BUP

One Step
Buprenorphine Test Device
Package Insert

A rapid, one step test for the qualitative detection of Buprenorphine in human urine.

For healthcare professionals including professionals at point of care sites.

For in vitro diagnostic use only.

INTENDED USE

The One Step Buprenorphine Test Device 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 is intended for use by professionals to assist in the determination of drug compliance.

This assay provides only a 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.[1] The plasma half life Buprenorphine is 2-4 hours.[1] While complete elimination of a single-dose of the drug can take as long as 6 days, the window of detection for the parent drug in urine is thought to be approximately 3 days.

Substantial abuse of Buprenorphine has also been reported in many countries where various forms of the drug are available. The drug has been diverted from legitimate channels through theft, doctor shopping, and fraudulent prescriptions, and been abused via intravenous, sublingual, intranasal and inhalation routes

The One Step Buprenorphine Test Device 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 One Step Buprenorphine Test Device yields a positive result when the Buprenorphine in urine exceeds 10 ng/ml.

PRINCIPLE

The One Step Buprenorphine Test Device 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. Buprenorphine, if present in the urine specimen below 10 ng/mL, will not saturate the binding sites of antibody-coated particles in the test device. 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 device contains mouse monoclonal anti-Buprenorphine antibody-coupled particles and Buprenorphine-protein conjugate. A goat antibody is employed in the control line system.

PRECAUTIONS

- For healthcare professionals including professionals at point of care sites.
- For *in vitro* diagnostic use only. Do not use after the expiration date.
- The test device 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 device should be discarded according to federal, state and local regulations.

STORAGE AND STABILITY

Store as packaged in the sealed pouch at 2-30°C. The test device is stable through the expiration date printed on the sealed pouch. The test device 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 96 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
- Disposable specimen droppers
- Package insert

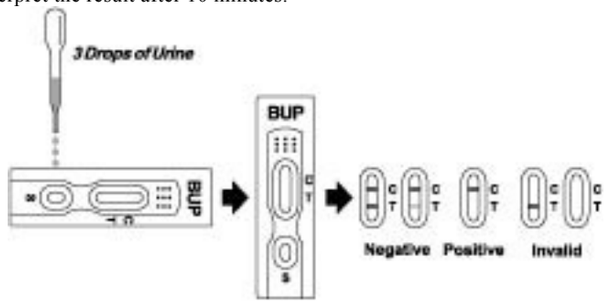
Materials Required But Not Provided

- Specimen collection container
- Timer
- External Controls

DIRECTIONS FOR USE

Allow test device, 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 device from the sealed pouch and use it as soon as possible.
2. Place the test device on a clean and level surface. Hold the dropper vertically and transfer 3 full drops of urine (approx. 100µl) 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.
3. Wait for the red line(s) to appear. The result should be read 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 red line should be in the control region (C), and another apparent red or pink line should be in the test region (T). This negative result indicates that the Buprenorphine concentration is below the detectable level (10 ng/mL).

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

POSITIVE: One red line appears in the control region (C). No line appears in the test 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 device. If the problem persists, discontinue using the lot immediately and contact the manufacturer.

QUALITY CONTROL

A procedural control is included in the test. A red line appearing in the control region (C) is considered an internal positive 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 One Step Buprenorphine Test Device 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 methods.[2]
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 or 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 cutoff level of the test.
6. Test does not distinguish between drugs of abuse and certain medications.

PERFORMANCE CHARACTERISTICS

Accuracy

226 urine samples were obtained and tested with the BUP One Step Buprenorphine Test Device and by LC/MS the results are summarized below:

Specimen Cutoff Range by LC/MS							
		Negative*	< -25% of cutoff	-25% cutoff to cutoff	Cutoff to +25% of cutoff	>+25% of cutoff	% Agreement
ACON BUP Device	Positive	0	0	2	5	50	98% (55/56) (90%-99%)**
	Negative	150	15	3	1	0	99% (168/170) (96%-99%)**

Total agreement with LC/MS: 223/226 = 99% (96%-99%)**

** Denotes 95% confidence interval

* Negative samples were confirmed negative using LC/MS by pooling these samples into groups of 15.

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 and 20 ng/mL. The assay cutoff level of 10 ng/mL was selected to correlate with the LC/MS analysis cutoff for Buprenorphine. The result demonstrates 99% accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

BUP Concentration (ng/mL)	Percent of Cutoff	n	Visual Result	
			Negative	Positive
0	0%	90	90	0
5	-50%	90	90	0
7.5	-25%	90	78	12
10	Cutoff	90	48	42
12.5	+25%	90	24	66
15	+50%	90	0	90
20	+100%	90	0	90

Specificity

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

Compound	Concentration (ng/mL)	Cross-Reactivity (%)
Buprenorphine	10	100
Norbuprenorphine	20	50
Buprenorphine 3-D-glucuronide	15	67
Norbuprenorphine 3-D-glucuronide	200	5

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 cut-off and 50% Buprenorphine above and below the 10 ng/mL cut-off were provided to each site. The following results were tabulated:

Buprenorphine conc. (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 (15) urine samples with specific gravity ranging from 1.004 to 1.034 were spiked with Buprenorphine to the concentrations of 5 ng/mL, 15 ng/mL and 20 ng/mL. The One Step Buprenorphine Test Device was tested in duplicate using the fifteen neat and spiked urine samples. The results demonstrate that varying ranges of urinary specific gravity does 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, 15 ng/mL and 20 ng/mL. The spiked, pH-adjusted urine was tested with the One Step Buprenorphine Test Device in duplicate. The results demonstrate that varying ranges of pH does 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 One Step Buprenorphine Test Device at a concentration of 100 µg/mL.

Non Cross-Reacting Compounds

4-Acetaminophenol	Acetone	Acetophenetidin
Acetylsalicylic acid	Albumin	Amitryptyline
Amobarbital	Amoxapine	Amoxicillin
d/l-Amphetamine	Ampicillin	Ascorbic acid
Aminopyrine	Apomorphine	Aspartame
Atropine	Benzilic acid	Benzoic acid
Benzphetamine	Bilirubin	Brompheniramine
Buspirone	Caffeine	Cannabidiol
Cannabinol	Cimetidine	Chloral hydrate
Chloramphenicol	Chlordiazepoxide	Chloroquine
Chlorothiazide	(+) – Chlorpheniramine	(±) - Chlorpheniramine
Chlorpromazine	Chlorprothixene	Cholesterol
Clomipramine	Clonidine	Cortisone
(-) Cotinine	Creatinine	Cyclobarbital
Cyclobenzaprine	Deoxycorticosterone	(-)Deoxyephedrine
R (-) Deprenyl HC1	Dextromethorphan	Diazepam
Diclofenac	Diflunisal	Digoxin
4-Dimethylaminoantipyrine	Diphenhydramine	Dicyclomine
5,5 –Diphenylhydantoin	Disopyramide	Doxylamine
Ecgonine HC1	Ecgonine Methylester	EDDP
EMDP	Efavirenz	Ephedrine
l-Ephedrine	(-) -Ψ -Ephedrine	[1R,2S] (-) Ephedrine
l-Epinephrine	(+/-) – Epinephrine	Erythromycin
β-Estradiol	Estrone-3-sulfate	Ethanol
Ethyl-p-aminobenzoate	Etodolac	Famprofazone
Fenfluramine	Fenoprofen	Fentanyl
Fluoxetine	Furosemide	Gentisic acid
d-Glucose	Guaiacol Glyceryl Ether	Guaiacol Glyceryl Ether Carbamate
Hemoglobin	Hydralazine	Hydrochlorothiazide
Hydrocodone	Hydrocortisone	Hydromorphone
o-Hydroxyhippuric acid	p-Hydroxymethamphetamine	p-Hydroxynorephedrine
3-Hydroxytyramine(Dopamine)	Hydroxyzine	Ibuprofen
Imipramine	Iproniazide	(-) Isoproterenol
Isoxsuprine	Kanamycin	Ketamine
Ketoprofen	Labetalol	Levorphanol
Lidocaine	Lindane	Lithium Carbonate
Loperamide	Maprotiline	Meperidine
Meprobamate	l-Methamphetamine	Methaqualone
Methadone	Methoxyphenamine	MDMA*
Methylphenidate	Mephentermine	Metoprolol
Morphine-3-β-D glucuronide	Morphine Sulfate	Methyprylon
Nalidixic acid	Naloxone	Naltrexone
α-Naphthaleneacetic acid	Naproxen	Niacinamide
Nifedipine	Norcodeine	Normorphine
Nimesulide	Norethindrone	d-Norpropoxyphene
Noscapine	d/l-Octopamine	Orphenadrine
Oxalic acid	Oxazepam	Oxolinic Acid
Oxycodone	Oxymetazoline	Oxymorphone
Papaverine	Pemoline	Penicillin-G
Pentazocine	Pentobarbital	Perphenazine
Phencyclidine	Phenelzine	Pheniramine
Phenobarbital	Phenothiazine	Phentermine
l-Phenylephrine	β-Phenylethylamine	(+/-) Phenylpropanolamine
Prednisolone	Prednisone	Procaine
Promazine	Promethazine	d-Propoxyphene
d/l-Propranolol	d-Pseudoephedrine	Quinacrine
Quinidine	Quinine	Ranitidine
Riboflavin	Salicylic acid	Secobarbital
Serotonin	Sodium Chloride	Sulfamethazine
Sulindac	Temazepam	Tetracycline
Tetrahydrocortexolone	Tetrahydrocortisone,3-acetate	Tetrahydrozoline
Thebaine	Theophylline	Thiamine
Thioridazine	l-Thyroxine	Tolbutamide
Cis-Tramadol	Trans-2-phenylcyclopropylamine	Trazodone
Trimethobenzamide	Triamterene	Trimipramine
Trifluoperazine	Trimethoprim	Tryptamine
d/l-Tryptophan	Tyramine	d/l-Tyrosine
Uric acid	Verapamil	Zomepirac

*(+) 3,4 Methylendioxymethamphetamine

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