Considerations When Risks Outweigh Benefits

How to Help Your Patients Taper from Benzodiazepines

Ten medical and professional societies¹ partnered to develop the *Joint Clinical Practice Guideline on Benzodiazepine Tapering* to help clinicians determine whether and how to taper benzodiazepine (BZD) medications.

Who should taper?

Regularly reassess the risks and benefits of ongoing BZD prescribing (eg, with each new BZD prescription or prescription renewal, at least every 3 months). Consider the risks and benefits outlined in <u>Table 1</u>. When determining the balance of risks and benefits, consider:

- Is the patient benefitting from the BZD? Could alternative interventions achieve similar benefits?
- How significant are the potential risks of BZD for the individual? What are the potential risks of tapering for the patient (eg, transition to the illicit market)?
- How imminent are the risks? How effectively can the risks be managed?

If the risks outweigh the benefits for the individual and they are likely to be physically dependent on BZD (see Table 2), the medication should be tapered. When there are resource constraints for BZD tapering, prioritize individuals at highest risk, including those:

- With recent adverse events related to BZD (eg, falls, cognitive concerns, motor vehicle accidents)
- With comorbidities that are negatively impacted by BZD
- With substance use disorder (SUD) or at risk for overdose
- Taking supratherapeutic doses (eg, higher than maximum recommended dose on the label)

Before you begin a taper

- Engage the patient (and their care partners) in a shared decision-making process. Consider:
 - Their perspective on the relative risks and benefits for them
 - Their concerns and preferences (eg, timing, pace, management of the underlying condition)
- Optimize treatment for underlying condition(s)
- Check the prescription drug monitoring program (PDMP)
- Coordinate with other providers, especially other who prescribe BZD, opioids, or other controlled medications

ommended dose on the label)

BZDs should never be abruptly

discontinued in a patient who is likely

to be physically dependent because

of the risk for severe and potentially

deadly withdrawal symptoms.

managed in an outpatient setting.

Consider a more intensive level of care when the patient is at imminent risk for harm that cannot be rapidly mitigated by the initial dose reduction and when the patient has comorbidities that are anticipated to significantly complicate tapering.

BZDs tapering can typically be

¹ American Academy of Family Physicians (AAFP); American Academy of Neurology (AAN); American Academy of Physician Associates (AAPA); American College of Medical Toxicology (ACMT); American Association of Nurse Practitioners (AANP); American Association of Psychiatric Pharmacists (AAPP); American College of Obstetricians and Gynecologists (ACOG); American Geriatrics Society (AGS); American Psychiatric Association (APA); American Society of Addiction Medicine (ASAM)

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Help the Patient Prepare for Tapering

One of the most important factors in the success of a taper is how supported the patient feels.

- Educate the patient on the <u>risks associated with BZDs</u>, the risk for withdrawal if BZD are rapidly reduced or stopped, and the tapering process. Reassure them that the tapering strategy will be adjusted based on their response to minimize their symptoms.
 - Providing written instructions and information on what to expect during tapering is helpful
- Offer or refer for psychosocial support (eg, cognitive behavioral therapy [CBT])

Support the Patient to Slowly Taper

There is no simple formula for BZD tapering. Different patients respond differently to dose reductions. There is no established way to accurately predict which patients may have more difficulty with the taper.

- Start slow
 - For the first reduction, consider the lower end of the dose reduction range (eg, 5%)
- Monitor patients after each dose reduction
 - See <u>Table 3</u> for common withdrawal signs and symptoms
 - Continue monitoring after BZD discontinuation for protracted withdrawal
 - o Check-ins can be virtual, including by telephone
- Adjust the pace of the taper based on the patient's response
 - Considering reduction of 5% to 10% every 2-4 weeks
 - Pause or slow the taper if significant symptoms emerge
 - Patients who have been taking lower doses for a shorter
 period of time may be able to tolerate a faster pace (ie, 10-25% every 2-4 weeks)

The Guideline recommends:

- Initial dose reductions of <u>5% to</u> 10%.
- Not exceeding 25% every 2 weeks.
- Tailoring tapering strategies to each patient and adjusting based on their response.

It may take months to years to fully taper off BZDs, particularly if patients have been taking a high dose for an extended period of time.

BZD Tapering Tips

- Consider strategies for slower dose reductions if the patient continues to experience significant symptoms (eg, reduce by 5% of current dose rather than 5% of original dose [ie, hyperbolic tapering], microtapering using liquid formulations)
- Consider switching to a longer acting BZD (eg, clonazepam), particularly for patients taking alprazolam
 - o For BZD dose equivalences, see <u>Table 4</u>
- Give the brain time to adjust. Adjunctive medications can be considered but generally try to avoid other GABAergic medications (eg, gabapentin, Z-drugs)
- Generally avoid returning to the previous dose, unless withdrawal symptoms remain intolerable despite adjustments to the tapering strategy (eg, pausing the taper, adjunctive medications)
- Achieving a lower dose may be sufficient to reduce the current risk of harm such that risks no longer outweigh benefits.
- Consider consulting with a medical toxicologist, addiction specialist, or clinical pharmacist, when needed

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Table 1. Potential Benefits and Risks of Continued BZD Use and BZD Tapering²

Potential Benefits	Potential Risks			
BZD Use	BZD Use	BZD Taper		
 Effectiveness in managing a patient's mental and physical health condition(s) Related functional improvements Quality of life improvements³ 	 Oversedation, including consideration of use with other sedating medications, alcohol, or other drugs Falls and related injuries Memory and cognitive impacts Motor vehicle accidents Medical safety concerns (eg, medication interactions) Impacts on co-occurring mental and physical health conditions Disrupted sleep patterns Impacts on work and family responsibilities Diversion Substance use disorder Overdose Fetal harm Suicidality 	 Withdrawal symptoms, including severe or complicated withdrawal (eg, seizures, delirium) Recurrence of the condition for which BZD were prescribed Impacts on co-occurring mental and physical health conditions Protracted withdrawal Return to illicit BZD use Transition to illicit BZD use (including risks associated with counterfeit BZDs from the illicit drug market [eg, contamination with fentanyl]). 		

A list of some of the potential benefits and risks to BZD use and tapering when considering whether to taper the medication.

Table 2. Risk for Clinically Significant BZD Withdrawal⁴

Duration of BZD Use	Frequency of BZD Use	Total Daily BZD Dose	Risk for Clinically Significant Withdrawal ⁵
Any	≤3 days per week	Any	Rare ⁶
<1 month	≥4 days per week	Any	Lower risk, but possible
1-3 months	≥4 days per week	Low ⁷	Lower risk, but possible
1-3 months	≥4 days per week	Moderate ⁸ to high ⁹	Yes, with greater risk with increasing dose and duration
≥3 months	≥4 days per week	Any	Yes, with greater risk with increasing dose and duration

This table summarizes estimates of risk for experiencing clinically significant withdrawal depending on the dose, duration, and frequency of BZD use.

² Clinicians should consider the likelihood of each benefit and risk for the individual patient. The narrative notes risk/hazard ratios available in the published literature.

³ Including compassionate use for end of life or palliative care.

⁴ This table is based on clinical consensus. It is intended to provide general guidance and should *not* replace clinical judgment.

⁵ Many factors influence the risk of physical dependence and BZD withdrawal syndrome, including but not limited to age, cooccurring physical and mental health conditions, other substance use, and prior history of withdrawal.

⁶ Half-lives are unknown for some novel synthetic benzodiazepines available in the illicit market.

 $^{^{7}}$ A low daily dose is estimated as 10 mg diazepam equivalents or less (eg, ≤0.5mg clonazepam, ≤2 mg lorazepam, ≤1 mg alprazolam). See Table 4 for BZD dose equivalents.

⁸ A moderate daily dose is estimated as 10–15 mg diazepam equivalents (eg, 0.5–1.5 mg clonazepam, 2–3 mg lorazepam, 1–2 mg alprazolam). See Table 4 for BZD dose equivalents.

⁹ A high daily dose is estimated as more than 15 mg diazepam equivalents (eg, >1.5 mg clonazepam, >3 mg lorazepam, >2 mg alprazolam). See Table 4 for BZD dose equivalents.

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Table 3. Potential Benzodiazepine Withdrawal Signs and Symptoms¹⁰

General	Affective	Cardiovascular	Gastrointestinal
 Elevated blood pressure Headaches Sweating, night sweats	Anxiety, panic attacksDepression, dysphoriaIrritability, agitation, aggression	Chest painPalpitationsTachycardia	Abdominal crampsDiarrheaNausea and vomiting
Neurological	Neuromuscular	Neuropsychiatric	Sleep
 Cognitive impairment (eg, poor memory, reduced concentration) Confusion, delirium† Perceptual disturbance Seizures† Sensory hypersensitivity (ie, to light, sound, taste, and smell) Tingling, numbness, altered sensation Tinnitus 	 Coordination, balance problems Dysesthesia, kinetic disorders Muscle pain (eg, tension, weakness, spasms) Muscle twitches, jerks, and fasciculations Tremors 	 Akathisia, restlessness Depersonalization, derealization Psychosis (eg, paranoia)† Suicidality and selfharm 	HypersomniaInsomniaNightmares

Examples of common BZD withdrawal signs and symptoms grouped by body system.

Table 4. Benzodiazepine Approximate Dose Equivalents to 10 mg Oral Diazepam¹¹

Benzodiazepine	ATC Therapeutic Class	VA/DoD SUD CPG (2021) ¹²	Ashton Manual (2002) ¹³
Alprazolam	Anxiolytic	1	0.5
Chlordiazepoxide	Anxiolytic	25	25
Clonazepam	Antiepileptic	1	0.5
Clorazepate	Anxiolytic	15	15
Diazepam	Anxiolytic	10	10
Estazolam	Sedative-Hypnotic	1	1-2
Flurazepam	Sedative-Hypnotic	15	15-30
Lorazepam	Anxiolytic	2	1
Oxazepam	Anxiolytic	30	20
Quazepam	Sedative-Hypnotic	10	20
Temazepam	Sedative-Hypnotic	15	20
Triazolam	Sedative-Hypnotic	0.25	0.5

Approximate dose equivalents of various BZD medications to a 10 mg dose of oral diazepam as determined by the VA/DoD SUD guideline and *The Ashton Manual*.

ATC: Anatomical Therapeutic Chemical classification system; CPG: clinical practice guideline; DoD: US Department of Defense; SUD: substance use disorder; VA: US Department of Veterans Affairs

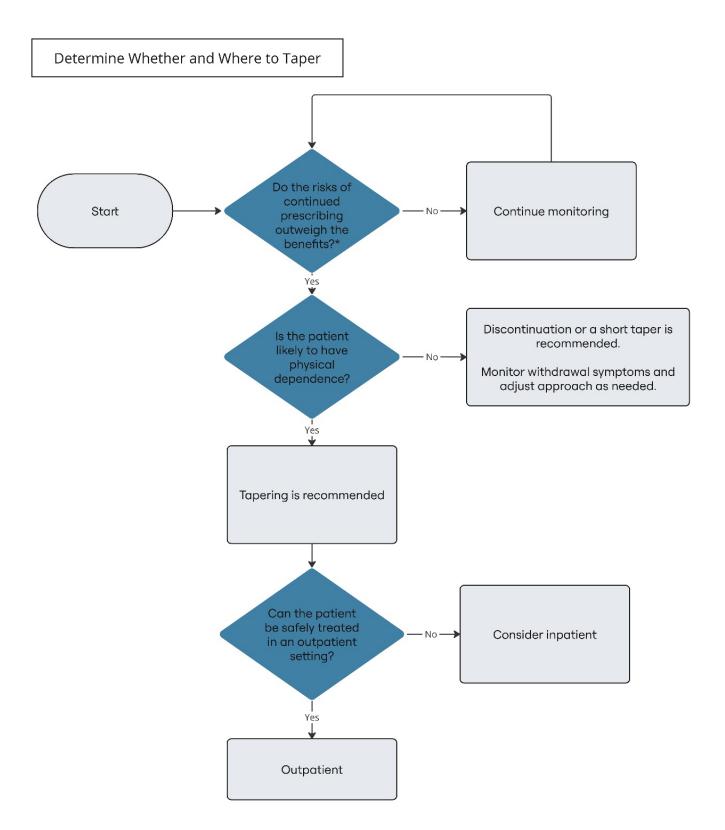
[†] Typically associated with abrupt cessation of high doses of BZDs

 $^{^{10}}$ Adapted from Soyka (2017), 2 Baldwin (2022), 80 Gold & Ward (2022), 84 and The Maudsley Deprescribing Guidelines. 82 This table does not represent a comprehensive list of withdrawal symptoms. See The Maudsley Deprescribing Guidelines. and The Ashton Manual.

¹¹ These doses are intended for guidance only. Clinical decisions on dose should be individualized based on the patient response. Determining the equivalent dose of an alternative BZD is inexact and can vary across patients. No precise strategies for conversion exist.

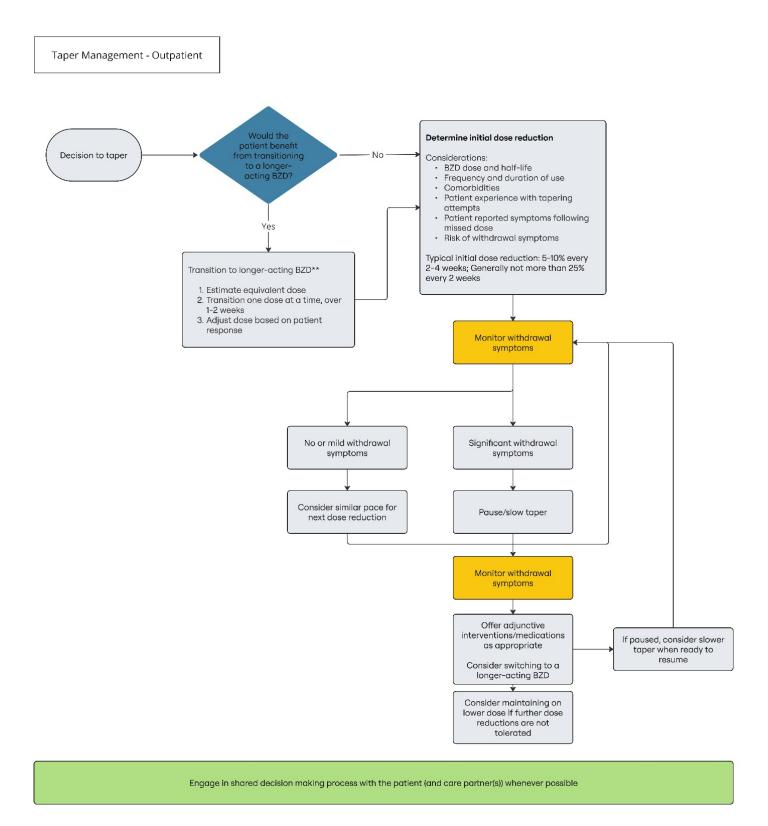
¹² Department of Veterans Affiars, Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. 2021. ¹³ Ashton CH. *Benzodiazepines: How They Work and How to Withdraw (The Ashton Manual)*. Institute of Neuroscience, Newcastle University; 2002. Same equivalents in Ashton, H. Benzodiazepine Equivalence Table [Online]. Revised April 2007. https://www.benzo.org.uk/bzequiv.htm and Ashton CH. The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatry*. 2005;18(3):249-255. doi:10.1097/01.yco.0000165594.60434.84

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^{*}Risks associated with BZD tapering should also be considered

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^{**}See Transitioning to a Longer-Acting Benzodiazepine section in the full Guideline