ZOP Rapid Test Dipstick (Urine)
Package Insert

REF DZOP-101	English

A rapid test for the qualitative detection of Zopiclone in human urine
For medical and other professional in vitro diagnostic use only

【INTENDED USE】

The ZOP Rapid Test Dipstick (Urine) is a rapid chromatographic immunoassay for the detection of Zopiclone in urine at a cut-off concentration of 50ng/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】

Zopiclone is a nonbenzodiazepine hypnotic agent used in the treatment of insomnia. It is a cyclopyrrolone, which increases the normal transmission of the neurotransmitter gamma-aminobutyric acid in the central nervous system, as benzodiazepines do, but in a different way. Zopiclone is indicated for the short-term treatment of insomnia where sleep initiation or sleep maintenance are prominent symptoms. Long-term use is not recommended, as tolerance, dependence, and addiction can occur with prolonged use. Zopiclone is partly extensively metabolized in the liver to form an active N-demethylated derivative (N-desmethylzopiclone) and an inactive zopiclone-N-oxide.

In urine, the N-demethyl and N-oxide metabolites account for 30% of the initial dose. Between 7 and 10% of zopiclone is recovered from the urine, indicating extensive metabolism of the drug before excretion. The terminal elimination half-life of zopiclone ranges from 3.5 to 6.5 hours (5 hours on average).[1] Time to peak plasma concentration is 1 - 2 h, the absorption rate constant is 1.3 h-1 and maximum plasma concentration after administration of 7.5 mg is 131μg/l.

Zopiclone may be measured in blood, plasma, or urine by chromatographic methods. Plasma concentrations are typically less than 100μg/l during therapeutic use, but frequently exceed 100μg/l in automotive vehicle operators arrested for impaired driving ability and may exceed 1000μg/l in acutely poisoned patients. Post mortem blood concentrations are usually in a range of 0.4-3.9 mg/l in victims of fatal acute overdose.[2,3,4]

The ZOP Rapid Test Dipstick (Urine) detects Zopiclone and/ or Zopiclone-N-oxide in urine at a cut-off concentration of 50ng/ml.

【PRINCIPLE】

The ZOP Rapid Test Dipstick (Urine) is an immunoassay based on the principle of competitive binding. Drugs which 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. Zopiclone, 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 Zopiclone-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 Zopiclone level exceeds the cut-off level, because it will saturate all the binding sites of anti-zopiclone 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-zopiclone antibody coupled particles and zopiclone-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 or label of the closed canister. The test must remain in the sealed pouch or closed canister 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 prolonged storage, specimens may be frozen and stored below -20°C. Frozen specimens should be thawed and mixed before testing.

【MATERIALS】

Materials Provided

- Test Dipsticks
- 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.

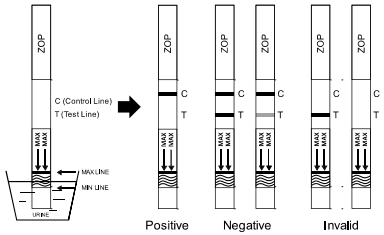
1. Bring the pouch to room temperature before opening it. Remove the Test Dipstick from the sealed pouch and use it within one hour.
2. With arrows pointing toward the urine specimen, immerse the Test Dipstick vertically in the urine specimen for at least 10-15 seconds. Do not pass the maximum line (MAX) on the Test Dipstick when immersing the strip. See the illustration below.
3. Place the Test Dipstick on a non-absorbent flat surface, start the timer and 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 the 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 zopiclone-N-oxide and zopiclone 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 zopiclone (including metabolite) 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】

1. The ZOP Rapid Test Dipstick (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.
2. It is possible that technical or procedural errors, as well as other interfering substances in the urine specimen may cause erroneous results.
3. 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.
4. A positive result indicates presence of the drug or its metabolites but does not indicate level of intoxication, administration route or concentration in urine.
5. 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.
6. Test does not distinguish between drugs of abuse and certain medications.

【EXPECTED VALUES】

This negative result indicates that the zopiclone (including metabolite) concentration is below the detectable level of 50ng/ml. Positive result means the concentration of zopiclone (including metabolite) is above the level of 50ng/ml. The ZOP Rapid Test Dipstick has a sensitivity of 50ng/ml

【PERFORMANCE CHARACTERISTICS】

A side-by-side comparison was conducted using The ZOP Rapid Test Dipstick and GC/MS at the cut-off of 50ng/ml. Testing was performed on 93 clinical specimens previously collected from subjects present for Drug Screen Testing. The following results were tabulated:

Method		GC/MS		Total Results
ZOP Rapid Test Dipstick	Results	Positive	Negative	
	Positive	19	2	21
	Negative	3	69	72
Total Results		22	71	93
% Agreement		86.4%	97.2%	94.6%

Analytical Sensitivity

A drug-free urine pool was spiked with Zopiclone at the following concentrations: 0ng/ml, 25ng/ml, 37.5ng/ml, 50ng/ml, 62.5ng/ml, 75ng/ml and 150ng/ml. The result demonstrates >99% accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Zopiclone Concentration (ng/ml)	Percent of Cut-off	n	Visual Result	
			Negative	Positive
0	0	30	30	0
25	-50%	30	30	0
37.5	-25%	30	27	3
50	Cut-off	30	17	13
62.5	+25%	30	4	26
75	+50%	30	0	30
150	3X	30	0	30

Analytical Specificity

The following table lists compounds that are positively detected in urine by the ZOP Rapid Test Dipstick (Urine) at 5 minutes.

Compound	Concentration (ng/ml)	Compound	Concentration (ng/ml)
Zopiclone-N-oxide	50	Zopiclone	50

Precision

A study was conducted at three hospitals by laypersons using three different lots of product to demonstrate the within run, between run and between operator precision. An identical Dipstick of coded specimens containing, according to GC/MS, no zopiclone, 25% above and below the cut-off and 50% above and below the cut-off of zopiclone was provided to each site. The following results were tabulated:

Zopiclone Concentration (ng/ml)	n per Site	Site A		Site B		Site C	
		-	+	-	+	-	+
0	10	10	0	10	0	10	0
25	10	10	0	10	0	10	0
37.5	10	9	1	8	2	9	1
62.5	10	2	8	2	8	2	8
75	10	0	10	0	10	0	10

Effect of Urinary Specific Gravity

Fifteen urine specimens of normal, high, and low specific gravity ranges were spiked with 25ng/ml and 75ng/ml of Zopiclone. The ZOP Rapid Test Dipstick (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 Zopiclone to 25ng/ml and 75ng/ml. The spiked, pH-adjusted urine was tested with The ZOP Rapid Test Dipstick (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 zopiclone (including metabolite) positive urine. The following compounds show no cross-reactivity when tested with The ZOP Rapid Test Dipstick (Urine) at a concentration of 100ug/ml.

Non Cross-Reacting Compounds

Aspartame	p-Hydroxymethampheta mine	AminopyrineAm inophenazone	Norethindrone
Asp-Phemethylester	Amitriptyline	Amobarbital	Norethisterone
Acetylsalicylic acid	Benzilic acid	Benzoic acid	Acetophenetidin
Atropine	Chlorothiazide	Chlorpromazine	Bilirubin
Chloramphenicol	Cholesterol	Clomipramine	Cortisone
Chloroquine	Cocaine	Creatinine	(-)Cotinine
Clonidine	Dexamethasone	Clindamycin	Digoxin
Cephalexin	(+)-cis-Diltiazem	Diclofenac	Dicumarol
Carisoprodol	Diphenhydramine	Doxylamine	Diazepam
Deoxycorticosterone	β-EstradiolEstradiol	Erythromycin	Diflunisal
Ethyl-p-aminobenzoate	Hydrochlorothiazide	Gentisic acid	Estrone-3- Sulfate
3-Hydroxytyramine	N-Acetylprocainamide	Furosemide	Fenoprofen
O-Hydroxyhippuric acid	Haloperidol	(-)Isoproterenol	Hydralazine
Hydrocodone	Maprotiline	Metronidazole	Methadone
Methoxyphenamine	Ibuprofen	Imipramine	Meperidine
Isoxsuprine	Caffeine	Protriptyline	Ketoprofen
Labetalol	Nalidixic acid	Nifedipine	Procyclidine
Metoclopramide	Naltrexone	Naproxen	Niacinamide
Naloxone	d,l- Octopamine	Oxazepam	Amoxcillin
d-Norpropoxyphene	Promethazine	Papaverine	Oxymetazoline
Procaine	Perphenazine	Phenelzine	Prednisone
Penicillin	Serotonin(5-Hydroxytryp tamine)	(1R,2S)-(-)-Eph edrine	Prednisolone
l-Phenylephrine	β-Phenylethylamine	Sulfamethazine	Trans-2-Phenylcyc lopropylamine
(R)-(-)-Phenylephrine	Thiamine	Thioridazine	Temazepam
Quinidine	Tolbutamide	Triamterene	Tetracycline
Tetrahydrozoline	Trimipramine	Tryptamine	d,l-Tryptophan
d,l-Tyrosine L-Tyrosine	(+/-)-Chlorpheniramine	Vancomycin	Uric acid
Trimethoprim	Quinine	Quinacrine	Zomepirac
Verapamil	Trazodone	Nimesulide	Phenobarbita
Ranitidine	5,5-Diphenylhydantoin	l-Thyroxine	Buspirone
Dicyclomine	Venlafaxine Hydrochloride	Lidocaine	Oxymorphone
2-ethylidene-1,5-dimethyl -3,3-diphenylpyrrolidine	Chlorprothixene	R(-)Deprenyl	Guaiacol Glyceryl Ether
Guaiacol Glyceryl Ether carbamate	3,4-Methylenedioxyethyl amphetamine	α-Naphthalene acetic Acid	Pheniramine
Amoxapine	Albumin	d (+) Glucose	(+/-) Epinephrine
4-Dimethylaminoantipyrin e	Cimetidine	Disopyramide	Sodium chloride
Phenothiazine	Kanamycin	Fluoxetine	Lindane
Pemoline	Chlorpropamide	Clozapine	Metoprolol
Etodolac	Digitoxin	Dimenhydrinate	Baclofen
Amantadine	Sulfamethoxazole	Indomethacin	Droperidol
Amikacin	Tobramycin	Sertraline	Sulfisoxazole
Gentamicin	R(+)-Methcathinone	R(+)-Cathinone	diacetylmorphine
Salbutamol	Spironolactone	Emetine	Barbital
S(-)-Methcathinone	Butethal	Butalbital	Aprobabital
Lansoprazole	Lorazepam glucuronide	Midazolam	Estazolam
Cyclopentobarbital	Alprazolam	Clobazam	Nitrazepam
Lorazepam	Doxepin	Desipramine	Triazolam
Riboflavin	(s)-(+)-mathoxy-α-mathe l-2-naphaleneacetic acid	Tramadol Hydrochloride	Nordoxepin
Nortriptyline	Quetiapine Fumarate	Trocamide	p-Acetamidopheny l-β-D-glucuronide
JWH-0185-pentanoic acid metabolite			Pregabalin
Cyclobenzaprine			

【BIBLIOGRAPHY】

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Index of Symbols

	Attention, see instructions for use		Tests per kit	EC REP	Authorized Representative
IVD	For in vitro diagnostic use only		Use by		Do not reuse
2°C 30°C	Store between 2-30°C	LOT	Lot Number	REF	Catalog #
	Do not use if package is damaged				

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