Diagnostic Automation / Cortez Diagnostics, Inc.
IMMUNO DIAGNOSTICS

CE

OneStep Tricyclic Antidepressants (TCA) RapiDip™ InstaTest

REF 121031-1-44

IVD See external Label 2°C 30°C 1 Test

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

INTENDED USE

The TCA RapiDip™ (Urine) is a lateral flow chromatographic immunoassay for the detection of Nortriptyline in human urine at a cut-off concentration of 1,000 ng/mL. This test will detect other related compounds, please refer to the Analytical Specificity table in this package insert.
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 high performance liquid chromatography (HPLC) 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 AND EXPLANATION

TCA (Tricyclic Antidepressants) are commonly used for the treatment of depressive disorders. TCA overdoses can result in profound central nervous system depression, cardiotoxicity and anticholinergic effects. TCA overdose is the most common cause of death from prescription drugs. TCAs are taken orally and sometimes by injection. TCAs are metabolized in the liver, both TCAs and their metabolites are excreted in urine mostly in the form of metabolites for up to ten days.
The TCA RapiDip™ (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 nortriptyline in urine. The TCA RapiDip™ (Urine) yields a positive result when the Nortriptyline in urine exceeds 1,000 ng/mL.

TEST PRINCIPLE

The TCA RapiDip™ (Urine) is a rapid chromatographic 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. Tricyclic Antidepressants, if present in the urine specimen below 1,000 ng/mL, will not saturate the binding sites of the antibody coated particles in the test. The antibodies coated particles will then be captured by immobilized Tricyclic Antidepressants 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 Tricyclic Antidepressants level exceeds 1,000 ng/mL because it will saturate all the binding sites of anti-Tricyclic Antidepressants 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 will generate a line in the test line region because of the absence of drug competition. 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.

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 clear specimen for testing.

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

REAGENTS

The test contains anti-Tricyclic Antidepressants particles and Tricyclic Antidepressants conjugate coated on the membrane. A goat antibody is employed in the control line system.

MATERIALS AND COMPONENTS

Materials provided with the test kits

- Test Dipsticks
- Package insert

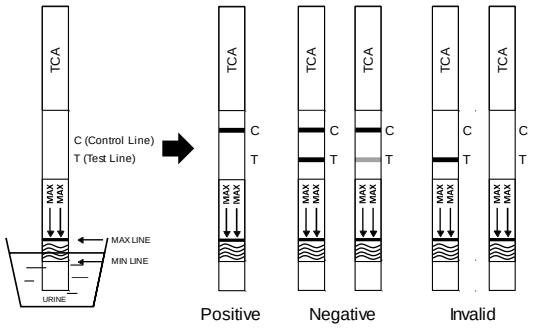
Materials required but not provided

- Specimen collection container
- Timer

ASSAY PROCEDURE

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 as soon as possible.
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.



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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 Tricyclic Antidepressant concentration is below the detectable level.

***NOTE:** The shade of color in the test line region (T) will vary, but it should always be considered as 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 Tricyclic Antidepressant concentration exceeds the detectable 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 using a new test. If the problem persists, discontinue using the lot immediately and contact your local distributor.

PERFORMANCE CHARACTERISTICS

Accuracy

A comparison was conducted using the TCA RapiDip™ (Urine) and GC/MS. The following results were tabulated:

Method		GC/MS		Total Results
TCA Rapid Test Dipstick	Results	Positive	Negative	
	Positive	91	13	104
	Negative	5	141	146
Total Results		96	154	250
% Agreement		94.8%	91.6%	92.8%

Analytical Sensitivity

A drug-free urine pool was spiked with at the following Nortriptyline concentrations: 0 ng/mL, 500 ng/mL, 750 ng/mL, 1,000 ng/mL, 1,250 ng/Ml, 1,500 ng/mL and 3,000 ng/mL. The result demonstrates >99% accuracy at 50% above and 50% below the cut-off concentration. The data are summarized below:

Nortriptyline Concentration (ng/mL)	Percent of Cut-off	n	Visual Result	
			Negative	Positive
0	0%	30	30	0
500	-50%	30	30	0
750	-25%	30	25	5
1,000	Cut-off	30	15	15
1,250	+25%	30	3	27
1,500	+50%	30	0	30
3,000	3X	30	0	30

Analytical Specificity

The following table lists compounds that are positively detected in urine by The TCA RapiDip™ (Urine) at 5 minutes.

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Nortriptyline	1,000	Imipramine	400
Nordoxepine	500	Clomipramine	50,000
Trimipramine	3,000	Doxepine	2,000
Amitriptyline	1,500	Maprotiline	2,000
Promazine	3,000	Promethazine	50,000
Desipramine	200	Perphenazine	50,000
Cyclobenzaprine	2,000	Dithiaden	10,000

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 panel of coded specimens containing, according to GC/MS, no Nortriptyline, 25% Nortriptyline above and below the cut-off and 50% Nortriptyline above and below the 1,000 ng/mL cut-off was provided to each site. The following results were tabulated:

Nortriptyline Concentration (ng/mL)	n per Site	Site A		Site B		Site C	
		-	+	-	+	-	+
0	10	10	0	10	0	10	0
500	10	10	0	10	0	10	0
750	10	9	1	8	2	8	2
1,250	10	1	9	1	9	1	9
1,500	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 500 ng/mL and 1,500 ng/mL of Nortriptyline. The TCA RapiDip™ (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 Nortriptyline to 500 ng/mL and 1,500 ng/mL. The spiked, pH-adjusted urine was tested with The TCA RapiDip™ (Urine) in duplicate and interpreted according to the package insert. 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 a drug-free urine pool and a drug-free urine pool spiked to contain a 1,500 ng/mL concentration of Nortriptyline. The following compounds show no cross-reactivity when tested with The TCA RapiDip™ (Urine) at a concentration of 100 µg/mL.

Non Cross-Reacting Compounds

Acetophenetidin	Dextromethorphan	Methadone	Phenylpropanolamine
N-Acetylprocainamide	Diazepam	D-methamphetamine	Prednisolone
Acetylsalicylic acid	Diclofenac	(L)-methamphetamine	Prednisone
Aminopyrine	Diflunisal	Methoxyphenamine	Procaine
Amobarbital	Digoxin	3,4-Methylenedioxyethyl-	D,L-Propanolol
Amoxicillin	Diphenhydramine	amphetamine	D-Propoxyphene
Ampicillin	Doxylamine	(±) 3,4-Methylenedioxy-	D-Pseudoephedrine
L-Ascorbic acid	Ecgonine hydrochloride	methamphetamine	Quinidine
Apomorphine	Ecgonine methylester	Methylphenidate	Quinine
Aspartame	(IR,2S)-(-)-Ephedrine	Morphine-3-β-D-	Ranitidine
Atropine	L-Ephedrine	glucuronide	Salicylic acid
D,L -Amphetamine	Erythromycin	Nalidixic acid	Secobarbital
L-Amphetamine	Ethyl-p-aminobenzoate	Naloxone	Serotonin
Benzilic acid	Fenfluramine	Naltrexone	(5-Hydroxytyramine)
Benzoic acid	Fenoprofen	Naproxen	Sulfamethazine
Benzoylecgonine	Furosemide	Niacinamide	Sulindac
Benzphetamine	Gentisic acid	Nifedipine	Temazepam
Bilirubin	Hemoglobin	Norcodein	Tetracycline
(±)-Brompheniramine	Hydralazine	(-)-ψ- Ephedrine	Tetrahydrocortisone,
Caffeine	Hydrochlorothiazide	Norethindrone	3 Acetate
Cannabidiol	Hydrocodone	D-Norpropoxyphene	Tetrahydrocortisone
Cannabinol	Hydrocortisone	Noscapine	3 (β-D glucuronide)
Chloralhydrate	p-Hydroxyamphetamine	D,L-Octopamine	Tetrahydrozoline
Chloramphenicol	O-Hydroxyhippuric acid	Oxalic acid	Thebaine
Chlordiazepoxide	3-Hydroxytyramine	β-Estradiol	Thiamine
Chlorothiazide	p-Hydroxy-	Oxycodone	Thioridazine
(±) Chlorpheniramine	methamphetamine	Oxymetazoline	Tolbutamine
Chlorpromazine	Ibuprofen	Papaverine	Triamterene
Chlorquine	(±)-Isoproterenol	Penicillin-G	Trifluoperazine
Cholesterol	Isoxsuprine	Pentazocine	Trimethoprim
Clonidine	Ketamine	Pentobarbital	D, L-Tryptophan
Cocaine hydrochloride	Ketoprofen	Phencyclidine	Tyramine
Codeine	Labetalol	Phenelzine	D, L-Tyrosine
Cortisone	Levorphanol	Phenobarbital	Uric acid
(-) Cotinine	Loperamide	Phentermine	Verapamil
Creatinine	Meperidine	L-Phenylephrine	Oxazepam
Deoxycorticosterone	Meprobamate	β-Phenylethlamine	Zomepirac

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QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control line region (C) is considered an internal positive procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique. In addition, if the test has been performed properly, the background will clear to provide a distinctive result.
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.

LIMITATION OF PROCEDURE

1. The TCA RapiDip™ (Urine) provides only a preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Gas chromatography/mass spectrometry (GC/MS) or high performance liquid chromatography (HPLC) are the preferred confirmatory methods.[1,2]
2. The TCA RapiDip™ (Urine) is a qualitative screening assay and cannot determine either the drug concentration in the urine or the level of intoxication.
3. It is possible that technical or procedural errors, as well as other interfering substances in the urine specimen may cause erroneous results.
4. 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.
5. A positive result indicates presence of the drug or its metabolites but does not indicate level or intoxication, administration route or concentration in urine.
6. 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.

EXPECTED VALUES

This negative result indicates that the Tricyclic Antidepressants concentration is below the detectable level of 1000ng/ml. Positive result means the concentration of Tricyclic Antidepressants is above the level of 1000ng/ml. The TCA RapiDip™ has a sensitivity of 1000ng/ml.

PRECAUTION

- 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

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.

REFERENCE

1. Rose,J.B., *Tricyclic antidepressants toxicity*. J. Toxicity Clin. Toxicol. 11,381-402,1977
2. Hawks RL, CN Chiang. *Urine Testing for Drugs of Abuse*. National Institute for Drug Abuse (NIDA), Research Monograph 73, 1986

ISO 13485
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