

CLINICAL PRACTICE GUIDELINES Prescribing and Monitoring of Benzodiazepines and Related Medications

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INTRODUCTION

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Prescriptions for benzodiazepine medications (primarily for anxiety or insomnia) filled in the United States increased by 320% between 1996 and 2013. Over this same interval, overdose deaths associated with these medications increased by over 500%.¹ A portion of this increase in mortality is likely attributable to the higher dose per prescription observed, as well as the marked increase in opioid prescribing over this same period. In Philadelphia, the concern was significant, with 2017 data showing that benzodiazepines were involved in 36% of overdose deaths overall.²

In response to these concerns, CBH developed guidelines to support safer prescribing of benzodiazepines. Since 2017, overdose deaths in Philadelphia involving benzodiazepines have decreased.^{3,4} Data from 2023 show that 12.3% of overdose deaths involved a benzodiazepine.⁴

These guidelines aim to reduce unsafe prescribing of benzodiazepines. The first consideration should be limiting the initiation of benzodiazepines when more effective or safer options are readily available, given the high liability for these medications to complicate recovery from substance use disorders or lead to iatrogenic benzodiazepine dependence. Tapering and discontinuing these medications once dependence has formed is challenging for several reasons, including the potential for a dangerous withdrawal syndrome. Safe tapering and discontinuation may require transfer to a higher level of care, increased contact with the prescribing physician or care team, and other individualized interventions. Please refer to Appendix A for additional information related to tapering benzodiazepines.

These guidelines apply to benzodiazepines as well as benzodiazepine receptor agonists (e.g., zolpidem), barbiturates, and other controlled sedative-hypnotics.

¹ Bachhuber et al., Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996–2013. Am J Public Health. Published online ahead of print February 18, 2016: e1–e3. doi:10.2105/AJPH.2016.303061

² <u>PA DOH Prescription Drug Monitoring Program Interactive Data Reports.</u>

³ <u>Unintentional Overdose Deaths by Specific Drugs 2010-2021.</u>

⁴ PA ODSMP, Substance Involved in Drug Overdose Deaths by county of death, 2017-2024.

1. GUIDELINE REGARDING MONOTHERAPY:

Benzodiazepines should not be initiated as monotherapy for the treatment of anxiety disorders.

While there is evidence that benzodiazepines can be used safely and effectively for the treatment of anxiety, evidence-based guidelines recommend their reservation as second-line agents.^{5,6,7,8,9,10,11} Other pharmacologic treatments, primarily Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) and Selective Serotonin Reuptake Inhibitors (SSRIs) have the benefit of a much stronger base of clinical trial evidence to support as first-line use and have significant safety advantages.

Benzodiazepines may be appropriate in the treatment of anxiety and depression for short-term use to achieve rapid symptom relief at the beginning of therapy, with subsequent tapering when the SNRI/SSRI takes effect.¹² Nonpharmacologic treatments may also be considered as first-line treatments for multiple anxiety disorders; those focusing on cognitive-behavioral and exposure-based models have the strongest supporting evidence.

Exceptions

СВН

Treatment should be individualized to help support individuals' recovery goals, and there may be rare instances in which benzodiazepine monotherapy is appropriate (e.g., in cases of documented intolerance or poor response to first-line treatments for anxiety disorders). In these instances, the rationale for the medication regimen should be documented in the member's medical record.

⁹ <u>APA Practice Guideline for the Treatment of Patients with Panic Disorder. 2009.</u>

¹⁰ DeGeorge, Grover, and Streeter. Generalized Anxiety Disorder and Panic Disorder in Adults. Am Fam Physician. 2022;106(2):157-164

¹¹ VA/DoD Clinical Practice Guidelines: Management of PTSD and ASD. 2023. Version 4.0. Provider Summary.

¹² Dunlop BW, Davis PG. Combination treatment with benzodiazepines and SSRIs for comorbid anxiety and depression: a review. Prim Care Companion J Clin Psychiatry. 2008;10(3):222-8. doi: 10.4088/pcc.v10n0307. PMID: 18615162; PMCID: PMC2446479.

⁵ Katzman, M.A., Bleau, P., Blier, P. et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry 14 (Suppl 1), S1 (2014). https://doi.org/10.1186/1471-244X-14-S1-S1

⁶ Borwin Bandelow, Leo Sher, Robertas Bunevicius, Eric Hollander, Siegfried Kasper, Joseph Zohar, Hans-Jürgen Möller. WFSBP Task Force On Mental Disorders In Primary Care and WFSBP Task Force on Anxiety Disorders, OCD and PTSD. Guidelines for the pharmacological treatment of anxiety disorders, OCD, and PTSD in primary care. Int J Psychiatry Clin Practice. 2012 Jun; 16 (2):77-84.

⁷ <u>APA Practice Guideline for the treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder. 2004.</u>

⁸ Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Post-Traumatic Stress Disorder. 2009.

2. GUIDELINE REGARDING INSOMNIA TREATMENT:

Benzodiazepines should not be used for the treatment of insomnia without appropriate evaluation and should not be used chronically.

Before the initiation of benzodiazepines or benzodiazepine receptor agonist medications, a thorough evaluation for underlying causes of secondary insomnia should be performed and documented.¹³ This evaluation should screen for sleep-related breathing disorders (e.g., obstructive sleep apnea), sleep-related movement disorders (e.g., restless legs syndrome), adverse medication or caffeine effects, behavioral causes (e.g., poor sleep hygiene), and psychiatric syndromes known to cause insomnia. Individuals should also be screened for other contraindications discussed in these guidelines.

The first-line treatment for chronic insomnia is cognitive behavioral therapy (CBT).¹⁴

When benzodiazepines or benzodiazepine receptor agonists are used for the treatment of insomnia, they should be used at the lowest possible effective dose and for the shortest duration. Continued prescriptions should not be given without evidence of continued need. Members should be educated about the risks of the medication, with emphasis on the member's individualized risk factors.

Exceptions

СВН

Some individuals may experience chronic insomnia that recurs with attempts to taper, beyond expectable and short-term rebound insomnia. In such cases, longer-term treatment may be acceptable, provided an appropriately documented rationale exists. Referral for sleep medicine evaluation or behavioral sleep therapy should also be considered.

¹³ Schutte-Rodin et al., Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults. J Clin Sleep Med 2008;4(5):487-504.

¹⁴ Qaseem et al. 2016. Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline from the American College of Physicians. Ann Intern Med. 2016 Jul 19;165(2):125-33. doi: 10.7326/M15-2175. Epub 2016 May 3.

3. GUIDELINE REGARDING PRESCRIBING TO THOSE WITH SUBSTANCE USE DISORDERS:

Benzodiazepines should not be prescribed to individuals with substance use disorders.

Individuals with current or past substance use disorders should rarely, if ever, be prescribed benzodiazepines.¹⁵ For such an evaluation, individual self-report cannot be the only source of information: a treatment history from CBH Member Services, collateral information from other providers, or urine drug screening (UDS) are acceptable objective assessment methods.

Exceptions

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There may be cases where therapy with benzodiazepines is medically necessary despite substance use, such as prevention of withdrawal symptoms linked to alcohol or other hypnotics.¹⁶ Thorough documentation of medical decision-making and the steps taken to protect the individual from harm is required. A plan to assess for abuse or diversion of medications in an ongoing fashion must also be documented.¹⁷ Urine drug screening is typically the most straightforward method. CBH recommends UDS monitoring occur upon initial benzodiazepine prescribing, and then periodically throughout treatment for these individuals. Evidence of persistent or repeated substance use, medication diversion, or other aberrant medication-related behavior should be addressed via behavioral contract, medication tapering, referral to an alternate level of care, or medical director/administrative review.

¹⁷ CMS Drug Diversion in the Medicaid Program: State Strategies for reducing Prescription Drug Diversion in Medicaid. 2012.



¹⁵ APA (American Psychiatric Association) (2009). Practice guidelines for the treatment of individuals with panic disorder. Arlington, VA: American Psychiatric Association.

¹⁶ Sachdeva A, Choudhary M, Chandra M. Alcohol Withdrawal Syndrome: Benzodiazepines and Beyond. J Clin Diagn Res. 2015 Sep;9(9):VE01-VE07. doi: 10.7860/JCDR/2015/13407.6538. Epub 2015 Sep 1. PMID: 26500991; PMCID: PMC4606320.

4. GUIDELINE REGARDING PRESCRIBING TO THOSE WITH OPIOID PRESCRIPTIONS:

Benzodiazepines should not be prescribed to individuals enrolled in Medication-Assisted Therapy (MAT) for opioid use disorders or to individuals who are prescribed chronic opioid medications for pain.

Given the danger (discussed above) represented by the combination of benzodiazepines and opioids, such a combination is contraindicated.¹⁸

Exceptions

C-B-H

Initiation of benzodiazepines for individuals receiving MAT or opioids must be accompanied by documentation that such prescribing adheres to all other parts of these guidelines, and a documented rationale establishing medical necessity. In these rare instances, risk may be mitigated by managing and prescribing medications by a single prescriber. If this is not possible, there should be ongoing collaboration between all involved prescribers. In cases where prescribing providers do not respond to collaboration requests, communication efforts should be clearly documented. In cases where the patient refuses consent to collaboration with the opioid prescriber, the benzodiazepine prescriber may proceed with a taper or discontinuation if the patient's safety is at risk. The patient should be informed that this is a potential outcome of refusing collaboration.

In some cases, individuals will be encountered who have been maintained on chronic opioids and chronic benzodiazepines. In such cases, a rapid discontinuation of either medication is neither practical nor safe. Continued treatment must be accompanied by documented collaboration between the providers of each medication and a documented plan to taper one or both medications (or documentation of why this is not possible). Thorough documentation of medical decision-making and the steps taken to protect the individual from harm is required. This includes education on the risks of overdose and provision of naloxone education and prescription, as well as monitoring parameters such as urine drug screens. CBH recommends UDS monitoring occur upon initial benzodiazepine prescribing, and then periodically throughout treatment for these individuals.

¹⁸ Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65:1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1



5. GUIDELINE REGARDING SPECIAL POPULATIONS:

Benzodiazepines should generally not be prescribed to children and adolescents, pregnant/lactating individuals, or senior citizens.

Exceptions

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There may be exceptional cases in which the prescription of benzodiazepines is deemed appropriate in the special populations mentioned above. In these cases, close consultation with other involved physicians (e.g., OB-GYN, pediatrician, etc.) is recommended. Treatment should be accompanied by a documented rationale for benzodiazepine use, individualized risk-benefit analysis, informed consent, safety monitoring mechanisms, and a tapering plan (or documentation of why this is not recommended or not possible).

Risks of benzodiazepine use in senior citizens include higher rates of falls, fractures, delirium, and increased risk of motor vehicle accidents. Benzodiazepines can also increase the risk of short-term cognitive impairment (memory, learning, attention), sedation, and drug-drug interactions.¹⁹

6. GUIDELINE REGARDING PDMP REQUIREMENTS:

Benzodiazepines and other controlled substances will be prescribed per state requirements related to the Prescription Drug Monitoring Program (PDMP).

In 2014, the Pennsylvania State Legislature passed <u>Act 191</u>, expanding the state's prescription drug monitoring program to include monitoring all Schedule II–V controlled substances. <u>Registration for the PDMP</u> is required for all PA prescribers.

Beginning in August 2016, all prescribers have legal responsibilities related to the use of the PDMP. Providers should stay current and ensure their practices comply with all PA PDMP requirements. Additional information is available on the <u>PA DOH Prescription Drug Monitoring Program Prescriber Q&A</u>. See below for an excerpt:

¹⁹ Markota et al. Mayo Clinic Concise Review for Clinicians: <u>Benzodiazepine Use in Older Adults: Dangers, Management, and</u> <u>Alternative Therapies</u>, 2017. Volume 91, Issue 11, 1632-1639.

Per Act 191 of 2014, lawfully authorized prescribers are required to query the PDMP for an existing patient when the following clinical situations apply:

- **1.** For each patient, the first time the patient is prescribed a controlled substance by the prescriber for purposes of establishing a baseline and a thorough medical record; or
- **2.** If a prescriber believes or has reason to believe, using sound clinical judgment, that a patient may be abusing or diverting drugs; or
- **3.** *Each time a patient is prescribed an opioid drug product or benzodiazepine by the prescriber.*

These requirements apply (1) to inpatient or outpatient settings; to acute or anticipated chronic controlled substance(s) prescriptions; to new or established patients; and in situations where the prescriber is seeing his/her own patient or is covering for a colleague. Writing a controlled substance(s) prescription for the first time to a patient is the basis for checking the PDMP in (1) above.

However, as part of good clinical practice, the Department of Health recommends that health care professionals check the system every time before a controlled substance(s) is prescribed or dispensed in any clinical setting.

Act 191 of 2014 states that a prescriber shall indicate the information obtained from the system in the individual's medical record if:

- **1.** The individual is a new individual; or
- **2.** The prescriber determines a drug should not be prescribed or furnished to an individual based on the information from the system.

CBH requests that, each time prescribers or their authorized delegates query the PDMP, they document in the medical record that this occurred. When a query of the PDMP reveals potential concerns, and controlled substances are still to be prescribed, documentation that guidelines 1-4 are being adhered to will be required.

It is also important to note that some controlled substances (e.g., methadone prescribed as MAT for OUD in some treatment settings) will not appear in PDMP reports. Thus, the PDMP system cannot be relied upon for information about such medications.

In addition, CBH providers are expected to perform medication reconciliation at the start of all treatment encounters in which medications are provided. Providers should complete informed consent before providing prescription medications.

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CBH IMPLEMENTATION REVIEW

CBH providers are expected to follow the above guidelines for Benzodiazepine Prescribing. CBH monitoring and oversight will assess adherence to the standards, including Quality, Clinical, and Compliance Department protocols. Components may be reviewed as part of initial and recredentialling reviews. In addition, some standards will be assessed via quantifiable metrics, which are specified in the table below:

CPG component	Metric	Data Source
Prescribing	Average rate of benzodiazepine prescribing	CBH Claims Data and CBH Pharmacy Claims data sent by the State
	Rate of Benzodiazepine prescribing to members also receiving opioid prescriptions	
	Rate of benzodiazepine prescribing to members receiving methadone	
	Rate of benzodiazepine prescribing to members receiving buprenorphine	
	Rate of Benzodiazepine prescribing to members with substance use disorder	



APPENDIX A: TAPERING BENZODIAZEPINES

Introduction

СВН

The guidelines above outline the significant safety concerns associated with benzodiazepine prescribing. However, despite these safety concerns, it is equally important to understand that benzodiazepines should not be stopped abruptly, particularly if they have been used long-term or at high doses. Risks of abrupt cessation include, but are not limited to, a potentially dangerous withdrawal syndrome, seizures, anxiety, insomnia, and agitation. Gradual tapering is recommended to avoid these symptoms and to minimize the likelihood of members seeking these medications from another source (prescribed or illicit).

Multiple evidence-based guidelines provide recommendations related to gradual tapering and discontinuing benzodiazepines (see references below). While tapering benzodiazepines can be challenging, it is important to remember that successful tapering and discontinuation are possible. Below is a summary of key points related to benzodiazepine tapering. Please use the additional resources to provide a more comprehensive picture, including example tapers and specific dosing regimens.

Key Points

- Benzodiazepines should not be stopped abruptly, particularly if they have been used chronically or at high doses, as there is a risk of dangerous withdrawal syndrome.
- Safe tapering and discontinuation may require transfer to a higher level of care, increased contact with the prescribing physician or care team, and other individualized interventions. Providers should assess the risk of benzodiazepine withdrawal to help determine the appropriate level of care. Factors to consider include, but are not limited to:
 - » Presence of benzodiazepine or alcohol withdrawal symptoms
 - » Dose, duration, and frequency of benzodiazepine use
 - » Comorbid alcohol or other substance use
 - » Prior episodes of withdrawal or withdrawal seizures
 - » Presence of high-risk medical conditions (TBI, epilepsy, recent illness/surgery, etc.)
 - » Expected duration of the tapering process
- Gradual <u>tapering of benzodiazepines</u> is recommended.
- Members should be engaged in discussions about the rationale for medication adjustments (including potential harms of benzodiazepine use) and participate in the creation of tapering plans if possible.
- Tapering plans and progress should be reviewed and documented at every prescriber encounter.

- **C**·**B**·**H**
 - Tapering and discontinuing benzodiazepines should be an ongoing, individualized clinical process that may require repeated adjustments. Prescriber documentation should reflect these individualized clinical decisions.
 - A team-based approach is recommended when tapering benzodiazepines.
 - Benzodiazepine tapering is a critical time to coordinate care with other prescribers, particularly of controlled substances.
 - Adequate use of PDMP is required. Pennsylvania PDMP must be queried every time a prescriber prescribes benzodiazepines.
 - For members who continue to receive benzodiazepine prescriptions, the appropriateness and efficacy of the benzodiazepines should be evaluated at every prescriber encounter. Treatment should be accompanied by a clearly documented rationale for benzodiazepine use, individualized risk-benefit analysis, informed consent, safety monitoring mechanisms, and a tapering plan (or documentation of why this is not recommended or not possible).
 - Other recommended interventions to assist with benzodiazepine tapering include cognitive behavioral therapy (CBT), self-help instructions, supportive therapies, educational interventions, and taper/discontinuation letters from clinicians.

APPENDIX B: REFERENCES

- <u>Effective Treatments for PTSD: Helping Patients Taper from Benzodiazepines</u>. National Center for PTSD. 2015.
- Pottie K, Thompson W, Davies S, et al. 2018. Canadian Family Physician. <u>Deprescribing</u> <u>benzodiazepine receptor agonists: Evidence-based clinical practice guideline</u>. (64) 339-351.
- Guaiana G and Barbui C. <u>Discontinuing benzodiazepines: best practices</u>. Epidemiology and Psychiatric Sciences. 2016. (25) 214-216.
- Oldenhof E, Anderson-Wurf J, Hall K, and Staiger P. <u>Beyond Prescriptions Monitoring</u> <u>Programs: The Importance of Having the Conversation about Benzodiazepine Use</u>. Journal of Clinical Medicine. 2019, 8, 2143.

