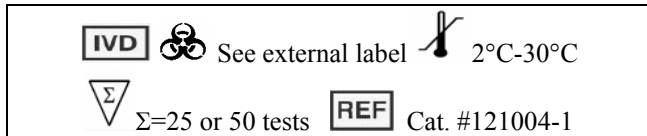




CORTEZ DIAGNOSTICS, INC.

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OneStep Buprenorphine RapiDip InstaTest

FOR THE QUALITATIVE ASSESSMENT OF
 BUPRENORPHINE
 IN HUMAN URINE

Catalog Number: 121004-1

INTENDED USE

The Cortez Diagnostics, Inc.BUP test strip is an immunochromatography based one step in vitro test. It is designed for qualitative determination of the major metabolite of buprenorphine, buprenorphine-3-β-d-glucuronide, in human urine specimens at cut-off level of 10 ng/ml. This assay has not been evaluated in the point of care location and is for use by Healthcare Professionals only.

This assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/ mass spectrometry (GC/MS) has been established as the preferred confirmatory method by the Substance Abuse Mental Health Services Administration (SAMHSA). Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are indicated.

SUMMARY AND EXPLANATION

Buprenorphine, a derivative of thebaine, is an opioid that has been marketed in the United States as the Schedule V parenteral analgesic Buprenex. In 2003, based on a reevaluation of available evidence regarding the potential for abuse, addiction, and side effect, DEA reclassified buprenorphine from a Schedule V to a Schedule III narcotic.

Buprenorphine resembles morphine structurally but has a longer duration of action than morphine and can be administered sublingually as an analgesic. In October 2002, FDA approved the use of a buprenorphine monotherapy product, Subutex, and a buprenorphine/naloxone combination product, Suboxone, for the treatment of opioid addiction. Subutex and Suboxone are the first narcotic drugs available under the US Drug Act (DATA) of 2003 for the treatment of opiate dependence that can be prescribed in the US in a physician's work place. It has also been shown that buprenorphine has abuse potential and may itself cause dependency. In addition, a number of deaths have been recorded as a result of overdose with intravenously injected buprenorphine in conjunction with other psychotropic drugs such as benzodiazepines. Buprenorphine is metabolized primarily by n-dealkylation to form glucuronide-buprenorphine and glucuronide-norbuprenorphine.

TEST PRINCIPLE

The Cortez Diagnostics, Inc.BUP test strip is based on the principle of specific immunochemical reaction between antibodies and antigens to analyze particular compounds in human urine specimen. The assay relies on the competition for binding antibody between drug conjugate and free drug which may be present in the urine specimen being tested. When drug is present in the urine specimen, it competes with drug conjugate for the limited amount of antibody-dye conjugate. When the amount of drug is equal or more than the cut-off, 10 ng/ml, it will prevent the binding of drug conjugate to the antibody. Therefore, a positive urine specimen will not show a colored band on the test line zone, indicating a positive result, while the presence of a colored band indicates a negative result.

A control line is present in the test window to work as procedural control. This colored band should always appear on the control line zone if the test device is stored in good condition and the test is performed appropriately.

MATERIALS PROVIDED

1. Instructions for use.
2. Cortez Diagnostics, Inc.BUP test device. The amount of each coated antigen and/or antibody on the strip is less than 1.0 mg for antigen conjugate and is less than 1.0 mg for goat anti-mouse IgG antibody.
 Test zone: contains buprenorphine bovine protein antigen conjugates.
 Control zone: contains Goat anti-mouse IgG antibody.
3. Conjugate pad: contains mice monoclonal anti-buprenorphine antibody.

MATERIALS REQUIRED BUT NOT PROVIDED

1. Urine collection container.
2. Timer or clock.

STORAGE AND STABILITY

The test device should be stored at 2 to 30°C and will be effective until the expiration date stated on the package. The product is humidity-sensitive and should be used immediately after being open. Any improperly sealed product should be discarded.

PRECAUTIONS

1. For in vitro diagnostic and forensic use only.
2. Do not use the product beyond the expiration date.
3. Handle all specimens as potentially infectious.
4. Humidity sensitive product, do not open foil pouch until it is ready to be tested.
5. Use a new urine specimen cup for each sample to avoid cross contamination.

SPECIMEN COLLECTION AND PREPARATION

It is required that approximately 150 µl of sample for each test. Fresh urine specimens do not need any special handling or treatment. Specimens should be collected in a clean, dry, plastic or glass container. If the assay is not performed immediately, urine specimen may be refrigerated at 2-8°C or frozen up to 7 days. Specimens should be thawed and brought to room temperature before testing. Urine specimens exhibiting a large amount of precipitate or turbidity should be centrifuged or allowed to settle before testing. Avoid contact with skin by wearing gloves and proper laboratory attire.

QUALITY CONTROL

Good Laboratory Practice recommends the daily use of control materials to validate the reliability of device. Control materials should be assayed as clinical specimen and challenging to the assay cutoff concentration, e.g., 25% above and below cutoff concentration. If control values do not fall within established range, assay results are invalid. Control materials which are not provided with this test kit are commercially available.

The Cortez Diagnostics, Inc. Drugs of Abuse Test provides a built-in process control with a different antigen/antibody reaction at the control region. This control line should always appear regardless the presence of drug or metabolite. If the control line does not appear, the test device should be discarded and the obtained result is invalid. The presence of this control band in the control region serve as 1) verification that sufficient volume is added, 2) that proper flow is obtained.

PROCEDURE

1. Bring all materials and specimens to room temperature.
2. Remove the test strip from the sealed foil pouch.
3. Dip the strip into the urine specimen with the arrow pointing toward the sample. The sample level should not be higher than the arrow pointed maximum line.
4. Hold the strip in the urine until a reddish color appears at the test area (approximately 20 seconds).
5. Withdraw the strip and place it face up on a clean, non-absorptive surface or leave the strip in urine if the urine level is not higher than arrow pointed maximum line.
6. Read the results at 5 minutes after adding the sample.

Do not interpret the result after 5 minutes

INTERPRETATION OF RESULTS

Negative:

Two colored bands form. The appearance of two colored bands, one in test line zone and the other in control line zone, indicates negative results. The negative result indicates that the buprenorphine concentration in the specimen is either zero or less than cut-off level.

Positive:

One colored band forms. One colored band appears in control line zone. No colored band is found in test line zone. This is an indication that the buprenorphine level in the specimen is above the cut-off level.

Invalid:

If there is no colored band in control line zone, the test result is invalid. Retest the sample with a new device.

Note: A borderline (+/-) in test line zone should be considered negative result.

LIMITATION OF PROCEDURE

The assay is designed for use with human urine only. A positive result with any of the tests indicates only the presence of a drug/metabolite and does not indicate or measure intoxication. There is a possibility that technical or procedural error as well other substances in certain foods and medicines may interfere with the test and cause false results. Please refer "SPECIFICITY" section for lists of substances that will produce either positive results, or that do not interfere with test performance. If a drug/metabolite is found present in the urine specimen, the assay does not indicate frequency of drug use or distinguish between drug of abuse and certain foods and medicines.

EXPECTED RESULTS

The Cortez Diagnostics, Inc.BUP Test is a qualitative assay. It identifies buprenorphine's major metabolite, Buprenorphine-3-β-d-glucuronide in human urine at a concentration of 10 ng/ml or

higher. The concentration of the Buprenorphine-3-β-d-glucuronide cannot be determined by this assay. The test is intended to distinguish negative result from presumptive positive result. All positive results must be confirmed using an alternate method, preferably GC/MS.

PERFORMANCE CHARACTERISTICS

A. Accuracy

The accuracy of the Cortez Diagnostics, Inc.BUP test was evaluated in comparison to GC/MS at a cut-off of 10 ng/ml of buprenorphine-3-β-d-glucuronide. One hundred and one urine specimens with confirmed buprenorphine-3-β-d-glucuronide concentrations were evaluated in this study. Borderline readings were recorded as negative. The results are summarized and presented below:

Cortez Diagnostics, Inc.BUP Test	(-)		(+)		Percent agreement with GC/MS
	GC/MS Negative (less than -25% cut off)	Near cutoff negative (between -25% and c/o	Near cutoff positive (between c/o and +25%	GC/MS Positive (greater than +25% cut off)	
Positive	1	1	10	39	96
Negative	41	9	0	0	100
Total	42	10	10	39	

Positive % agreement: 96, Negative % agreement: 100.

Two specimens were found discrepant between the Cortez Diagnostics, Inc.BUP and GC/MS method. When compared those data, 50% (1 out of 2) of the discrepancy specimens were found between cut-off and +25% cut-off concentration (7.5 – 12.5 ng/ml).

B. Sensitivity

The cut-off concentration (sensitivity level) of Cortez Diagnostics, Inc.BUP test is determined to be 10 ng/ml of buprenorphine-3-β-d-glucuronide or 10 ng/ml of buprenorphine.

C. Precision

The precision study was performed by three individuals observing the test result to determine the random error of visual interpretation. The test results were found to have no significant differences between the three observers.

Device	Control Con. ng/ml	No. of Tested	No. of positive			No. of borderline #			No. of negative		
			1*	2*	3*	1*	2*	3*	1*	2*	3*
BUP	5	42							42	42	42
	7.5	42				2		2	40	42	40
	10	42	29	27	24	13	15	18			
	12.5	42	42	42	42						
	15	42	42	42	42						

The precision study was performed by three individuals observing the test results to determine the random error of visual interpretation. The results were found to have no significant differences between three observers.

D. Specificity

The specificity for Cortez Diagnostics, Inc.BUP test was tested by adding various drugs, drug metabolites, and other compounds that are likely to be present in urine. All compounds were prepared in drug-free normal human urine.

1. Interference testing

The Cortez Diagnostics, Inc.BUP test performance at cut-off level is not affected when pH and Specific Gravity ranges of urine specimen are at 4.0 to 8.0 and 1.005 to 1.035.

The following substances were tested and confirmed not to interfere with Cortez Diagnostics, Inc.BUP test at the listed concentrations.

Glucose	2000 mg/dl,
Human albumin	2000 mg/dl
Human hemoglobin	10 mg/dl,
Urea	4000 mg/dl
Uric acid	10 mg/dl

2. Specificity

The following table lists compounds that are detected by Cortez Diagnostics, Inc.BUP test which produced positive results when tested at levels equal or greater than the concentrations listed below:

Compounds	Concentration	Cross reactivity
Buprenorphine-3-β-d-glucuronide	10 ng/ml	100%
Buprenorphine	200 ng/ml	5%

Each listed substance that commonly found in the urine was evaluated and indicated negative result at concentration of 100 µg/ml.

Acetaminophen	4-Acetamidophenol	Acetylsalicylic acid
Amikacin		

Amitriptyline	Amobarbital	Amphetamine	Arterenol
Aspartame	Ascorbic acid	Atropine	
Camphor	Caffeine	Chloroquine	Chlopheniramine
deoxyephedrine	Cortisone	Dextromethorphan	Digitoxin
Digoxin		Diphenhydramine	Egonine
Ecgoinine methyl ester		Ephedrine	
Epinephrine		Gentisic	Guaiacol glycer ester
	Histamine		
Hydrochlorothiazide		Homatrophine	Imipramine
	Ibuprofen		
Isoproterenol		Ketamine	Lidocaine
	Meperidine	Methodone	Methamphetamine
	3,4=MDMA	Methaqualone	Methylphenidate
	Neomycin	Niacinamide	Oxazepam
Perphenazine	Penicillin G	Phencyclidine	Phenylethylamine-α
Phenylpropanolamine	Promethazine	Pseudoephedrine	Quinine antidine
Salicylic acid	Tetracycline		Tetrahydrozoline
	Theophylline		
11-nor-Δ ⁸ -THC-9-COOH (10 µg/ml)			11-nor-Δ ⁸ -THC-9-COOH (10 µg/ml)
Thioridazine	Trifluoperazine		Tryptophan
	Tyramine		

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ISO 13485-2003

Revision Date: 6-3-06