

## NPS Benzodiazepines

New Psychoactive Substances (NPS) are emerging drugs that are synthesized to mimic psychoactive substances that have been banned. The identification of NPS benzodiazepines in biological and drug samples has been increasing in recent years. Most have never undergone human testing and pose an unknown risk to the user. Some of the NPS benzodiazepines have recently been designated as DEA Schedule 1 drugs in the U.S. or controlled status is pending. NPS benzodiazepines are usually sold via the internet as research chemicals (powders or liquids) or as tablets that sometimes resemble traditional pharmaceutical benzodiazepine tablets. They are purchased and consumed for their sedative effect, to manage unwanted adverse effects from stimulant drugs, and to self-medicate when traditional benzodiazepines are unavailable. Like traditional benzodiazepines, they have a high risk of dependency and abuse.

The U.S. has seen increasing numbers of substances containing NPS benzodiazepines. For example, the number of substances analyzed by the DEA as containing etizolam increased from 3 in 2012 to 1,517 in 2020. ([DEA Etizolam, 2020](#); [NFLIS Snapshot Dec 2020](#); [Bollinger K. Forensic Sci Internat 2021;3:100138](#)) The Center for Forensic Science Research and Education (CFSRE) analyzes biological samples and seized materials to identify NPS. In their 2021 1<sup>st</sup> quarter Trend Report, 65% of all NPS identified were benzodiazepines compared to 45% in the same quarter of 2020. Of the 12 different NPS benzodiazepines detected, etizolam was the most prevalent followed by flualprazolam and clonazolam. Almost 85% of the positive samples were found in combination with other drugs, such as fentanyl, stimulants, and traditional benzodiazepines (e.g., alprazolam, diazepam). ([Trend Report: Q1 2021 NPS Benzodiazepines](#))

Benzodiazepines enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABA<sub>A</sub> receptor, resulting in sedative, hypnotic, anti-anxiety, anticonvulsant, and muscle relaxant effects. Overdoses are characterized by CNS depression ranging from drowsiness to coma. Respiratory depression is rare with benzodiazepines alone but may be seen in massive overdoses or when other drugs such as opioids are coingested. Hypotension, hypothermia, and rhabdomyolysis may occur with high doses. Case reports of NPS benzodiazepine overdoses thus far suggest poisoning is similar to traditional benzodiazepines; however, the effects that new NPS benzodiazepines might produce are unknown, and counterfeit drugs often contain other drugs that differ in toxic effects. In-hospital testing and identification is limited. Urine drug screens may not be positive for benzodiazepines in the presence of NPS since typical assays do not test for them.

Treatment is primarily supportive (e.g., assisted ventilation). Flumazenil, a competitive antagonist at the benzodiazepine site on the GABA<sub>A</sub> receptor, reverses CNS and respiratory depression. If NPS benzodiazepine toxicity is suspected based on history, flumazenil may be utilized in select patients who are at low risk for adverse effects from flumazenil. Call the poison center for help in assessing whether a patient can safely be given flumazenil. More information on flumazenil can be found at <http://bit.ly/FlumazAFS>.



Counterfeit alprazolam tablets containing flualprazolam

Source: DEA. 2020 National Drug Threat Assessment. March, 2021.

### Did you know?

There are at least 29 NPS benzodiazepines reported in 49 countries and territories.

Some include adinazolam, clonazolam, bromazolam, deschloroetizolam, diclazepam, etizolam, flualprazolam, flubromazepam, flubromazolam, phenazepam, and pyrazolam. This is according to the United Nations Office on Drugs and Crime (UNODC) Current NPS Threats report, October 2020. The UNODC also reported that 64% of NPS identified in toxicology cases from January 2019 to April 2020 were NPS benzodiazepines. ([UNDOC Current NPS threats Volume III, October 2020. Retrieved from https://www.unodc.org/documents/scientific/Current\\_NPS\\_Threats\\_Vol.3.pdf](#))

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