Benzodiazepine Withdrawal Syndrome (BZWS) An Evidence-based Summary for Professionals

I would like to discuss my benzodiazepine prescription with you, and I am concerned

- that you might not listen to or believe me.
- that I will be on these drugs for the rest of my life.
- · of dependence, tolerance, and withdrawal.
- about tapering too quickly.

I want us to work together, and I want to talk to you about high quality evidence-based studies and literature reviews indicating:

- Physiological dependence on benzodiazepines (BZDs) or non-benzodiazepines (Z-drugs) can develop in as little as 2-4 weeks.^[1]
- After 4 weeks of use, up to 47% of patients will go through withdrawal. [2][3]
- Withdrawal symptoms can present while the patient is on a consistent dose (tolerance withdrawal), and can persist for months or even years after deprescription of BZDs.^[4]
- Over 130 varied and intermittent symptoms are associated with BZD dependence and withdrawal.^[5] This variability can often lead to misdiagnosis.

Diagnosing BZD or Z-drug Dependence and Withdrawal

Patient has history of BZD or Z-drug use

- · Higher dose and/or longer use increase risk
- > 4 weeks use typical
- Intermittent use, or 2-4 weeks use (lower probability) Symptoms (over 130 symptoms have been identified)^[5]
- Symptoms are varied and intermittent, with no apparent pattern.



For details and references: Scan or go to benzoreform.org/resources-forprescribers/

Selected Psychological BZWS Symptoms

Anxiety states, Agitation, Irritability/restlessness, Depersonalization/ Derealization, Depression / Sadness / Suicidality, Excitability / Mood swings, Paranoia /Feelings of persecution

Selected Neurophysiologic BZWS Symptoms

Hyperacusis / Tinnitus, Cutaneous sensory alterations, Dizziness / Lightheadedness, Dyscognition, Muscular / Neuromuscular symptoms, Pain – Ache /Neuropathic / Local or diffuse, Sexual dysfunction, Sleep problems, Smell, taste and visual alterations

Selected Somatic BZWS Symptoms

Cardiovascular: Flushing / Palpitations / Tachycardia / BP ↑ or ↓

Appetite change / Weight gain or loss, Dry mouth / Thirst, Menstrual abnormalities / Breast engorgement, Fatigue / Malaise, Food intolerance

GI: Gas / Constipation /Diarrhea / Dysphagia / Nausea / Vomiting, Hyperventilation or Dyspnea

Urinary: Frequency / Incontinence / Polyuria

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This pamphlet does not provide patient medical advice. It is provided for informational purposes only. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition.

Treatment of BZD Dependence

- 1. SEIZURE RISK Do not abruptly discontinue BZDs.
- 2. Before BZD discontinuation, establish a plan with the patient which includes support.
- 3. If tolerated, transition patient to a long-acting BZD (diazepam is preferred, as a liquid). [6]
- 4. Slowly taper the patient off of the BZD often it takes more time than for opioids.
 - Patient-led tapers with prescriber guidance are the most successful.
 - Many patients can reduce by no more than 10% or less per month, some patients by 10% or more per week. Allow the patient to decide where to start.
 - Follow the patient's lead to adjust (up or down) the amount and interval of subsequent reductions. Tapering may take a year or more to complete. [7]
 - The taper rate usually must be slowed as the remaining dosage decreases.
- 5. Never up-dose or use PRN BZDs.
- 6. Add other management techniques, as needed. For example, cognitive behavioral therapy is more effective in anxiety management than BZDs and can help with withdrawal. [8] Start these early in the withdrawal process, as they usually take time to be effective.
- 7. Often, symptoms do not fully abate immediately after tapering. In some cases, symptoms can continue for years post-taper.^[9] Patients need reassurance that this is normal.
- 8. Many other alternative treatments and references can be found at www.benzoreform.org.
- 9. The most authoritative work on BZDs is *Benzodiazepines: How They Work and How to Withdraw*, also known as the "Ashton Manual", by Heather Ashton, MD. (at www.benzo.org/uk/manual/)

BZD and Z-drug prescription guidelines. [5]

- Benzodiazepines are important for alcohol withdrawal, status epilepticus, and in anesthesia. They have <u>no role</u> for anxiety in PTSD, OCD, and most life situations. They can be used <u>as a bridge</u> until other treatments get underway for crisis, functionally disabling anxiety and/or insomnia. [6]
- Prescribe the lowest effective dose for the shortest duration possible.
- Limit prescribing to no more than 4 weeks.
- Benzodiazepine efficacy often diminishes after 4 weeks of use.
- Physiological dependence is common after 4 weeks' use.
- A guided withdrawal process is usually needed after physiological dependence is established.

References

- [1] Pharmacological Treatment of Mental Disorders in Primary Health Care, Geneva: World Health Organization; 2009. Available at https://www.ncbi.nlm.nih.gov/books/NBK143202/
- [2] de las Cuevas C. Benzodiazepines: more "behavioural" addiction than dependence. Psychopharmacology (Berl). 2003 May Abstract
- [3] Lugoboni F, Quaglio G. Exploring the dark side of the moon: the treatment of benzodiazepine tolerance. Br J Clin Pharmacol. 2014 Article
- [4] Ashton H. "Benzodiazepines: How They Work and How to Withdraw". 2002
- [5] Lader M. Withdrawing Benzodiazepines in Patients With Anxiety Disorders. Curr. Psychiatry Rep. 2016 Jan;18(1):8. Abstract
- [6] Clinical Practice Guidelines: Management of Anxiety Disorders. Can J Psychiatry. 2006; 51 (Supplement 2): 29S, 54S. Abstract
- [7] Pottie, K. Deprescribing benzodiazepine receptor agonists: evidence-based clinical practice guideline. Canadian Fam Phys. 2018 Article
- [8] APA Guidelines for Panic Disorder. Practice Guideline (January 2009) Full guidelines
- [9] Durham RC Long-term outcome of eight clinical trials of CBT for anxiety disorders: symptom profile of sustained recovery and treatment-resistant groups. J Affect Disord. 2012 Feb;136(3):875-81. doi: 10.1016/j.jad.2011.09.017. Epub 2011 Oct 19. Abstract
- [10] 16 prescription guidelines exist for BZDs. They are all listed and linked at https://benzoreform.org/links/. This is a list of the items that are common to all of these guidelines.
- [11] Ashton H. Protracted withdrawal syndromes from benzodiazepines, J of Substance Abuse Trtmt, Vol 8, #1-2, 1991, P19-28, Abstract