Diagnostic Automation / Cortez Diagnostics, Inc.
IMMUNO DIAGNOSTICS

CE

OneStep Benzodiazepines Urine RapiDip™ InstaTest

REF 121063-1-19

IVD See external Label 15-30°C ∑=1 Test

For medical and other professional in vitro diagnostic use only.

INTENDED USE

OneStep Benzodiazepines Urine RapiDip™ InstaTest is a qualitative immunoassay intended to provide qualitative screening results for benzodiazepine abuse by detecting oxazepam in human urine at a cutoff concentration of 300ng/ml (oxazepam). It is for health care professional use only.

This assay provides only a preliminary result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography / Mass Spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are obtained.

SUMMARY AND EXPLANATION OF THE TEST

Benzodiazepines, including Alprazolam, Diazepam, Lorazepam, Triazolam, Chlordiazepoxide, Flurazepam and Temazepam are sedative, hypnotic and anti-anxiety drugs commonly being used as oral tranquilizers. Most benzodiazepine are extensively metabolized in the liver and excreted in the urine as metabolites. Benzodiazepines have a low potential for physical or psychological dependence. However, the same as other central nervous system stimulating drugs, they may induce drowsiness and muscle relaxation. Chronic abuse of benzodiazepine may result in intoxication, similar to drunken behavior. Overdose and extended usage of benzodiazepine may lead to coma and possibly death. Benzodiazepines may remain effective for 4-8 hours. The members of the Benzodiazepine family are absorbed at different rates and their effects may vary with the absorption rate. They are excreted in the urine primarily as their parent compounds or an inactive metabolite, oxazepam glucuronide, that are only detectable for one (1) to two (2) days. Oxazepam, a common metabolite of many benzodiazepine, is also a marketed drug (Serax); It may remain detectable in urine for up to one week. That makes oxazepam a useful marker of benzodiazepine abuse.

TEST PRINCIPLE

This assay is a one-step lateral flow chromatographic immunoassay. The test strip includes 1) a burgundy-colored conjugate pad containing mouse anti-oxazepam antibodies coupled to colloidal gold; and 2) nitrocellulose membrane containing a Test (T) line and a Control (C) line. The Test line is coated with benzodiazepines-BSA, and the Control line is coated with goat anti-rabbit IgG antibody.

This test is a competitive binding immunoassay. The oxazepam in the urine specimen competes with the benzodiazepines–BSA antigen coated on the nitrocellulose membrane for the limited binding sites of the conjugated anti-oxazepam antibodies.

When an adequate amount of urine specimen is applied to the sample pad of the device, the urine specimen migrates by capillary action through the test strip. If the level of oxazepam in the urine specimen is below the cutoff (300 ng/ml), the Test line appears as a visible burgundy line. If the level of oxazepam in the urine specimen is at or above the cutoff, no Test line develops.

The C line binds to the gold-conjugated rabbit IgG and forms a burgundy color line, regardless of the presence of oxazepam.

SPECIMEN COLLECTION AND PREPARATION

1. Each urine specimen must be collected in a clean container. Do not mix specimens
2. Specimens may be kept at 15-30°C (59-86°F) for 8 hours, at 2-8°C for up to 3 days and at -20°C or lower for long term storage.

MATERIALS AND COMPONENTS

Materials provided with the test kits

- 50 test strips each sealed in a pouch with desiccant.
- 1 package insert (Instructions for Use).

Materials required but not provided

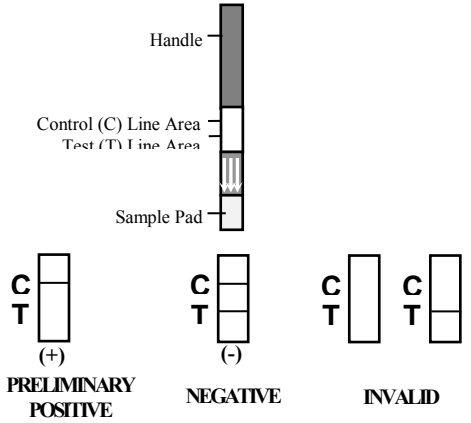
- Specimen collection containers
- Timer

ASSAY PROCEDURE

1. Refrigerated specimens and other test materials, including devices, **must be equilibrated to room temperature before testing**.
2. Open the foil pouch at the notch and remove the test device.
3. Dip the device in the specimen for at least 10 seconds. Keep the specimen surface at the level indicated by the arrow sign on the device.
4. Remove the device from the specimen, and place it on a flat, dry surface.
5. Read the test result between four (4) to seven (7) minutes after adding the specimen.

RESULTS

***IMPORTANT*: Do not read test results after seven (7) minutes. The T Line should always be interpreted independently of the C Line.**



Positive:
If only the C line appears, the test indicates that the oxazepam level in the sample is at a cutoff of 300 ng/ml or higher.
Samples with preliminary positive results should be confirmed with a more specific method before a positive conclusion is made.

Negative:
If both the C line and T line appear, the test indicates that the oxazepam level is below 300 ng/ml.
Note: A faint T line should be considered negative.

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Invalid:
If no C line develops within 5 minutes, repeat the assay with a new test device.

PERFORMANCE CHARACTERISTICS

1. Accuracy

A study was performed at three different Physician's Office Laboratories (POL) and a Reference Laboratory. One hundred (100) clinical samples were blind labeled and tested. Each sample was tested at each site, and compared with GC/MS results.

The results agreed 100% with the GC/MS data of specimens at levels below 75% of the cutoff (negative) and above the cutoff (positive). Seven (7) discrepancies were observed on the specimens at the level between 75% of the cutoff and the cutoff.

The overall agreement was 98.3%.

		Benzodiazepines RapiDip™ InstaTest		Total	Agreement
		Positive	Negative		
GC/MS (ng/ml)	Drug-free	0	168	168	100%
	<75% (0~225)	0	24	24	100%
	75%~Cutoff (225~300)	7	25	32	78%
	Cutoff~125% (300~375)	32	0	32	100%
	Positive (>375)	144	0	144	100%
Total		183	217	400	98.3%

2. Precision

The precision was determined by replicate assays of four different levels of samples with three different production lots. The device was tested for five consecutive days five times each, for a total of 25 assays for each control.

The results indicate 100 % precision for the replicate within each lot and no appreciable interlot variation occurred across the three (3) different lots of devices.

3. Cross-Reactivity

To determine the cross-reactivity of the structurally related compounds with the device, the following compounds were spiked into known drug-free urine pools and tested. Those compounds showed a positive response at the concentration indicated in the following table:

Description	Concentration (ng/ml)
Alprazolam	*300*
Bromazepam	*500*
Clobazem	*1500*
Chlonazepam	*500*
Diazepam	*200*
Desmethyldiazepam	*300*
Flurazapam	*300*
Lorazepam	*450*
Lormetazepam	*300*
Medazepam	*300*
Nitrazepam	*250*
Nordiazepam	*400*
Prazepam	*250*
Triazolam	*300*
Oxazepam	*300*

4. Interference

To determine the interference of structurally unrelated analytes, the following analytes were spiked into known drug-free urine pools, as well as the oxazepam positive (spiked with oxazepam to the level of 300 ng/ml) urine pools and were tested. No significant interference with either negative or positive results was observed at the concentrations listed below:

Compounds listed in this table found not to interfere with the test results at the concentration of 1mg/ml:	
Acetaminophen	*Dextromethorphan*
Acetylsalicylic Acid	*Ethanol*
Amikacin	*Lidocaine*
Amitriptyline	*Methadone*
Ampicillin	*Methanol*
Arterenal	*Oxalic Acid*
Aspirin	*Penicillin-G (Benzylpenicillin)*
Atropine	*Phenylpropanalamine*
Benzoic Acid	*Ranitidine*
Caffeine	*Salicyclic Acid*
(+)-Chlorpheniramine	*Thioridazine*
Codeine	*Trifluoperazine*
Cortisone	

Biological Analytes	Concentration
Albumin	*2 mg/ml*
Bilirubin	*1 mg/ml*
Creatine	*1 mg/ml*
Hemoglobin	*1 mg/ml*
Glucose	*2 mg/ml*
pH	*5.0 – 9.0*
Vitamin C (L-Ascorbic Acid)	*1 mg/ml*
Uric Acid	*1 mg/ml*

There is a possibility that other substances and/or factors not listed may interfere with the test and cause false results.

STORAGE

Store the kit at room temperature 15-30°C (59-86°F). Each device may be used until the expiration date printed on the label if it remains sealed in its foil pouch containing desiccant.

Do not freeze and/or expose the kit to temperatures over 30°C (86°F). 15°C 30°C

QUALITY CONTROL

- **Built-in Control Features**
  OneStep Benzodiazepines Urine RapiDip™ InstaTestThis test contains a built-in control feature, the C line. The presence of the C line indicates that an adequate sample volume was used and that the reagents migrated properly. If a C line does not form, the test is considered invalid. In this case, review the whole procedure and repeat the testing with a new device.

- **External Quality Control**
  Users should always follow the appropriate federal, state, and local guidelines concerning the running of external quality controls. SAMHSA[3] recommends that the concentration of drug(s) in positive and negative controls be approximately 25% above and below the cutoff concentration of the assay.

LIMITATIONS OF PROCEDURE

1. OneStep Benzodiazepines Urine RapiDip™ InstaTest is for *professional in vitro* diagnostic use only.
2. Results obtained by this device provide only a preliminary qualitative result. A more specific alternate chemical method must be used in order to obtain a confirmed result.
3. This product is designed for testing human urine only.
4. Adulterants such as bleach or other strong oxidizing agents may produce erroneous test results if present in the sample. When suspected, collect a fresh specimen and repeat the test with a new device.
5. Samples in which bacterial contamination is suspected should not be used. These samples may interfere with the test and cause false results.

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EXPECTED VALUES

OneStep Benzodiazepines Urine RapiDip™ InstaTest is designed to detect oxazepam in human urine at a cutoff concentration of 300ng/ml.

PRECAUTION

1. The instructions must be followed exactly to obtain accurate results.
2. Do not open the sealed pouch, unless ready to conduct the assay.
3. Do not use expired devices.
4. Dispose of all specimens and used assay materials in as potentially biohazardous.

REFERENCE

1. FDA Guidance for Labeling Urine Drugs of Abuse Screening Testing, Kshit Mohan, 7/21/87.
2. Urine Testing for Drugs of Abuse. National Institute on Drug Abuse (NIDA): Research Monograph 73, 1986.
3. Baselt, R.C. Disposition of Toxic Drugs and Chemicals in Man, 4th ED., Biomedical Publ., Davis, CA; p569-570, 1995.
4. Department of Health and Human Services, Mandatory Guidelines for Federal Workplace Drug Testing Programs, Fed. Register. 53 (69): 11970 (1988).
5. Wilson, John, Abused Drugs II, a Laboratory Pocket Guide., AACC Press. Washington, DC; 1994.

ISO 13485
ISO 9001

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