

IS BENZODIAZEPINE USE BEING OVERLOOKED DURING THE OPIOID EPIDEMIC?

- Q:** Recently, I've seen an increase in the number of requests for a prescription benzodiazepine by the patients that I am treating. Are there any concerning trends regarding the rate at which benzodiazepines are prescribed or abused?
- A:** Though the Opioid Epidemic has captured the attention of the public, a similarly concerning trend involving increased availability, use, misuse, and abuse of benzodiazepines is occurring simultaneously. Providers must be aware of the dangers associated with the use of benzodiazepines, especially in patients that are concomitantly using other licit or illicit central nervous system (CNS) depressants.

The Opioid Epidemic has dominated headlines for the past few years. Numerous organizations, including, but not limited to, the National Institute of Health (NIH), the National Institute on Drug Abuse (NIDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Food and Drug Administration (FDA) are actively researching and developing strategies to combat the Opioid Epidemic. Thus far, the steps taken to curtail overprescribing and abuse of opioids appear to be having a positive impact on the Opioid Epidemic. That being said, consideration should be given to expanding these best practices to another class of CNS depressants, benzodiazepines. Benzodiazepines have been on the market since 1960 and are prescribed to treat a variety of medical conditions, including generalized anxiety disorder, epilepsy, and insomnia.¹ There are twelve benzodiazepines available in the U.S. Though all have unique pharmacokinetic properties, with some carrying highly specific indications, each drug has a relatively similar adverse effect profile. One of the most common side effects associated with this drug class is CNS depression, which is discussed in greater detail below. The risk for adverse effects secondary to benzodiazepine use becomes much greater when used in combination with other substances capable of potentiating common side effects of this class of drugs.²

Despite little national attention, the growth in benzodiazepine prescribing is startling. From 1996-2013, there was a 67% increase in the number of prescriptions filled for benzodiazepines, in addition to a three-fold increase in the quantity dispensed per prescription.³ An upsurge in availability coincided with an increase in the number of opioid co-prescriptions, benzodiazepine-related medical expenditures, and overdose deaths involving this class of medications.⁴⁻⁹ These findings garnered the attention of the FDA, which issued new black box warnings in 2016 that implore providers to use extreme caution when treating patients concomitantly with opioids and other CNS depressants.¹⁰ Despite these alerts, a review of internal data demonstrated that out of nearly 90,000 urine, blood, and oral fluid samples submitted to Aegis® in May 2018 for testing of both benzodiazepines and opioids, 16.5% reflected recent ingestion of at least one medication from both classes, a prevalence rate substantiated by findings from other laboratories.^{11,12}

As the rates of patient-reported adverse events and abuse associated with benzodiazepine use continue to rise, healthcare providers must be able to recognize common side effects of benzodiazepines.^{13,14} An overview of adverse effects, as well as the short- and long-term risks associated with benzodiazepine use can be seen below:

COMMON ADVERSE EFFECTS ASSOCIATED WITH ROUTINE USE ¹⁵	SHORT-TERM RISKS ASSOCIATED WITH USE ¹⁶	LONG-TERM RISKS ASSOCIATED WITH USE ¹⁷
Cognitive disorder	Increased risk of falls	Depression
Confusion	Overdose	Emotional blunting
Dysarthria	Suicide	Ataxia
Incoordination	Vehicle crashes	Aggression
Lightheadedness		Irritability
Memory impairment		Nervousness
Sedation		Sedation
Somnolence		Cognitive impairment
Fatigue		
Drug withdrawal seizure		

There are a few recently published perspectives of healthcare professionals that shed light on best practices for managing patients that are chronically prescribed these medications.^{18,19} Implementation of improved educational programs regarding the dangers of chronic benzodiazepine use for both patients and providers is a common thread amongst these publications. Additionally, authors draw attention to the importance of utilizing prescription drug monitoring programs (PDMPs) to assess for the use of dangerous drug combinations. Though most states require healthcare providers to review PDMPs at the initiation of opioid therapy and periodically throughout treatment, there is often less structure and consistency in these requirements in relation to prescribing and dispensing of benzodiazepines. Finally, for those patients where treatment with benzodiazepines is either no longer medically necessary or too risky, discontinuation of the drug using an appropriate taper and transition to an alternative therapy may be warranted.²⁰ While it is well understood that abrupt cessation of benzodiazepines should be avoided, it does not appear that a consensus exists on the most effective pharmacological therapy available to assist in safe and effective discontinuation.²¹

The data discussed above demonstrates a concerning trend in the rate at which benzodiazepines are prescribed and used by the general public. Due to the propensity for serious adverse effects to occur secondary to the use of benzodiazepines, especially when taken simultaneously with other CNS depressants, providers must remain keenly aware of what medications their patients are using. Medication compliance testing can be an effective means to determine if patients are taking prescribed or non-prescribed benzodiazepines with or without other CNS depressants. Benzodiazepines tested at Aegis include:

PARENT DRUG	MAY BE DETECTED AS	THRESHOLD
Chlordiazepoxide (Reported as “Benzodiazepine Metabolites”)	Nordiazepam Oxazepam	50 ng/ml
Clorazepate (Reported as “Benzodiazepine Metabolites”)	Nordiazepam Oxazepam	50 ng/ml
Diazepam (Reported as “Benzodiazepine Metabolites”)	Nordiazepam Temazepam Oxazepam	50 ng/ml
Temazepam (Reported as “Benzodiazepine Metabolites”)	Temazepam Oxazepam	50 ng/ml
Oxazepam (Reported as “Benzodiazepine Metabolites”)	Oxazepam	50 ng/ml
Alprazolam	Alprazolam Alpha-hydroxy-alprazolam	50 ng/ml
Clonazepam	7-amino-clonazepam	50 ng/ml
Lorazepam	Lorazepam	50 ng/ml
Flurazepam	2-hydroxy-flurazepam	50 ng/ml

Please call our clinical scientists at 1-877-552-3232 if you require additional information.

NOTICE: The information above is intended as a resource for health care providers. Providers should use their

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