Clinical Guidelines:

Prescribing and Monitoring of Benzodiazepines and Related Medications

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Community Behavioral Health
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INTRODUCTION

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 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 of opioid prescribing over this same period. The role of benzodiazepines in opioid overdose deaths nationwide increased from 18% of opioid overdose deaths in 2004 to 31% in 2011.[2] In Philadelphia, the issue is even more significant, with a 2016 report finding that approximately 90% of all opioid overdose deaths also involved benzodiazepines.[3] Reporting from the Philadelphia Department of Public Health in 2017 states that use of the dangerous combination of opioids and benzodiazepines remains common, with approximately one third of people currently using prescription opioids also using a benzodiazepine.[4]

Accordingly, 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 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 benzodiazepine receptor agonists (e.g., zolpidem) as well, in the case of sleep, and to barbiturates and other less-commonly prescribed, controlled sedative-hypnotics, where even greater risks may exist.

The full text of each guideline statement occurs in bold at the start of each section.

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[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] *Jones CM, McAninch JK. Emergency department visits and overdose deaths from combined use of opioids and benzodiazepines. Am J Prev Med. 2015;49(4): 493–501.*

[3] *Philadelphia Department of Public Health. Overdose deaths involving opioids in Philadelphia. CHART 2016;1(1):1-8.*

[4] *Philadelphia Department of Public Health. Prescription Opioid and Benzodiazepine Use in Philadelphia. CHART 2018; 2(9):2-6.*

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] 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.[7] 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

Treatment should be individualized when possible to help support individuals' recovery goals. When there is documented intolerance or poor response to first-line treatments for anxiety disorders (see table below), benzodiazepine monotherapy may be appropriate.

FDA Approved (On Label) First-line Pharmacologic Therapy for Anxiety Disorders					
	Panic Disorder	*Generalized Anxiety Disorder*	*Social Anxiety Disorder*	*Obsessive Compulsive Disorder*	*Post-Traumatic Stress Disorder*
Selective Serotonin Reuptake Inhibitors (SSRI)					
Citalopram	X				
Escitalopram	X	X	X	X	
Fluoxetine	X			X	X

[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] *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.*

FDA Approved (On Label) First-line Pharmacologic Therapy for Anxiety Disorders					
	Panic Disorder	*Generalized Anxiety Disorder*	*Social Anxiety Disorder*	*Obsessive Compulsive Disorder*	*Post-Traumatic Stress Disorder*
Fluvoxamine	X		X	X	
Paroxetine	X	X	X	X	X
Sertraline	X	X	X	X	X
Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)					
Venlafaxine	X	X	X		X
Duloxetine		X			

Table adapted from Bandelow et al., 2012. First-line here refers to medications supported fully by clinical trial evidence and that gave a good risk/benefit ratio. Discussion of methods for grading of evidence and risk/benefit discussed more fully in Bandelow et al., 2008.

2. GUIDELINE REGARDING INSOMNIA TREATMENT:

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

Prior to the initiation of benzodiazepines or benzodiazepine receptor agonist medications, a thorough evaluation for underlying causes of secondary insomnia should be performed and documented.[8] 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. When benzodiazepines are used for the treatment of insomnia, an initial treatment period of 2-4 weeks is recommended, as many individuals will remain asymptomatic after tapering at this point.

[8] *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.*

Exceptions

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 there is appropriately documented rationale. Referral for sleep medicine evaluation or behavioral sleep therapy should also be considered.

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

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

Benzodiazepines have a significant liability for misuse; in order to avoid complicating the recovery of individuals with substance use disorders, a thorough screening for past and current substance use disorder must be documented prior to the prescribing of benzodiazepines.[9] For the purposes of 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 are acceptable methods of objective assessment. Individuals with current or past substance use disorders should rarely, if ever, be prescribed benzodiazepines.

Exceptions

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.[10] 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.[11] Urine drug screening is typically the simplest method. 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.

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

[10] *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.*

[11] ***CMS Drug Diversion in the Medicaid Program: State Strategies for reducing Prescription Drug Diversion in Medicaid**. 2012.*

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.[12]

Exceptions

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, documented rationale establishing medical necessity, and ongoing collaboration between both prescribing providers. In cases where prescribing providers do not respond to collaboration requests, communication efforts should be documented.

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. 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 this is a potential outcome of refusing collaboration.

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[12] *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 the elderly.

Exceptions

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

6. GUIDELINE REGARDING PDMP REQUIREMENTS:

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

In 2014, the Pennsylvania State Legislature passed **Act 191**, expanding the state's prescription drug monitoring program to include monitoring of all Schedule II–V controlled substances. **Registration for the PDMP** 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 up-to-date and ensure their practices are compliant with all PA PDMP requirements. Additional information is available on **the PA Department of Health website**. See below for an excerpt:

> *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 0f 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 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 controlled substances prescribed for some MAT of opioid use disorders (e.g., methadone) will *not* appear in PDMP reports, and this system cannot be relied upon for information about such medications.

CBH IMPLEMENTATION REVIEW

CBH providers are expected to follow the above guidelines for Benzodiazepine Prescribing. Adherence to the standards will be assessed through CBH monitoring and oversight, including Quality, Clinical, and Compliance Department protocols. Components may be reviewed as part of NIAC 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
	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

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 dose. 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).

There are multiple evidence-based guidelines that 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 of benzodiazepines is possible. Provided below is a summary of key points related to benzodiazepine tapering. Please use the additional resources for 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 dose, as there is 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 for risk of benzodiazepine withdrawal to help determine the appropriate the level of care. Factors to consider include, but are not limited to:
  - presence of benzodiazepine or alcohol withdrawal symptoms
  - dose, duration, 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 tapering process
- Gradual **tapering of benzodiazepines** is recommended.
- Members should be engaged in discussions about rationale for medication adjustments (including potential harms of benzodiazepine use) and participate in creation of tapering plans if possible.
- Tapering plans and progress should be reviewed and documented at every prescriber encounter.

- The process of tapering and discontinuing benzodiazepines should be an ongoing individualized clinical process, which may need repeated adjustments. Prescriber documentation should reflect these individualized clinical decisions.
- A team-based approach is recommended when tapering benzodiazepines.
- Benzodiazepine tapering is an important time to coordinate care with other prescribers, particularly of controlled substances.
- Adequate use of PDMP is required. Pennsylvania PDMP must be queried every time that a prescriber writes a prescription for benzodiazepines.
- For members who continue to receive a benzodiazepine prescription, appropriateness and efficacy of the benzodiazepines should be evaluated at every prescriber encounter. Treatment should be accompanied by clearly documented rationale for benzodiazepine use, individualized risk-benefit analysis, informed consent, and safety monitoring mechanisms, and 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, taper/discontinuation letters from clinicians.

APPENDIX B: REFERENCES

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