

BENZODIAZEPINES

(Street Names: Benzos, Downers, Nerve Pills, Tranks)

Introduction:

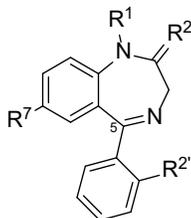
Benzodiazepines are a class of drugs that produce central nervous system (CNS) depression and are most commonly used to treat insomnia and anxiety. Benzodiazepines have the potential for dependence and abuse, particularly by individuals with a history of multi-substance abuse. The five benzodiazepines that are most commonly prescribed and encountered on the illicit market are Alprazolam (e.g., Xanax[®]), lorazepam (e.g., Ativan[®]), clonazepam (e.g., Klonopin[®]), diazepam (e.g., Valium[®]), and temazepam (e.g., Restoril[™]). In recent years, the trafficking and abuse of “novel designer benzodiazepines”—including clonazolam, diclazepam, flubromazolam, flualprazolam, etizolam, and bromazolam—has dramatically increased. Serious adverse effects associated with the use of such “novel designer benzodiazepines” have been documented and include CNS depression, loss of motor coordination, respiratory depression, memory loss, and blackouts.

Licit Uses:

Benzodiazepines are widely prescribed drugs. According to the IQVIA National Prescription Audit[™], total prescriptions dispensed in the United States in 2024 were approximately 30.5 million for alprazolam, 21.4 million for clonazepam, 19.8 million for lorazepam, 8.2 million for diazepam, and 3.8 million for temazepam. In the United States, benzodiazepines are prescribed for their sedative-hypnotic (e.g., temazepam, triazolam, flurazepam, estazolam), anti-anxiety (e.g., alprazolam, chlordiazepoxide, clorazepate, diazepam, lorazepam, oxazepam), muscle relaxant (e.g., diazepam), and anti-convulsant (e.g., diazepam, clonazepam) effects. Benzodiazepines are also used as an adjunct to anesthesia (e.g., midazolam) and for the treatment of alcohol withdrawal (e.g., chlordiazepoxide) and panic disorders (e.g., alprazolam, clonazepam). Most benzodiazepines are available as tablet and capsule preparations; several are also available as injectable preparations and syrup.

Chemistry:

All benzodiazepines are composed of a benzene ring fused to a seven-member diazepine ring. Most benzodiazepines also possess a phenyl ring attached at the 5-position of the diazepine ring. Small modifications of this basic structure account for the varied pharmacologic effects of these drugs.



Pharmacology:

Benzodiazepines produce CNS depression by enhancing the effects of the major inhibitory neurotransmitter gamma-aminobutyric acid, thereby decreasing brain activity. Benzodiazepines are classified by their duration of action, which ranges from less than 6 hours to more than 24 hours. Some benzodiazepines have active metabolites that prolong their effects.

Adverse effects include increased reaction time, motor incoordination, anterograde amnesia, slurred speech, restlessness, delirium, aggression, depression, hallucinations, and paranoia. Unlike barbiturates, large doses of benzodiazepines are rarely fatal unless combined with other CNS depressant drugs (e.g., alcohol, opioids). Adverse effects can be reversed by flumazenil administration (injection).

Tolerance often develops after long-term use, requiring larger doses to achieve the desired effect. Physical and psychological dependence may develop, whether taken under a doctor's orders or used illicitly. Withdrawal symptoms include anxiety, insomnia, dysphoria, tremors, and seizures. The severity of withdrawal symptoms is dependent on the dose, duration of use, and drug used. Withdrawal can be precipitated by flumazenil administration to individuals who are dependent on benzodiazepines.

Illicit Uses:

Benzodiazepines, particularly those with rapid onset, are abused to produce a euphoric effect. Abuse of benzodiazepines is often associated with multiple-substance abuse. Diazepam and alprazolam are used in combination with methadone to potentiate methadone's euphoric effect. Those who misuse cocaine or other stimulants may also use benzodiazepines to relieve side effects (e.g., irritability, agitation) associated with cocaine or stimulant binges. Benzodiazepines are also used to augment alcohol's effects and modulate withdrawal states. Those who misuse sedative hypnotics often use prescription benzodiazepines in excess of the recommended therapeutic dose. Additionally, benzodiazepines have long been associated with drug-facilitated sexual assault through the use of prescription medication (e.g., diazepam, temazepam, flunitrazepam). More recently, “novel designer benzodiazepines”—including flualprazolam, etizolam, clonazolam, flubromazolam, diclazepam, and bromazolam—have become increasingly popular, appearing in a significant number of driving under the influence of drug (DUID) cases, toxicology reports, and death investigations.

According to the United Nations Office on Drugs and Crime, benzodiazepine-type novel psychoactive substances (NPS) continue to constitute the greatest number of NPS reported to the Tox-Portal, accounting for 47% of all NPS cases associated with postmortem investigations and 67% of all DUID cases. In 2022, the American Association of Poison Control Centers reported 44,346 case mentions; 15,911 single exposures; and 13 deaths associated with benzodiazepines. Among these, 10,396 cases were intentional.

Illicit Distribution:

Individuals who abuse benzodiazepines obtain these substances by collecting prescriptions from several doctors, forging prescriptions, or buying diverted pharmaceutical products on the illicit market, which includes domestic and foreign products. One of the top three prescription drugs diverted from the licit market is alprazolam.

The Drug Enforcement Administration's National Forensic Laboratory Information System (NFLIS) Drug database collects scientifically verified data on drug items and cases submitted to and analyzed by participating federal, state, and local forensic drug laboratories. NFLIS-Drug received 12,218 alprazolam; 5,305 bromazolam; 4,393 clonazepam; 1,249 diazepam; 949 clonazolam; 788 lorazepam; 425 etizolam; 292 flualprazolam; 61 flubromazolam; and 53 temazepam reports in 2023.

Control Status:

Benzodiazepines are controlled in schedule IV of the Controlled Substances Act, with the exception of flualprazolam, etizolam, clonazolam, flubromazolam, and diclazepam, which are placed in schedule I. Flunitrazepam is unique among the benzodiazepines, which is a schedule IV substance with schedule I penalties.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 571-362-4250, Telephone 571-362-3249, or Email DPE@dea.gov.