment and Management of Alcohol Use Disorder*, for details to help you choose among them.	• Benzodiazepines are the drugs of choice for management of alcohol withdrawal.[9] • Parenteral forms of diazepam and lorazepam are available.
Anxiety	• No agent clearly superior in regard to efficacy.[3] • Consider agent with medium or long half-life which has been used more extensively for anxiety disorders: clonazepam, lorazepam, or diazepam.[3] Shorter acting agents pose higher risk of withdrawal, rebound, and abuse.[3,10]	• Ideally, for short-term use only (e.g., for two to four weeks, until antidepressant starts to work, then taper).[3,11] • Can be used to treat patients who have failed first-line medications (e.g., SSRI, SNRI) and nonpharmacologic therapies.[11] • Alprazolam is one of the most abused benzodiazepines; a quick onset leads to euphoria.[3] Accounts for one in ten ER visits in US due to drug misuse.[12] More toxic in overdose than other benzos.[12] Missed doses or discontinuation can cause significant withdrawal quickly.[10] May be difficult to taper/discontinue.[3] Risk of breakthrough anxiety with immediate-release product.[3] Sustained-release product (U.S.) may have less abuse potential.[3] • Diazepam has fastest onset (<1 hour).[2] Diazepam's duration of effect shorter than lorazepam's despite its long half-life; it is lipophilic and quickly redistributes out of the brain.[3,13] • Consider propranolol for performance anxiety.[3] • For more information on treatment of anxiety, see our chart, *Pharmacotherapy of Anxiety Disorders in Adults*.
Insomnia	• Temazepam (*Restoril*, generics) (favorable benefit vs risk).[14]	• See our chart, *Comparison of Insomnia Treatments* for non-benzodiazepine alternatives.
Panic attacks	• Alprazolam, clonazepam, lorazepam, or diazepam (most evidence of efficacy).[27]	• Ideally, for short-term use only (e.g., for two to four weeks, until antidepressant starts to work, then taper).[3,11] • Can be used to treat patients who have failed first-line medications (e.g., SSRI, SNRI) and nonpharmacologic therapies.[11] • See comments under "Anxiety" regarding alprazolam. • Avoid clonazepam in older adults due to long duration of action.[11]

Condition	Preferred Benzodiazepine	Comments
Low back pain	• Most evidence for diazepam.[15]	• See our chart, *Muscle Relaxants*, for details regarding use. • For alternatives, see our charts, *Treatment of Acute Low Back Pain* and *Treatment of Chronic Low Back Pain*.

Tips for Prescribing and Deprescribing Benzodiazepines

Goal	Suggested Strategies or Resources
Educate patients about benzodiazepine safety.	• In the U.S., benzodiazepines are dispensed with a MedGuide that covers risks.[17] • Consider these **patient counseling points** when talking to patients about starting a benzodiazepine: o Like all medications, benzos have risks. These risks include: ▪ Feeling sleepy, dizzy, clumsy, or confused.[6] This can cause falls or accidents.[22] ▪ If you take a benzo at bedtime, you might get up without being fully awake and do something you do not know you are doing. This could include driving, eating, talking, or sleepwalking.[1] ▪ Tolerance. This means that over time, your benzo might not work as well as it once did.[16] ▪ Dependence. This means that some patients don't feel well when they stop using benzos. This occurs most often when the benzo is taken regularly for several days to weeks.[17] ▪ Mood or behavior problems.[7] ▪ Misuse or abuse.[17] o To use benzos safely, you should: ▪ Avoid alcohol. Also avoid narcotic pain meds like oxycodone or hydrocodone. These mixtures can cause you to become too sedated, or even slow your breathing to a dangerous level.[17] ▪ Take your benzo exactly as prescribed. Do not increase the dose on your own.[7] ▪ Report unusual changes in behavior or mood.[7] ▪ Seek immediate medical care for trouble breathing.[17] ▪ Keep your benzo in a safe place. Tell only a few people you trust that you are taking it. Do not share it with others.
Safely initiate a benzodiazepine.	• Consider all therapeutic options for management of the patient's condition, and provide information about non-drug alternatives.[17] • Limit dosages and durations to the minimum required.[21] Have an exit plan.[23] • Some experts suggest follow-up in one to four weeks. • Screen for potentially problematic drug interactions (e.g., opioids).[19,21] • Before prescribing and throughout treatment, assess the patient's risk of abuse, misuse, and addiction.[17] Screening and assessment tools are available at: https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools.

Goal	Suggested Strategies or Resources
Educate patients about benzodiazepine **discontinuation** and get patient buy-in.	• First, ask patients what their goals and preferences are regarding their benzodiazepine.[16] Involve the caregiver, or care team in a long-term care setting.[22] Consider addressing the following benefits of discontinuation: o Discontinuation of your benzodiazepine may improve alertness and thinking, and reduce fall risk.[16] o There may be options for treating your condition that are better for you than your benzo.[17] ▪ These options may or may not be a medication. For example, there are things you can do to help sleep, anxiety, and low back pain that do not involve pills. • Regarding the discontinuation process, consider addressing the following points: o You must not stop your benzo on your own. If you are dependent on your benzo and stop it all of a sudden, you might have withdrawal symptoms. Examples include: ▪ More common: anxiety, irritability, trouble sleeping, sweating, gastrointestinal symptoms.[16,18] ▪ Possible but uncommon: seizures, seeing or hearing things that aren't there.[16,17] • The condition your benzo is being used to treat might get worse during discontinuation. We will work together to control it to the extent possible before stopping your benzo.[22] • Depending on the dose, how often you take it, and for how long you have been taking it, you may need to slowly decrease (taper) the dose. You will be given specific advice for the taper. If you feel worse during this process, don't be discouraged. Your plan can be adjusted if this happens. Most symptoms are mild and short-term (days to weeks).[16] • If the benzodiazepine cannot be completely discontinued, a dose reduction is still a partial success.[22] • Consider sharing the validated EMPOWER brochure, available at https://www.deprescribingnetwork.ca/patient-handouts.[18]
Identify patients for whom benzodiazepines should be tapered.	• Patients ≥65 years of age[18] • Patients <65 years of age who have used a benzo most days of the week for >4 weeks.[16] • Be aware that case reports describe a wide range of time to dependence, with some reporting the onset as early as days to weeks after the start of a benzodiazepine.[17]
Identify strategies for a successful benzodiazepine taper. *Continued…*	• Monitor every one to two weeks.[16] • Be prepared to address severe or life-threatening withdrawal reactions include catatonia, seizures, delirium tremens, depression, suicidal or homicidal thoughts, mania, or psychosis.[17] • Also watch for a protracted withdrawal syndrome that persists beyond initial benzodiazepine withdrawal. Symptoms may last as long as 12 months, and include depression, cognitive impairment, insomnia, anxiety, motor symptoms, paresthesia, or tinnitus.[17] • In case of worsening of underlying condition or withdrawal symptoms, maintain benzodiazepine dose or increase to the previous step for one to two weeks, then taper more slowly.[16,17,22] • Incorporate non-drug approaches to manage underlying conditions (e.g., sleep hygiene, cognitive behavioral therapy).[16]

Goal	Suggested Strategies or Resources
Successful benzodiazepine tapering strategies, continued	• For patients on both an opioid and benzodiazepine, the decision to taper the opioid or benzodiazepine first should be individualized.[19] Benzodiazepine tapering can be destabilizing for patients who are benefiting from them, benzodiazepine withdrawal is riskier than opioid withdrawal, and tapering opioids can be associated with anxiety.[19,28] For these reasons, it might be easier and safer to taper the opioid first.[28] • Depending on patient reliability, consider having the pharmacist dispense only a week's worth of medication (or less) at a time.[26] • Provide a written tapering plan to improve chance of success.[18]
Formulate a benzodiazepine tapering plan for your patient.	• There is no one tapering schedule suitable for all patients.[17] In general: o Low doses might be tapered by 20% per week, but high doses (e.g., alprazolam >4mg/day) should be tapered over at least eight to 12 weeks.[20,24] o Also consider a slower taper for patients taking alprazolam; patients taking a benzo for >2 to 3 months; and for patients with panic disorder or a seizure disorder.[2,3,25] o Try to complete the taper within six months so that the patient does not become unduly focused on the taper.[29] o When the lowest available dose is reached, progressively reduce dosing frequency (e.g., for insomnia, schedule drug-free nights).[16] o Switching and stabilizing on a longer-acting agent (e.g., clonazepam) before tapering is sometimes done, but may not be superior.[16,22,26] The "Benzodiazepine Dosing and Pharmacokinetics" table above provides approximate equivalent doses. • Suggested tapering regimens include: o Reduce dose by 25% every one to two weeks (commonly used).[28] When 25% to 50% of the dose remains, consider reducing by 12.5% every four to seven days.[16,20] ▪ If the dosage form does not allow for a 25% reduction, consider a 50% reduction initially, then switch to lorazepam or oxazepam for the end of the taper.[16] o Taper by no more than 5 mg diazepam equivalent per week. When 20 mg diazepam equivalent is reached, slow the taper to 1 to 2 mg diazepam equivalent per week.[26] The "Benzodiazepine Dosing and Pharmacokinetics" table above provides approximate equivalent doses. o **Alprazolam**: decrease by no more than 0.5 mg increments. If taking ≥6 mg/day, consider decreasing by 0.5 mg every two to three weeks. When at 2 mg/day, decrease by 0.25 mg every two to three weeks.[24] o In **panic disorder**, taper the benzodiazepine over two to four months, by no more than 10% of the dose weekly.[25] o Some patients may need an especially conservative "hyperbolic taper," wherein the dose is reduced by 5% to 10% **of the most recent dose** monthly.[30] A liquid formulation may be needed to achieve required dosages.

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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Appropriate Opioid Use

(modified December 2024)

This toolbox provides resources to help clinicians managing chronic pain with opioids, one of the most challenging areas of clinical practice. **Also check with your licensing body for information on state or provincial regulations pertaining to dosing limits, screening, monitoring, etc**. Note that CDC guidance regarding opioid prescribing does not apply to patients with cancer, sickle cell disease, or at the end of life.[1]

Goal	Suggested Strategies or Resources
Limit opioid use for acute pain.	• Adequate treatment of acute pain (sudden onset; duration <1 month) or subacute pain (unresolved acute pain lasting one to three months) is important to prevent transition to chronic pain (pain lasting >3 months), but care should be taken to ensure that patients do not accidentally transition from using opioids for acute pain to prolonged use.[1,2] • Do not use opioids first-line for most kinds of acute pain. Nonopioids are at least as effective as opioids for low back pain, neck pain, musculoskeletal injuries (e.g., strains, sprains, tendonitis, bursitis), headaches, dental pain, minor surgery, and kidney stones.[1] See our chart, *Analgesics for Acute Pain in Adults*, for preferred treatments. • Prescribe the lowest effective dose.[1] Prescribe only enough for the anticipated duration of severe pain, then re-evaluate.[1] • Advise patients that short-term use can lead to unnecessary long-term use, so the opioid will be discontinued as soon as appropriate.[1] • Do not prescribe extended-release opioids for acute pain.[3]
Identify appropriate/ inappropriate uses for subacute or chronic opioids.	• Nonopioids are preferred for subacute and chronic pain.[1] • Opioids are most appropriate for patients with moderate to severe pain that affects function or quality of life with unsatisfactory response to non-opioids (e.g., acetaminophen or NSAIDs for osteoarthritis, tricyclics, duloxetine, or anticonvulsants for neuropathic pain).[2,4] • Generally avoid opioids in pelvic pain, fibromyalgia, headaches, migraine, back pain, temporomandibular disease, irritable bowel syndrome, ill-defined pain syndromes.[1,5]

Identify patients at risk for opioid misuse before prescribing.
 	
Continued…
	• Screen for opioid abuse risk factors (e.g., age <45 years, widespread pain without objective findings, current or past misuse of alcohol or other substances, major psychosocial issues, refusal to accept a multimodal approach).[4]
	  ○ The Patient Health Questionnaire, a screening tool for depression, is available at https://cde.drugabuse.gov/sites/nida_cde/files/PatientHealthQuestionnaire-2_v1.0_2014Jul2.pdf.
	  ○ The Primary Care PTSD Screen is available at http://www.ptsd.va.gov/professional/assessment/screens/pc-ptsd.asp.
	• Be wary of patients insisting on specific products or claiming allergies to specific analgesics; this can be a red flag for drug-seeking behavior.[6] Use our chart, *Opioid Allergy*, for help finding the best options for potentially allergic patients.
	• Risk assessment tools include:
	  ○ the one-minute **ORT** (Opioid Risk Tool: https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf).

Goal	Suggested Strategies or Resources
Identify patients at risk for opioid misuse, continued	○ **SOAPP-R** (Screener and Opioid Assessment for Patients with Pain, revised: https://d1li5256ypm7oi.cloudfront.net/colospine/2016/08/SOAPP-R-Screener-and-Opioid-Assessment-for-Patients-with-Pain-Revised-160816-57b258fc9a277.pdf). ○ **DIRE** (Diagnosis, Intractability, Risk, Efficacy: http://www.agencymeddirectors.wa.gov/Files/AssessmentTools/11-DIRE_score.pdf). ○ **PMQ** (Pain Medication Questionnaire). A systematic review recommended the PMQ, but not the ORT, and deemed SOAPP-R potentially useful.[7] • In the **US**, check your state's prescription drug monitoring program to identify patients who may be improperly using or diverting opioids and other controlled substances, or getting a benzodiazepine prescription from another prescriber. In **Canada**, use your provincial drug information system or prescription monitoring program, if available. ○ The CDC recommends checking before the initial prescription, before each prescription, or at minimum, every 3 months.[1]
Reduce risk of overdose.	• Screen for, and address, mental health problems (e.g., depression, substance use disorder).[2] • Avoid opioids in patients with active mental illness or a history of substance use disorder, including alcohol.[9] Optimize non-opioids instead.[9] • Consider limiting quantities in at-risk patients.[9,14] • Keep in mind that women are at higher risk of overdose than men.[2] • If possible, avoid other respiratory/central nervous system depressants (e.g., benzodiazepines, barbiturates, diphenhydramine, muscle relaxants, promethazine).[2,8] Our toolbox, *Appropriate Use of Oral Benzodiazepines*, has tips for deprescribing. • Reserve long-acting opioids for severe, continuous subacute or chronic pain, in opioid-tolerant patients who have been benefiting from certain dosages (consult product labeling) of short-acting agents for at least one week.[1] ○ There's no proof long-acting opioids are safer or more effective.[1] In fact, the risk of unintentional overdose is two-fold higher, especially during the first two weeks.[10] Long-acting opioids are also associated with higher all-cause mortality compared to anticonvulsants or antidepressants in chronic noncancer pain.[4] ○ Try to avoid combining short- and long-acting opioids.[1] For example, for breakthrough pain that occurs near the end of the dosing interval, the fentanyl patch can be dosed every 48 hours, and *MS Contin* or *OxyContin* every eight hours.[11,12] • Consider the partial opioid agonist buprenorphine for patients who need an opioid for chronic pain, but for whom an opioid with a wider margin of safety than a full agonist is desirable. • A trial of a different opioid (opioid rotation) can be considered for uncontrolled pain, to improve pain and function.[9] ○ Use caution when switching between opioids.[9] See our chart, *Equianalgesic Dosing of Opioids for Pain Management.* • Advise patients/caregivers to hold the dose and contact the prescriber in the event of somnolence, or if an opioid reversal agent is used (**see opioid reversal agents section, below**). • Ensure that patients and caregivers understand not to break, split, or crush sustained-release formulations.

Goal	Suggested Strategies or Resources
Dose opioids safely.	• Start with a low dose of a short-acting opioid (e.g., oxycodone 5 mg every 4 to 6 hours as needed).[4,9,13] • Consider limiting the initial opioid trial to oral morphine 50 mg/day, or its equivalent.[9] • The CDC guidelines recommend careful reassessment of benefits and risks before increasing the daily dose, especially to ≥50 mg morphine or its equivalent (e.g., hydrocodone 50 mg [US], hydromorphone 10 mg, oxycodone 30 mg).[1] Most patients do not achieve additional benefit from higher doses, but do incur increased risk.[1] Doses ≥50 MME/day double the risk of death from an opioid overdose compared to <20 MME/day.[1] o Some healthcare systems, payers, and state medical boards have protocols related to dosage thresholds, although the CDC guidance is not intended to set standards related to dosages or durations.[1] o Also see "Follow-up and Evaluation" section, below. • Few trials have evaluated ≥90 mg morphine or its equivalent.[1] o Be aware that overdose risk increases 2 to 8.9-fold oral morphine ≥100 mg/day, or its equivalent, compared to the risk with doses <20 mg/day.[1,a] • **Reserve methadone for patients who have failed other opioids, and only prescribed by clinicians experienced in its use**.[4] Methadone safety guidelines can be found at http://www.jpain.org/article/S1526-5900(14)00522-7/pdf. • When opioids other than morphine are used: o See the CDC site to calculate MME/day: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. o Download the CDC app for MME calculations: https://www.cdc.gov/opioids/healthcare-professionals/prescribing/app.html.
Provide an opioid reversal agent.	• Offer naloxone or nalmefene (US), especially for patients with sleep apnea, history of overdose or substance use, concomitant benzodiazepine use, or use of relatively high opioid doses (e.g., or ≥50 MME/day). • Use our *Opioid Reversal Agents Quick Start Guide* as a stepwise approach to identify candidates for take-home naloxone or nalmefene (US). • For more detailed information our FAQ, *Meds for Opioid Overdose*, addresses common questions that arise in practice regarding naloxone for opioid overdose.
Manage patient expectations.	• Set goals with the patient for functional improvement, and document them for future monitoring purposes; this is how efficacy will be determined.[9] Think SMART: the goals should be Specific, Measurable, Action-oriented, Realistic, Time-dependent.[13] • Explain that improving pain and function by about 30% is a success.[1] • Explain that evidence of long-term benefit is lacking and delineate risks.[1] • View the opioid prescription as a time-limited trial; you are testing benefit to the patient, not committing to long-term opioid use.[9] Discuss how the opioid will be discontinued if benefits do not outweigh risks.[1]

Goal	Suggested Strategies or Resources
Educate patients about opioid safety.	• An educational poster from the CDC promoting non-opioid alternatives is available at http://www.cdc.gov/drugoverdose/pdf/guidelines_patients_poster-a.pdf. • A patient fact sheet from the CDC discussing opioid risks, opioid alternatives, and measures to improve opioid safety is available at http://www.cdc.gov/drugoverdose/pdf/guidelines_factsheet-patients-a.pdf. • ISMP Canada provides information to consumers on safe medication use, including opioids: https://www.safemedicationuse.ca/tools_resources/tips.html. • Patient counseling should include advice to avoid driving during dose increases or if they are sedated. Patients should be told to avoid using alcohol or sedating drugs. If they do use these substances, they should not drive.[9] • Patients should be counseled on how to safely store and dispose of opioids.[1] Treatment agreements often include an expectation of secure storage. • Apprise patients of the risks of opioid use (e.g., hypogonadism, sleep apnea, tolerance, hyperalgesia [i.e., pain sensitization caused by chronic opioid use], withdrawal, and opioid use disorder) at baseline and periodically.[1,9]

Prevent and identify misuse at follow-up.	• Consider a treatment agreement, at minimum, for patients at high risk of misuse, or patients not well known to the prescriber.[14] Some experts feel that a treatment agreement is needed for all patients receiving opioids for chronic noncancer pain.[4] Treatment agreements have not been proved to prevent opioid misuse.[4,9]
	• Require in-person follow-up in order for patients to obtain a refill or new prescription.[4]
	• Consider pill counts.[14]
	• **COMM** (Current Opioid Misuse Measure) can be used to screen for abuse in **current** opioid users.[7]
	• Consider **urine drug testing**.
	  o Consider baseline and periodic (at least annually) urine drug testing, although this is not evidence-based.[1,9]
	  o Consider testing three or four times per year in patients at high risk per the ORT or taking >120 mg of morphine daily.[10]
	  o Approximately 30% of urine drug screening will show unexpected results, mostly due to not detecting the prescribed opioid or presence of tetrahydrocannabinol.[9] If urine testing is planned, either at baseline or follow-up, know how to interpret the results and plan how you will apply them.[4]
	• Consider abuse-deterrent formulations. Keep in mind these products have not been proven to prevent opioid misuse.[9]

Ensure appropriate follow-up and evaluation of opioid therapy. *Continued…*	• Schedule follow-up at least every one to four weeks while determining the optimal dose, then at least every three months.[1] Treatment agreements generally require in-person follow-up in order for patients to obtain a refill or new prescription.[4] o A trial of three to six months is reasonable, but efficacy wanes after three months.[9] Patient perception of benefit past three months may be related to relief of interdose withdrawal as opposed to pain relief.[9] • Chronic pain is often accompanied by impaired function, multiple medical conditions, and psychological disorders.[1,4] Address these areas in addition to evaluation of efficacy (i.e., improved function and pain control), adverse effects, and evidence of misuse.[1]

Goal	Suggested Strategies or Resources
Appropriate follow-up and evaluation, continued	○ An assessment tool for function, the SF36 Health Survey, is available at http://www.rand.org/health/surveys_tools/mos.html. ○ A checklist for adverse effects, function, and opioid dependence is available from the Utah Department of Health at http://health.utah.gov/prescription/pdf/guidelines/checklist%20for%20adverse%20effects.pdf. ○ An assessment tool for pain, the Brief Pain Inventory (Short Form), is available at http://www.health.utah.gov/prescription/pdf/guidelines/BriefPainInvNPEC.pdf. ○ The two-item version of the Graded Chronic Pain Scale is available at http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf (See Figure B). It measures pain intensity and related disability. • Canadian opioid management tools and guidelines are available at: http://nationalpaincentre.mcmaster.ca/guidelines.html. • **Re-evaluate therapy** before increasing the daily dose to 50 mg of oral morphine or its equivalent.[1,a] (Canada: before escalating the daily dose to ≥90 mg, consider referral for a second opinion.[9]) ○ Assess diagnosis, pain control, function, and adverse effects.[1] ○ Maximize non-opioids and offer an opioid taper, explaining risks and benefits.[1] ○ Increase monitoring frequency.[1] ○ Consider offering an opioid reversal agent.[1] • If misuse occurs, evaluate whether continuation of chronic opioid therapy is appropriate. Restructuring of therapy (e.g., more intensive monitoring, opioid tapering with optimization of non-opioid modalities, education/counseling) or referral may be indicated.[4,10,17]
Use appropriate non-opioid and adjunctive therapies.	• Maximize non-opioid pain medications before opioids are used.[1,9] • Integrate interdisciplinary therapy.[2] This usually involves exercise and psychological therapy.[2] ○ Therapies that require patient participation (e.g., exercise, cognitive behavioral therapy) may have better long-term benefit than passive therapies (e.g., massage) on pain and function.[1] ○ Supervised therapy for stretching, strengthening, and aerobic exercise may be appropiate.[10] • Sleep hygiene is recommended.[10] • To **prevent** constipation, fluids, dietary fiber, and exercise can be recommended. Consider "prophylactic treatment" with daily use of an osmotic laxative (polyethylene glycol [PEG] 3350). Avoid bulk-forming laxatives.[16] • Ensure associated comorbidities are treated (e.g., depression, obesity).[1]

Goal	Suggested Strategies or Resources
Taper dose or discontinue opioids when appropriate.	• Discontinue the opioid as pain resolves, with tapering if the opioid has been used around the clock for more than a few days.[1] The taper can be brief if the opioid was prescribed short-term, for acute pain.[1] For hospitalized patients, coordinate tapering: o A taper may not be appropriate if the opioid is discontinued due to a life-threatening issue.[1] • For opioids started in the hospital, discuss the tapering plan with the patient and outpatient provider.[1] • Consider dose reduction or tapering and discontinuation in the event of inefficacy despite a three-month trial, suspected side effects that outweigh benefits, comorbidities or drug interactions that increase risks (e.g., fall risk, kidney impairment), evidence of misuse or diversion, or signs of intoxication, overdose, or suspected hyperalgesia.[1,4,10] Alternatively, rotation to another opioid could be attempted in case of inefficacy or side effects, or to facilitate dose reduction.[9] • For practical tapering tips and protocols, see our FAQ, *Opioid Tapering: Tips for Success*.
Advise safe opioid disposal.	• **US**: Learn where and how to dispose of unused meds at https://www.fda.gov/consumers/consumer-updates/where-and-how-dispose-unused-medicines. • **Canada**: Learn about getting rid of old meds at the Health Products Stewardship Association site https://healthsteward.ca/ or call 844-535-8889.
Offer treatment for opioid use disorder.	• Medication-assisted treatment of opioid use disorder has the most evidence and helps prevent withdrawal symptoms and decreases illicit opioid use, overdose death, and criminal activity.[18] • Find a physician in your area authorized to prescribe buprenorphine for opioid dependence at http://www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator. • In Canada, consult federal-, provincial-, and territorial-funded programs.
Manage opioids appropriately in the inpatient setting, including at discharge. *Continued…*	• In the emergency department (ED), urgent care, or at discharge: o watch for red flags for abuse (e.g., frequent ED visits, non-opioid allergies, requesting specific opioids).[20] o prescribe only enough opioid doses to cover the number of days that the pain is expected to be severe enough to require opioids.[21] For example days' supply for different types of surgery, see https://michigan-open.org/prescribing-recommendations/. o do not prescribe long-acting opioids (except in hospice patients, with hospice consultation).[19] o check your state/provincial prescription drug monitoring program before writing an opioid.[19] o communicate tapering plans at transitions of care so that opioids started in the hospital do not end up being continued chronically.[22] • See The Joint Commission's pain assessment and management standards for hospitals: https://www.jointcommission.org/-/media/tjc/documents/standards/r3-reports/r3_report_issue_11_2_11_19_rev.pdf.

Goal	Suggested Strategies or Resources
Opioids in the inpatient setting, continued	• Generally, continue long-term, pre-op opioids in surgical patients.[10] Coordinate post-op pain care with the outpatient prescriber.[10] • In the ED, Alternatives to Opioids ("ALTO") include acetaminophen, NSAIDs, lidocaine (e.g., renal colic pain), and ketamine. See our chart, *Analgesics for Acute Pain in Adults*, for details. • Use multimodal, opioid-sparing analgesia (e.g., acetaminophen, an NSAID, gabapentin or pregabalin, lidocaine, local or regional anesthesia, ketamine) perioperatively.[15] ○ Post-op, consider around-the-clock oral acetaminophen as the "backbone" of analgesia.[15] • If an opioid is needed, the oral route is preferrable when possible.[15] • Instruct patients on disposing any leftover doses.[23]
Where permitted by law, ensure appropriate use of cannabinoids for pain.	• A clinical practice guideline for medical cannabis or cannabinoids for chronic pain is available at https://www.bmj.com/content/bmj/374/bmj.n2040.full.pdf. • See the College of Family Physicians of Canada's cannabis resources for family physicians at https://www.cfpc.ca/en/education-professional-development/practice-tools-guidelines/cannabis-resources-for-family-physicians.

a. See our chart, *Equianalgesic Dosing of Opioids for Pain Management*.

Abbreviations: ED = emergency department; MME = morphine milligram equivalents; NSAID = nonsteroidal anti-inflammatory drug; ORT = Opioid Risk Tool; PTSD = post-traumatic stress disorder

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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