

BUP

One Step

Buprenorphine Test Device (Urine)

Package Insert

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

INTENDED USE

The BUP One Step Buprenorphine Test Device (Urine) is a lateral flow 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. 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 One Step Buprenorphine Test Device (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 One Step Buprenorphine Test Device (Urine) yields a positive result when the Buprenorphine in urine exceed 10 ng/mL.

PRINCIPLE

The BUP One Step Buprenorphine Test Device (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 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-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 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 precipitates should be centrifuged, filtered, or allowed 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 assay. 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 devices
- Droppers
- Package insert

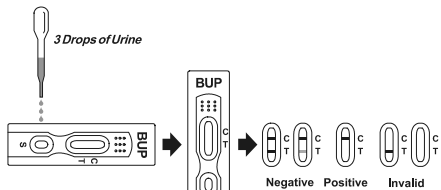
Materials Required But Not Provided

- 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 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 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

- The BUP One Step Buprenorphine Test Device (Urine) provides only a qualitative, preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Liquid chromatography/mass spectrometry (LC/MS) is the preferred confirmatory methods.
- 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 or 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 cutoff level of the test.
- Test does not distinguish between drugs of abuse and certain medications.

PERFORMANCE CHARACTERISTICS

Accuracy

A correlation study was conducted on fifty-eight (58) clinical specimens from patients reporting Buprenorphine use and one-hundred fifty (150) urine specimens collected from presumed non-drug users. Using the BUP One Step Buprenorphine Test Device (Urine), the specimens were tested and compared to the self-reported use of Buprenorphine. All specimens, including the ones showing negative results, were then confirmed by LC/MS. The following results were tabulated:

Method	Patient Self-Report		Total Results
	Positive	Negative	
BUP One Step Test Device	Results Positive	51	51
	Negative	7	157
	Total Results	58	208
% Agreement	88%	>99%	97%

When compared at 10 ng/mL with LC/MS, the following results were tabulated:

Method	LC/MS		Total Results
	Positive	Negative	
BUP One Step Test Device	Results Positive	55	57
	Negative	1	169
	Total Results	56	226
% Agreement	98%	99%	99%

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 and 15 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 of Cut-off	n	Visual Result	
			Negative	Positive
0	0%	90	90	0
5	-50%	90	90	0
7.5	-25%	90	78	12
10	Cut-off	90	48	42
12.5	+25%	90	24	66
15	+50%	90	0	90

Analytical Specificity

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

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Buprenorphine	10	Buprenorphine 3-D-Glucuronide	15
Norbuprenorphine	20	Norbuprenorphine 3-D-Glucuronide	200

Precision

A study was conducted at 3 physician's offices by untrained operators 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	15	15	0	15	0	15	0
5	15	15	0	15	0	15	0
7.5	15	8	7	10	5	9	6
12.5	15	0	15	1	14	0	15
15	15	0	15	0	15	0	15

Effect of Urinary Specific Gravity

Fifteen urine samples with specific gravities ranging from 1.004 to 1.034 were spiked with Buprenorphine to the concentrations of 5 ng/mL, and 15 ng/mL. The BUP One Step Buprenorphine 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 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 One Step Buprenorphine 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 Buprenorphine positive urine. The following compounds show no cross-reactivity when tested with the BUP One Step Buprenorphine Test Device (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	Loperamide	L-Phenylephrine
Acetophenetidin	Doxylamine	Maprotiline	B-Phenylethylamine
Acetylsalicylic acid	Ecgonine hydrochloride	Meperidine	Phenylpropanolamine
N-Acetylprocainamide	Ecgonine methyl ester	Mephentermine	(D,L-norephedrine)
Albumin	EDDP	Meprobamate	(±) Phethylpropranolamine
Amigopyrine	Evirent (Sustiva)	Methadone	Prednisolone
Amitriptyline	EMDP	D-Methamphetamine	Prednisone
Amobarbital	Ephedrine	L-Methamphetamine	5 beta-pregname3alpha17alpha-21trio1 21
Amoxapine	(1r,2s)-(-)-Ephedrine	Methaqualone	Procaine
Amoxicillin	(-)-ψ-Ephedrine	Methoxyphenamine	Promazine
L-Amphetamine	(±)-Epinephrine	(-)-3,4-Methylenedioxyamphetamine (MDA)	Promethazine
Ampicillin	Erythromycin	(+) 3,4-Methylenedioxy-methamphetamine	D,L-Propranolol
Apoporphine	β-Stradiol	Methylphenidate	D-Propoxyphene
Aspartame	Estrone-3-sulfate	Methylphenidate	D-Pseudoephedrine
Atropine	Ethanol (Ethyl alcohol)	Methyprylon	Quinacrine
Benzilic acid	Ethyl-p-aminobenzoate	Methazolone	Quinidine
Benzoic acid	Etodolac	Methazolone	Quinine
Benzofluorone	Famprofazone	Metoprolol	Rantidine
Benzphetamine	Fenfluramine	Morphine sulfate	Riboflavin
Bilirubin	Fenpropfen	Morphine-	Salicylic acid
(±)-Brompheniramine	Fentanyl	3-β-D-glucuronide	Secobarbital
Bupirone	Fluoxetine	Nalidixic acid	Serotonin
Caffeine	Furosemide	Nalorphine	(5-hydroxytryptamine)
Cannabidiol	Gentisic acid	Naloxone	Sodium chloride
Cannabinol	D (+) Glucose	Naltrexone	Sulfamethiazole
Chloralhydrate	Guaiaicol Glyceryl Ether	Methyprylon	Sulfindac
Chloramphenicol	Guaiaicol Glyceryl Ether	Metoprolol	Temazepam
Chlorazepoxide	carbamate	Nimesulide	Tetracycline
Chloroquine	Hemoglobin	Norcodolone	Tetrahydrocortisone,
Chlorothiazide	Hydralazine	Morphine sulfate	3-acetate
(+) Chlorpheniramine	Hydrochlorothiazide	Alpha-	Tetrahydrozoline
(±)-Chlorpheniramine	Hydrocodone	Naphthaleneacetic Acid	Thebaine
Chlorpromazine	Hydrocortisone	Norethindrone	Theophylline
Chlorprothixene	Hydromorphone	Normorphine	D,L-Octopamine
Cholesterol	p-Hydroxyamphetamine	D-Norpropraxophene	Thiamine
Cimetidine	O-Hydroxyhippuric acid	Noscapine	Thioridazine
Clomipramine	p-Hydroxymethamphetamine	p-Hydroxynorephedrine	(chlorpromazine)
Clonidine	p-Hydroxynorephedrine	Orphenadrine	Oxazepam
Cocaine HCl	Hydroxyzine	Oxalic acid	Oxolinic acid
Codaine	3-Hydroxytryptamine	Oxazepam	Oxycodone
Cortisone	Ibuprofen	Oxolinic acid	Oxymetazoline
(-) Cotinine	Imipramine	Oxycodone	Papaverine
Creatinine	Iproniazid	Oxymetazoline	Pemoline
Cyclobarbitol	(-) Isoproterenol	Oxymorphone	Penicillin-G
Cyclobenzaprine	Isosuprine	Papaverine	Ketoprofen
Deoxycorticosterone	Kanamycin	Pemoline	Labelalol
(-) Deoxyephedrine	Ketamine	Penicillin-G	L-Ascorbic acid
R (-) Deprenyl HCl	Ketoprofen	Pentobarbital	L-Ephedrine
Dextromethorphan	Labelalol	Perphenazine	Dicyclanide
Diazepam	L-Ascorbic acid	Phenazone	L-Epinephrine
Diclofenac	L-Ephedrine	Phencyclidine	L-Epinephrine
Dicyclomine	L-Epinephrine	Phenelzine	Lidocaine
Diffusinal	Lorviranolol	Pheniramine	Lindane
Digoxin	Lidocaine	Phenobarbital	(hexachlorocyclohexane)
4-Dimethylaminoantipyrine	Lindane	Phenothiazine	Phentermine
Diphenhydramine	(hexachlorocyclohexane)	Phentermine	

BIBLIOGRAPHY

- Glass, IB. *The International Handbook of Addiction Behavior*. Routledge Publishing, New York, NY. 1991, 216
- Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*. 6th Ed. Biomedical Publ., Davis, CA., 129, 2002.
- Hawks RL, CN Chiang. *Urine Testing for Drugs of Abuse*. National Institute for Drug Abuse (NIDA), Research Monograph 73, 1986.