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Directory of Toxicology

Toxicology Topics

Benzodiazepines

Benzodiazepines belong to a broad classification of CNS (central nervous system) depressant drugs known as sedatives/hypnotics. They are prescribed as anxiolytic, sleeping agents, anticonvulsants, and muscle relaxers, and have a high potential for abuse. For this reason, some employers include benzodiazepines in their employment drug-screening procedures. One of the major problems with testing for benzodiazepines is the variety of benzodiazepine class drugs that are available.

The initial testing procedure is intended to provide a qualitative assay of benzodiazepines in urine using nitrazepam as the primary calibrator with a cutoff level of 300 ng/mL. Benzodiazepines may be detected at these levels for up to 10 days following the last use of the medication. This assay will react with over 20 different benzodiazepine products currently available including alprazolam (Xanax®), bromazepam, chlordiazepoxide (Librium®), clonazepam (Clonopin®) cloazepate (Tranxene®), diazepam (Valium®), flunitrazepam, flurazepam, lorazepam (Ativan®), nitrazepam, oxazepam (Serax®), and temazepam (Restoril®).

Specimens that have an initial positive immunoassay test for benzodiazepines are then subjected to confirmation testing by solid phase extraction and analysis of the extract by GC/MS. The confirmation procedure is designed to look for the primary metabolites of the most common benzodiazepines, nordiazepam, temazepam and oxazepam. One or more of these benzodiazepine metabolites can be detected following the ingestion of a variety of benzodiazepines, including chlordiazepoxide (Librium®), cloazepate (Tranxene®), diazepam (Valium®), halazepam (Paxipam®), prazepam (Centrax®) and temazepam (Restoril®).

Specimens containing benzodiazepines which do not yield the metabolites that are assayed will fail to confirm for the presence of those specific benzodiazepines even when those benzodiazepines may be present. For example, a donor who has been taking Ativan® may screen positive for benzodiazepines, but will fail to confirm because lorazepam does not metabolize to form any of the targeted metabolites.

In cases where there is interest in a specific benzodiazepine a targeted assay may be performed but typically is more costly and may require referral of the specimen to another laboratory.

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Which Benzodiazepines do we test for?

Currently we have confirmation procedures for Oxazepam, Temazepam Nordiazepam and Alprazolam (α –hydroxyalprazolam). The following drugs may produce one or more of the 4 metabolites that we currently test for by GC/MS

1. Temazepam (methyloxazepam, Normison, Temaz, Razepam, Restoril)
May causes sedation and drowsiness in normal doses.
2. Prazepam (Centrax, Verstran)
Anxiolytic agent
3. Oxazepam (Serax)
Anxiolytic agent less potent than valium(Diazepam)
4. Medazepam (Nobrium)
Anxiolytic agent and precursor to Diazepam
5. Halazepam (Paxipam)
Short term anxiolytic agent
6. Diazepam (Valium, Valrelease, Vazepam)
Anxiolytic agent, muscle relaxant or anticonvulsant
7. Clorazepate (Tranxene, Gen-XENE)
Same as diazepam
8. Chlordiazepoxide (Librium, Libritabs, Sereen)
Sedative-hypnotic drug, used as anxiolytic agent
9. Alprazolam (Xanax)
Short acting antidepressant and anxiolytic agent effectively used in treating panic attacks and panic disorders

Table one is a list of the 4 metabolites confirmed by GC/MS and a list of drugs that break down into these metabolites and the % that is broken down into the metabolite.

Nordiazepam	Oxazepam	Temazepam	α-Hydroxyalprazolam
	Prazepam 59%		Alprazolam 17%
	Oxazepam 61%		
	Medazepam 55%		
Halazepam 2%	Halazepam 10%		
Diazepam 10%	Diazepam 33%	Diazepam 10%	
Clorazepate 1%	Clorazepate 80%		
	Temazepam 7%	Temazepam 73%	
	Chlordiazepoxide 97%		

Drugs that do not metabolize into the groups tested for at DLI but may result in a positive immunoassay screen

1. Triazolam (Halcion)
2. Tetrazepam (Megavix, Musaril, Myolastan, Panos)
3. Quazepam (Doral)
4. Nitazepam (Mogadon)
5. Lorazepam (Ativan)
6. Loprazolam (Dormonox, Somnovit)
7. Flurazepam (Dalmane)
8. Estazolam (Prosom)
9. Clonazepam (Clonopin, Klonopin, Rivotril)
10. Bromazepam (Lectopam, Lexotan, Ro5-3350)