

Benzodiazepines

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The **benzodiazepines** are one of the main substances tested for in treatment centers as a drug of abuse. They interact additively with other drugs both pharmaceutical and those of abuse. The combination of benzodiazepines and opiates, especially heroin, are often a cause of fatalities. They were reported as the largest group of recreationally used drugs in 1997¹, and remain one of the most abused.

The first benzodiazepine, chlordiazepoxide (Librium®), was discovered serendipitously in 1954 by the Austrian scientist Dr. Leo Sternbach (1908-2005), working for the pharmaceutical company Hoffmann-La Roche.² Initially, he discontinued his work on the compound *Ro-5-0690*, but he "rediscovered" it in 1957 when an assistant was cleaning up the laboratory. Although initially discouraged by his employer, Sternbach conducted further research that revealed the compound was a very effective tranquilizer.

They began to be widely prescribed for stress-related ailments in the 1960s and 1970s. In 1963 approval for use was given to diazepam (Valium) - a simplified version of Librium - primarily to counteract anxiety symptoms. Nitrazepam (Mogadon) was introduced in 1965 and flurazepam (Dalmane) in 1973 to

assist in addressing sleep related problems.

Mechanism of Action

They are believed to act on the GABA receptor GABA_A, the activation of which dampens higher neuronal activity by stimulating inhibitory neurons.

Classifications

Benzodiazepines are commonly divided into three groups: **Short-acting compounds** act for less than six hours and have few residual effects if taken before bedtime, but rebound insomnia may occur and they might cause wake-time anxiety. **Intermediate-acting compounds** have an effect for 6-10 hours, may have mild residual effects but rebound insomnia is not common. **Long-acting compounds** have strong sedative effects that persist. Accumulation may occur.

The various benzodiazepines listed are in order of the shortest acting to the longest acting (by the approximate elimination half-life of the drug), however this time may greatly vary between persons.

- triazolam (Halcion®) - 2 hours
- midazolam (Versed®, Hypnovel®) - 2-6 hours

- oxazepam (Serax®) - 4-15 hours
- chlordiazepoxide (Librium®) - 5-25 hours
- alprazolam (Xanax®) - 6-12 hours
- temazepam (Restoril®) 8-20 hours
- lorazepam (Ativan®) 10-20 hours
- bromazepam (Lexotan®) 10-20 hours
- estazolam (ProSom®) 10-24 hours
- lunitrazepam (Rohypnol®) 18-26 hours. (Withdrawn from the market in some countries; considered a "date-rape drug")
- clonazepam (Klonopin®, Rivotril®) 18-50 hours
- nitrazepam (Mogadon®) 20-40 hours
- quazepam (Doral®) 25-100 hours
- clorazepate (Tranxene®) 36-100 hours
- medazepam (Nobrium®) 36-150 hours
- razepam (Centrax®) 36-200 hours
- diazepam (Valium®) 36-200 hours
- flurazepam (Dalmane®) 40-250 hours

The following are not benzodiazepines, but have similar effects:

- zolpidem (Ambien®)
- zaleplon (Sonata®)
- meprobamate (Miltown®)

Part 2 of this article will appear in the December issue of Toxicology Times.

??? Did You Know ???

SAMHSA has delineated four major dimensions that support a life in recovery:

- **Health**—overcoming or managing one's disease(s) or symptoms—for example, abstaining from use of alcohol, illicit drugs, and non-prescribed medications if one has an addiction problem—and, for everyone in recovery, making informed, healthy choices that support physical and emotional well-being
 - **Home**—having a stable and safe place to live
 - **Purpose**—conducting meaningful daily activities, such as a job, school volunteerism, family caretaking, or creative endeavors, and the independence, income, and resources to participate in society
 - **Community**—having relationships and social networks that provide support, friendship, love, and hope
- Source: SAMHSA

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Question of the Month

Question: My patient is prescribed Ultram – will that show as an Opiate on a drug screen?

Answer: No, it will not be detected with the regular Opiate drug screen. Ultram (Tramadol) has Opiate like activity (mu receptor) and is used for mild pain management, but is not actually an Opiate. There is a specific screening test for Tramadol (much like Oxycodone) that can be performed upon request.