

Benzodiazepines Drug Information

Classification

The benzodiazepines are a class of drugs primarily classified as anti-anxiety, sedatives, or hypnotics. All contain a benzene ring fused to a 7-membered diazepine ring, hence the term benzodiazepine. Various modifications and substitutions of the ring structure yield compounds of similar activities. The clinical effects of these drugs result from actions on the central nervous system and these effects include sedation, hypnosis, muscle relaxation, and anticonvulsant activity.

Metabolism

The benzodiazepines are well absorbed after oral administration and are rapidly distributed throughout the body. They are extensively metabolized by the liver, and in general, slowly excreted in the urine as pharmacologically inactive conjugated metabolites. Some metabolites may possess some pharmacological activity of their own, thus displaying the "next day" effects of some benzodiazepines. Oxazepam is a common urinary metabolite of several benzodiazepines such as diazepam and temazepam. Duration of detectability in urine is varied. Ingestion of therapeutic dosages may be detectable for 1-3 days while extended usage over a period of months or years can extend excretion times up to 4-6 weeks after cessation of use (depends on dosage & benzodiazepine)

Abuse

The benzodiazepines are considered one of the most widely prescribed drugs in the United States, thus leading to its widespread abuse. Diazepam (Valium®) and alprazolam (Xanax®) are two of the most widely abused of the benzodiazepines. Many abusers will attempt to accentuate the effects of benzodiazepines by the concomitant use of alcohol or other CNS depressant drugs. As a result, benzodiazepines are involved in approximately one third of all drug self induced poisonings. Other commonly abused benzodiazepines are chlordiazepoxide, flurazepam, clonazepam, and lorazepam. Prolonged high doses of benzodiazepines can cause dependency and a withdrawal syndrome may occur following abrupt cessation of use.

Chemical Name	Trade Name
Alprazolam	Xanax®
Chlordiazepoxide	Librium®
Clonazepam	Klonopin®
Clorazepate	Tranxene
Diazepam	Valium®
Flunitrazepam	Rohypnol®

Chemical Name	Trade Name
Flurazepam	Dalmane®
Lorazepam	Ativan®
Midazolam	Versed®
Oxazepam	Serax®
Prazepam	Centrax®
Temazepam	Restoril®
Triazolam	Halcion®

Laboratory drug testing: Methods of Analysis

There are many problems associated with a comprehensive approach to the analysis of the benzodiazepines. The benzodiazepines are a very diverse and complex group of compounds which are extensively metabolized in urine. For this reason, it is not always possible to determine the parent drug with urine testing. In addition, dosage levels and half-life varies substantially between the benzodiazepines affecting the ability to detect therapeutic use of some benzodiazepines. Therefore, the analytical detection limits may preclude the detection of therapeutic use.

The most common analytical methods to screen for the presence of benzodiazepines in urine are the immunoassay methods such as enzyme immunoassay (EIA). The immunoassay methods are class specific in that they detect oxazepam, a common metabolite of many benzodiazepines. However, many other structurally similar benzodiazepines may also be detected.

While immunoassay cross-reactivity to non-benzodiazepine compounds is extremely rare, most immunoassay manufacturers recommend that positive results be confirmed by alternate specific analytical method such as gas chromatography/mass spectrometry (GC/MS) or liquid chromatography/tandem mass spectrometry (LC/MS/MS). Most routine confirmation methods are targeted to detect the group of benzodiazepines which share a common metabolic pathway and metabolize to nordiazepam and oxazepam thus making these methods class specific. However, common benzodiazepines such as alprazolam (Xanax®), lorazepam (Ativan®), and clonazepam (Klonopin®) do not share this metabolic pathway and must be confirmed by specific techniques, such as GC/MS or LC/MS/MS. It is essential to understand the advantages and limitations of the various laboratory analytical methods to ensure proper detection of benzodiazepines. If a case history indicates the use of a particular benzodiazepine, then a method must be chosen which will have the necessary sensitivity and specificity to identify the drug of interest.

