Appropriate Use of Oral Benzodiazepines

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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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