ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Not a Luxury Good: Designer Benzodiazepines

Since its discovery in the mid-1950s, benzodiazepines (BZDs) have been commonly prescribed and used for its anti-epileptic, sedative, and anxiolytic effects due to its GABAA receptor agonism (*Neurol Int. 2022;14(3):648-663*). However, BZDs have been abused at supratherapeutic doses to enhance the euphoric effects of other substances such as opioids, used to treat the "unwanted" side effects from stimulants or hallucinogens, and as self-medication for symptoms of opioid or alcohol withdrawal (*Drug Alcohol Depend. 2025;272:112708*). Designer benzodiazepines (DBZDs) are considered novel psychoactive substances (NPS) and share the same chemical structure core as FDA -approved BZDs with slight alterations to increase its potency at the $GABA_A$ receptor. These illicit substances are typically purchased through the illegal drug market under the guise of "research-grade" substances and can be manufactured to resemble FDA-approved BZDs such as alprazolam. Although fatalities from DBZDs alone are rare, when taken with other CNS depressants the risk of heavy sedation, respiratory depression, and subsequent death greatly increases.

The life cycle of DBZDs in the illicit drug market varies between years. The Center for Forensic Science Research and Education (CFSRE) analyze toxicology specimens and drug materials to trend the prevalence of NPS in the U.S. Between the 3rd and 4th quarter trend report of 2022, there was a shift from flualprazolam and etizolam to bromazolam dominating the DBZD space. The 2nd quarter 2025 trend report identified 38% of the specimens analyzed to contain BZDs, with bromazolam being the most common (*NPS Discovery Q2 2025 Trend Reports*). From April 2023 to May 2024, the Drug Overdose Toxico-Surveillance (DOTS) Reporting Program found that within patients with confirmed bromazolam exposure, 92.9% of samples contained adulterants (e.g. xylazine, quinine, doxylamine), 85.7% contained fentanyl and fentanyl analogs, and 60.7% contained stimulants (*Drug Alcohol Depend. 2025;274:112776*). Pharmacokinetic data on bromazolam is limited but is predicted to have ~10-fold greater binding affinity to the $GABA_A$ receptor than alprazolam, an onset of action of 15-45 minutes, and 5-8 hours duration of action (*Clin Toxicol (Phila). 2025;63(5):330-336*). The observed effects of bromazolam are typically heavy sedation and possibly BZD-induced respiratory depression. There have been reports of patients experiencing hyperthermia, seizures, and myocardial injury after ingesting bromazolam disguised as alprazolam (*MMWR Morb Mortal Wkly Rep. 2024;72(5253):1392-1393*). A recent outbreak in July 2025 at Penn North Baltimore resulted in 27 people going to the hospital due to a "bad batch" of fentanyl mixed with N-methylclonazepam, a BZD derivative similar in structure and potency to clonazepam.

Management for DBZD toxicity is supportive in nature with an emphasis on managing airway and respiratory status. It is reasonable to administer naloxone in patients with undifferentiated respiratory depression as DBZDs are commonly abused alongside opioids. The antidote flumazenil acts as a competitive $GABA_A$ antagonist at the BZD site to reverse the effects of DBZDs. However, the utilization of flumazenil should be taken with extreme caution. By competitively inhibiting the $GABA_A$ receptor, reversing the GABA-ergic effects of the DBZD may unmask the effects of other substances, precipitate withdrawal in chronic or non-BZD-naive patients, and can result in seizures and dysrhythmias.

If designer benzodiazepines are suspected or for further guidance on management of DBZDs, please contact your local poison center at 1-800-222-1222.

Did you know?

The DEA placed the DBZDs flualprazolam, etizolam, clonazolam, flubromazolam, and diclazepam in schedule I of the Controlled Substances Act including any salts, isomers, and salts of isomers of these substances.

These substances were initially categorized as schedule I in 2023 and extended to last to July 26, 2026. Currently there is a proposal to make this ruling permanent, but it has not been finalized. (https://www.federalregister.gov/d/2025-14022)

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