

# SureStep™ BZO

## One Step Benzodiazepines Test Device (Urine) Package Insert English

A rapid, one step test for the qualitative detection of Benzodiazepines in human urine. For medical and other professional *in vitro* diagnostic use only.

### INTENDED USE

The BZO One Step Benzodiazepines Test Device (Urine) is a lateral flow chromatographic immunoassay for the detection of Oxazepam (major metabolite) in urine at a cut-off concentration of 300 ng/mL. This test will detect other related compounds, please refer to the Analytical Specificity table in this package insert.

This assay provides only a qualitative, preliminary analytical test 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 used.

### SUMMARY

Benzodiazepines are medications that are frequently prescribed for the symptomatic treatment of anxiety and sleep disorders. They produce their effects via specific receptors involving a neurochemical called gamma aminobutyric acid (GABA). Because they are safer and more effective, Benzodiazepines have replaced Barbiturates in the treatment of both anxiety and insomnia. Benzodiazepines are also used as sedatives before some surgical and medical procedures, and for the treatment of seizure disorders and alcohol withdrawal.

Risk of physical dependence increases if Benzodiazepines are taken regularly (e.g., daily) for more than a few months, especially at higher than normal doses. Stopping abruptly can bring on such symptoms as trouble sleeping, gastrointestinal upset, feeling unwell, loss of appetite, sweating, trembling, weakness, anxiety and changes in perception. Only trace amounts (less than 1%) of most Benzodiazepines are excreted unaltered in the urine; most of the concentration in urine is conjugated drug. The detection period for the Benzodiazepines in the urine is 3-7 days.

The BZO One Step Benzodiazepines Test Device (Urine) is a rapid urine-screening test that can be performed without the use of an instrument. The test utilizes the antibody to selectively detect elevated levels of Benzodiazepines in urine. The BZO One Step Benzodiazepines Test Device (Urine) yields a positive result when the Benzodiazepines in urine exceeds the cut-off level.

### PRINCIPLE

The BZO One Step Benzodiazepines Test Device (Urine) is an immunoassay based on the principle of competitive binding. Drugs that may be present in the urine specimen compete against the drug conjugate for binding sites on the antibody.

During testing, a urine specimen migrates upward by capillary action. Benzodiazepines, if present in the urine specimen below the cut-off level, will not saturate the binding sites of the antibody in the test. The antibody coated particles will then be captured by immobilized Benzodiazepines-protein conjugate and a visible colored line will show up in the test line region. The colored line will not form in the test line region if the Benzodiazepines level exceeds the cut-off level, because it will saturate all the binding sites of anti-Benzodiazepines antibody.

A drug-positive urine specimen will not generate a colored line in the test line region because of drug competition, while a drug-negative urine specimen or a specimen containing a drug concentration less than the cut-off will generate a line in the test line region. To serve as a procedural control, a colored line will always appear at the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

### REAGENTS

The test contains mouse monoclonal anti-Benzodiazepines antibody coupled particles and Benzodiazepines-protein conjugate. A goat antibody is employed in the control line system.

### PRECAUTIONS

- For medical and other professional *in vitro* diagnostic use only. Do not use after the expiration date.
- The test should remain in the sealed pouch until use.
- All specimens should be considered potentially hazardous and handled in the same manner as an infectious agent.
- The used test should be discarded according to local regulations.

### STORAGE AND STABILITY

Store as packaged in the sealed pouch either at room temperature or refrigerated (2-30°C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

### SPECIMEN COLLECTION AND PREPARATION

#### Urine Assay

The urine specimen must be collected in a clean and dry container. Urine collected at any time of the day may be used. Urine specimens exhibiting visible particles should be centrifuged, filtered, or allowed to settle to obtain a clear specimen for testing.

#### Specimen Storage

Urine specimens may be stored at 2-8°C for up to 48 hours prior to testing. For long-term storage, specimens may be frozen and stored below -20°C. Frozen specimens should be thawed and mixed before testing.

### MATERIALS

#### Materials Provided

- Test devices
- Droppers
- Package insert

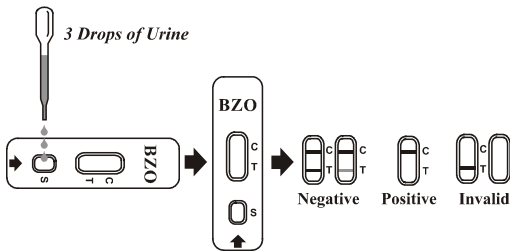
#### Materials Required But Not Provided

- Specimen collection container
- Timer

### DIRECTIONS FOR USE

Allow the test, urine specimen and/or controls to reach room temperature (15-30°C) prior to testing.

- Bring the pouch to room temperature before opening it. Remove the test device from the sealed pouch and use it as soon as possible.
- Place the test device on a clean and level surface. Hold the dropper vertically and transfer 3 full drops of urine (approx. 100 µL) to the specimen well (S) of the test device, and then start the timer. Avoid trapping air bubbles in the specimen well (S). See the illustration below.
- Wait for the colored line(s) to appear. Read results at 5 minutes. Do not interpret the result after 10 minutes.



### INTERPRETATION OF RESULTS

(Please refer to illustration above)

**NEGATIVE:** \* Two lines appear. One colored line should be in the control line region (C), and another apparent colored line should be in the test line region (T). This negative result indicates that the Benzodiazepine concentration is below the detectable cut-off level.

\*NOTE: The shade of color in the test line region (T) may vary, but it should be considered negative whenever there is even a faint colored line.

**POSITIVE:** One colored line appears in the control line region (C). No line appears in the test line region (T). This positive result indicates that the Benzodiazepine concentration exceeds the detectable cut-off level.

**INVALID:** Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

### QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control line region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique. Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as good laboratory testing practice to confirm the test procedure and to verify proper test performance.

### LIMITATIONS

- The BZO One Step Benzodiazepines Test Device (Urine) provides only a qualitative, preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method.
- It is possible that technical or procedural errors, as well as other interfering substances in the urine specimen may cause erroneous results.
- Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results regardless of the analytical method used. If adulteration is suspected, the test should be repeated with another urine specimen.
- A positive result indicates presence of the drug or its metabolites but does not indicate level of intoxication, administration route or concentration in urine.
- A negative result may not necessarily indicate drug-free urine. Negative results can be obtained when drug is present but below the cut-off level of the test.
- Test does not distinguish between drugs of abuse and certain medications.

### PERFORMANCE CHARACTERISTICS

#### Accuracy

A side-by-side comparison was conducted using the BZO One Step Benzodiazepines Test Device (Urine) and a leading commercially available BZO rapid test. Testing was performed on 298 clinical specimens previously collected from subjects present for Drug Screen Testing. Ten percent of the specimens employed were either at -25% or +25% level of the cut-off concentration of 300 ng/mL Oxazepam. Presumptive positive results were confirmed by GC/MS. The following results were tabulated:

Method	Other BZO Rapid Test		Total Results
	Positive	Negative	
BZO One Step Test Device	Positive	130	135
	Negative	14	163
<b>Total Results</b>	<b>144</b>	<b>154</b>	<b>298</b>
<b>% Agreement</b>	<b>90%</b>	<b>97%</b>	<b>94%</b>

When compared to GC/MS at the cut-off of 300 ng/mL, the following results were tabulated:

Method	GC/MS		Total Results
	Positive	Negative	
BZO One Step Test Device	Positive	130	136
	Negative	5	164
<b>Total Results</b>	<b>135</b>	<b>165</b>	<b>300</b>
<b>% Agreement</b>	<b>96%</b>	<b>96%</b>	<b>96%</b>

#### Analytical Sensitivity

A drug-free urine pool was spiked with Oxazepam at the following concentrations: 0 ng/mL, 150 ng/mL, 225 ng/mL, 300 ng/mL, 375 ng/mL and 450 ng/mL. The result demonstrates >99% accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Oxazepam Concentration (ng/mL)	Percent of Cut-off	n	Visual Result	
			Negative	Positive
0	0	30	30	0
150	-50%	30	30	0
225	-25%	30	26	4
300	Cut-off	30	12	18
375	+25%	30	3	27
450	+50%	30	0	30

#### Analytical Specificity

The following table lists compounds that are positively detected in urine by the BZO One Step Benzodiazepines Test Device (Urine) at 5 minutes.

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Alprazolam	196	Estazolam	2,500
a-hydroxylprazolam	1,262	Flunitrazepam	390
Bromazepam	1,562	(±) Lorazepam	1,562
Chlordiazepoxide	1,562	RS-Lorazepam glucuronide	156
Clobazam	98	Midazolam	12,500
Clonazepam	781	Nitrazepam	98
Clorazepate dipotassium	195	Norchlordiazepoxide	195
Delorazepam	1,562	Nordiazepam	390
Desalkylflurazepam	390	Oxazepam	300
Diazepam	195	Tetrazepam	98
		Triazolam	2,500

### Precision

A study was conducted at three physicians' offices by untrained operators using three different lots of product to demonstrate the within run, between run and between operator precision. An identical panel of coded specimens containing, according to GC/MS, no Oxazepam, 25% Oxazepam above and below the cut-off and 50% Oxazepam above and below the 300 ng/mL cut-off was provided to each site. The following results were tabulated:

Oxazepam Concentration (ng/mL)	n per Site	Site A		Site B		Site C	
		-	+	-	+	-	+
0	15	15	0	15	0	15	0
150	15	14	1	14	1	15	0
225	15	11	4	14	1	14	1
375	15	0	15	1	14	3	12
450	15	0	15	0	15	0	15

### Effect of Urinary Specific Gravity

Fifteen urine specimens of normal, high, and low specific gravity ranges were spiked with 150 ng/mL and 450 ng/mL of Oxazepam. The BZO One Step Benzodiazepines Test Device (Urine) was tested in duplicate using the fifteen neat and spiked urine specimens. The results demonstrate that varying ranges of urinary specific gravity do not affect the test results.

### Effect of Urinary pH

The pH of an aliquoted negative urine pool was adjusted to a pH range of 5 to 9 in 1 pH unit increments and spiked with Oxazepam to 150 ng/mL and 450 ng/mL. The spiked, pH-adjusted urine was tested with the BZO One Step Benzodiazepines Test Device (Urine) in duplicate. The results demonstrate that varying ranges of pH do not interfere with the performance of the test.

### Cross-Reactivity

A study was conducted to determine the cross-reactivity of the test with compounds in either drug-free urine or Oxazepam positive urine. The following compounds show no cross-reactivity when tested with the BZO One Step Benzodiazepines Test Device (Urine) at a concentration of 100 µg/mL.

### Non Cross-Reacting Compounds

Acetaminophen	Deoxycorticosterone	MDE	β-Phenylethylamine
Acetophenetidin	Dextromethorphan	Meperidine	Phenylpropanolamine
N-Acetylprocainamide	Diclofenac	Meprobamate	Prednisolone
Acetylsalicylic acid	Diffunilal	Methadone	Prednisone
Aminopyrine	Digoxin	L-Methamphetamine	Procaine
Amitypyline	Diphenhydramine	Methoxyphenamine	Promazine
Amobarbital	Doxylamine	(±) - 3,4-Methylenedioxy-amphetamine	Promethazine
Amoxicillin	Egonine	(±) - 3,4-Methylenedioxy-methamphetamine	D,L-Propranolol
Ampicillin	Egonine methylester	(±) - 3,4-Methylenedioxy-methamphetamine	D-Propoxyphene
L-Ascorbic acid	(-) - ψ - Ephedrine		D-Pseudoephedrine
D,L-Amphetamine sulfate	[1R,2S] (-) Ephedrine	Morphine-3-β-D glucuronide	Quinacrine
D,L-Amphetamine	(L) - Ephedrine	Morphine sulfate	Quinidine
Aspartame	Erythromycin	Nalidixic acid	Quinine
Atropine	β-Estradiol	Naloxone	Ranitidine
Benzilic acid	Estrore-3-sulfate	Naltrexone	Salicicylic acid
Benzoic acid	Ethyl-p-aminobenzoate	Naproxen	Secobarbital
Benzoylcegonine	Fenoprofen	Niacinamide	Serotonin
Benzphetamine	Furazemide	Nifedipine	Sulfamethazine
Bilirubin	Genistic acid	Norcocaine	Sulindac
(±) - Brompheniramine	Hemoglobin	Norethindrone	Tetracycline
Caffeine	Hydralazine	D-Norpropoxyphene	Tetrahydrocortisone
Cannabidiol	Hydrochlorothiazide	Noscapine	3-Acetate
Cannabinal	Hydrocodone	D,L-Octopamine	Tetrahydrocortisone
Chloralhydrate	Hydrocortisone	Oxalic acid	3-(β-D-glucuronide)
Chloramphenicol	O-Hydroxyhippuric acid	Oxolinic acid	Tetrahydrozoline
Chlorothiazide	p-Hydroxyamphetamine	Oxydometin	Thiamine
(±) - Chlorpheniramine	p-Hydroxy-methamphetamine	Oxymetazoline	Thioridazine
Chlorpromazine	methamphetamine	Papaverine	D,L-Tyrosine
Chlorquine	3-Hydroxytyramine	Penicillin-G	Tolbutamide
Cholesterol	Ibuprofen	Pentazocine	Triamterene
Clomipramine	Imipramine	Perphenazine	Trifluoperazine
Clonidine	Iproniazid	Perphenazine	Trimethoprim
Cocaine	(±) - Isoproterenol	Phenacyclidine	Trimipramine
Cocaine	Isosuprine	Phenelzine	Tryptamine
Cocaine	Ketamine	Phenobarbital	D,L-Tryptophan
Cortisone	Ketoprofen	Phentermine	Tyramine
(+) Cotinine	Labeltol	Trans-2-phenylcyclo-propylamine hydrochloride	Uric acid
Creatinine	Loperamide	L-Phenylephrine	Verapamil
	Maprotiline		Zomepirac

### BIBLIOGRAPHY

- Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*. 2nd Ed. Biomedical Publ., Davis, CA. 1982; 488
- Hawks RL, CN Chiang. *Urine Testing for Drugs of Abuse*. National Institute for Drug Abuse (NIDA), Research Monograph 73, 1986

### Index of Symbols

	Attention, see instructions for use		Tests per kit		Authorized Representative
	For <i>in vitro</i> diagnostic use only		Use by		Do not reuse
	Store between 2-30°C		Lot Number		Catalog #

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