

BUP Rapid Test Dipstick (Urine) Package Insert

REF DBU-101/111 [English]

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

[INTENDED USE]

The BUP Rapid Test Dipstick (Urine) is a rapid chromatographic immunoassay for the detection of Buprenorphine in human urine at a cut-off concentration of 10 ng/mL. 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) or Liquid Chromatography/mass spectrometry (LC/MS) are the preferred confirmatory methods. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

[SUMMARY]

Buprenorphine is a potent analgesic often used in the treatment of opioid addiction. The drug is sold under the trade names Subutex,™ Buprenex,™ Temgesic,™ and Suboxone™ which contain Buprenorphine HCl alone or in combination with Naloxone HCl. Therapeutically, Buprenorphine is used as a substitution treatment for opioid addicts. Substitution treatment is a form of medical care offered to opiate addicts (primarily heroin addicts) based on a similar or identical substance to the drug normally used. In substitution therapy, Buprenorphine is as effective as Methadone but demonstrates a lower level of physical dependence. Concentrations of free Buprenorphine and Norbuprenorphine in urine may be less than 1 ng/mL after therapeutic administration, but can range up to 20 ng/mL in abuse situations. The plasma half-life of Buprenorphine is 2-4 hours. 1 While complete elimination of a single-dose of the drug can take as long as 6 days, the detection window for the parent drug in urine is thought to be approximately 3 days.

The BUP Rapid Test Dipstick (Urine) is a rapid urine screening test that can be performed without the use of an instrument. The test utilizes a monoclonal antibody to selectively detect elevated levels of Buprenorphine in urine. The BUP Rapid Test Dipstick (Urine) yields a positive result when Buprenorphine in urine exceeds 10 ng/mL.

[PRINCIPLE]

The BUP 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. Buprenorphine, if present in the urine specimen below 10 ng/mL, will not saturate the binding sites of antibody-coated particles in the test. The antibody-coated particles will then be captured by immobilized Buprenorphine 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 Buprenorphine level exceeds 10 ng/mL because it will saturate all the binding sites of anti-Buprenorphine antibodies.

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 lower 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 in 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-Buprenorphine antibody-coupled particles and Buprenorphine-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 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.

NOTE: Once the canister has been opened, the remaining test(s) are stable for 50 days only.

[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 precipitates should be centrifuged, filtered, or allowed settle to obtain a clear specimen for testing.

Specimen Collection

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

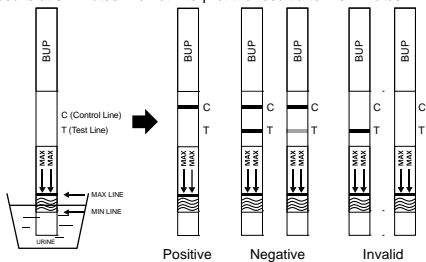
[MATERIALS]

- Test Dipsticks
- Materials Provided
 - Package insert
- Materials Required But Not Provided
 - Timer
- Specimen collection container

[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 distinct colored 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 Buprenorphine concentration is below the detectable level (10 ng/mL).

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

POSITIVE: One colored line appears in the control region (C). No line appears in the test line region (T). This positive result indicates that the Buprenorphine concentration exceeds the detectable level (10 ng/mL).

INVALID: Control line (C) 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 using a new test. If the problem persists, discontinue using the lot immediately and contact your local distributor.

[QUALITY CONTROL]

A procedural control is included in the test. A colored line appearing in the control 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 practice to confirm the test procedure and to verify proper test performance.

[LIMITATIONS]

1. The BUP 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) or liquid chromatography/mass spectrometry (LC/MS) are the preferred confirmatory methods.
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 Buprenorphine concentration is below the detectable level of 10ng/mL. Positive result means the concentration of Buprenorphine is above the level of 10ng/mL. The BUP Rapid Test Dipstick has a sensitivity of 10ng/ml

[PERFORMANCE CHARACTERISTICS]

Accuracy

A side-by-side comparison was conducted using BUP Rapid Test Dipstick and a commercially available BUP rapid test. Testing was performed on 94 clinical specimens previously collected from subjects present for Drug Screen Testing. The following results were tabulated:

Method	Other BUP Rapid Test		Total Results	
	Results	Positive		Negative
BUP Rapid Test Dipstick	Positive	43	0	43
	Negative	0	51	51
	Total Results	43	51	94
% Agreement		>99.9%	>99.9%	>99.9%

A side-by-side comparison was conducted using The BUP Rapid Test Dipstick and GC/MS at the cut-off of 10ng/mL. Testing was performed on 250 clinical specimens previously collected from subjects present for Drug Screen Testing. The following results were tabulated:

Method	GC/MS		Total Results	
	Results	Positive		Negative
BUP Rapid Test Dipstick	Positive	105	0	105
	Negative	1	144	145
	Total Results	106	144	250
% Agreement		99.1%	>99.9%	99.6%

Analytical Sensitivity

A drug-free urine pool was spiked with Buprenorphine at the following concentrations: 0 ng/mL, 5 ng/mL, 7.5 ng/mL, 10 ng/mL, 12.5 ng/mL 15 ng/mL and 30 ng/mL. The result demonstrates >99% accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Buprenorphine Concentration (ng/mL)	Percent Cut-off	n	Visual Result	
			Negative	Positive
0	0%	30	30	0
5	-50%	30	30	0
7.5	-25%	30	26	4
10	Cut-off	30	14	16
12.5	+25%	30	3	27
15	+50%	30	0	30
30	3X	30	0	30

Analytical Specificity

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

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Buprenorphine	10	Buprenorphine 3-D-Glucuronide	50
Norbuprenorphine	50	Norbuprenorphine 3-D-Glucuronide	100

A study was conducted at 3 hospitals by laypersons using 3 different lots of product to demonstrate the within run, between run and between operator precision. An identical panel of coded specimens containing no Buprenorphine, 25% Buprenorphine above and below the cutoff and 50% Buprenorphine above and below the 10 ng/mL cutoff were provided to each site. The following results were tabulated:

Buprenorphine Concentration (ng/mL)	n per Site	Site A			Site B			Site C		
		-	+	-	+	-	+			
0	10	10	0	10	0	10	0	10	0	
5	10	10	0	10	0	10	0	10	0	
7.5	10	9	1	9	1	8	2	9	1	
12.5	10	1	9	1	9	1	9	1	9	
15	10	0	10	0	10	0	10	0	10	

Effect of Urinary Specific Gravity

Fifteen urine samples with specific gravities were spiked with Buprenorphine to the concentrations of 5 ng/mL and 15 ng/mL. The BUP 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 the 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 Buprenorphine to 5 ng/mL and 15 ng/mL. The spiked, pH-adjusted urine was tested with The BUP 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 Buprenorphine positive urine. The following compounds show no cross-reactivity when tested with The BUP Rapid Test Dipstick (Urine) at a concentration of 100 µg/mL.

Non Cross-Reacting Compounds

4-Acetamidophenol	5,5-Diphenylhydantoin	Lithium carbonate	Trans-2- phenyl cyclopropylamine
Acetone	Disopyramide	Lorazepam	D,L-Propranolol
Acetophenetidin	Doxylamine	Maprotiline	D-Proproxyphene
Acetylsalicylic acid	Ecgonine hydrochloride	Mepiridine	D-Pseudoephedrine
N-Acetylprocainamide	Ecgonine methylester	Mephentermine	Quinacrine
Albumin	EDDP	Meprobamate	Quinidine
Aminopyrine	Efavirenz (Sustiva)	Methadone	Quinine
Amirityline	EMDP	D-Methamphetamine	Prednisolone
Amobarbital	Ephedrine	L-Methamphetamine	Prednisone
Amoxapine	(1R,2S)-(-)Ephedrine	Methaqualone	5 beta-pregnane3alpha17alpha-
Amoxicillin	(-)ψ-Ephedrine	Methoxyphenamine	21triol 21
L-Amphetamine	(-)Epinephrine	(±) 3,4-Methylenedioxy-amphetamine (MDA)	Procaine
Ampicillin	Erythromycin	(+) 3,4-Methylenedioxy-methamphetamine	Promazine
Apomorphine	β-Estradiol		Promethazine
Aspartame	Estrone-3-sulfate		Methylphenidate
Atropine	Ethanol (Ethyl alcohol)		Methypyrrolon
Benzilic acid	Ethyl-p-aminobenzoate		Methaqualone
Benzoic acid	Famprofazone		Metoprolol
Benzoylcegonine	Benzphetamine		Morphine sulfate
Benzphetamine	Bilirubin		Morphine
Buprenorphine	(±)-Brompheniramine		3-β-D-glucuronide
Buspirone	Buspirone		Nalidixic acid
Caffeine	Furosemide		Naloxone
Camnabitol	Gentisic acid		Naltrexone
Camnabitol	D (+) Glucose		Naloxonium
Chloralhydrate	Guaiacol Glyceryl Ether		Methypyrrolon
Chloramphenicol	Guaiacol Glyceryl Ether carbamate		Sodium chloride
Chloridiazepoxide	Carbamate		Sulfamethazine
Chloroquine	Hemoglobin		Sulindac
Chlorothiazide	Hydralazine		Morphine sulfate
(±)-Chlorpheniramine	Hydrochlorothiazide		Alpha-Naphthaleneacetic Acid
(-) Chlorpheniramine	Hydrocodone		Tetrahydrocortisone, 3-acetate
Chlorpromazine	Hydrocortisone		Norethindrone
Chlorpropoxene	Hydromorphone		Normorphone
Cholesterol	O-Hydroxyamphetamine		D-Norpropoxyphene
Cimetidine	O-Hydroxyhippuric acid		Noscapine
Clomipramine	p-Hydroxymethamphetamine		D,L-Octopamine
Clonidine	p-Hydroxyorephedrine		Orphenadrine
Cocaine HCl	Hydroxyzine		Oxalic acid
Cocaine	3-Hydroxytyramine		Oxazepam
Codine	Cortisone		Oxolinic acid
Cortisone	(-) Cotinine		Oxycodone
(-) Cotinine	Creatinine		Oxymetazoline
Creatinine	Cyclobarbitol		Oxymorphone
Cyclobarbitol	Cyclobenzaprine		Papaverine
Cyclobenzaprine	Deoxycorticosterone		Pemoline
Deoxycorticosterone	Ketamine		Penicillin-G
(-) Deoxyephedrine	Ketoprofen		Pentacocine
R (-) Deprenyl HCl	Labeltalol		Perfenbutarbitol
Dextromethorphan	Diazepam		Perphenazine
Diazepam	Diclofenac		Phencyclidine
Diclofenac	Dicyclomine		Phenelzine
Dicyclomine	Diffunilal		Pheniramine
Diffunilal	Digoxin		Phenobarbital
Digoxin	4-Dimethylaminoantipyrine		Phenothiazine
4-Dimethylaminoantipyrine	Diphenhydramine		Phenylephrine
Diphenhydramine	Lindane		Phenylephrine
Lindane	(hexachlorocyclohexane)		Phenylephrine

[BIBLIOGRAPHY]

1. Glass, IB. *The International Handbook of Addiction Behavior*. Routledge Publishing, New York, NY, 1991, 216
2. Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*. 6th Ed. Biomedical Publ., Davis, CA., 129, 2002
3. 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 in vitro diagnostic use only		Use by		Do not reuse
	Store between 2-30°C		Lot Number		Catalog #
	Do not use if package is damaged				



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