TML Rapid Test Dipstick (Urine)
Package Insert

REF DTM-101/111 | **English**

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

【INTENDED USE】

The TML Rapid Test Dipstick (Urine) is a rapid chromatographic immunoassay for the qualitative detection of Tramadol in human urine at a cut-off concentration of 100 ng/mL. It is a prescription assay intended for use by healthcare professionals including those at point of care sites. This test will detect other related compounds, please refer to the Analytical Specificity table in this package insert.

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) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

【SUMMARY】

Tramadol(TML) is a quasi-narcotic analgesic used in the treatment of moderate to severe pain. It is a synthetic analog of codeine, but has a low binding affinity to the mu-opioid receptors. Large doses of tramadol can develop tolerance and physiological dependency and lead to its abuse. Tramadol is extensively metabolized after oral administration. Approximately 30% of the dose is excreted in the urine as unchanged drug, whereas 60% is excreted as metabolites. The major pathways appear to be N- and O- demethylation, glucoronidation or sulfation in the liver.

The TML Rapid Test Dipstick (Urine) is a rapid urine-screening test that can be performed without the use of an instrument. The test utilizes the antibody to selectively detect elevated levels of Tramadol in urine. The TML Rapid Test Dipstick (Urine) yields a positive result when Tramadol in urine exceeds 100 ng/mL. At present, the Substance Abuse and Mental Health Services Administration (SAMHSA) does not have a recommended screening cutoff for Tramadol positive specimens.

【PRINCIPLE】

The TML 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. Tramadol, if present in the urine specimen below 100 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 Tramadol 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 Tramadol level exceeds 100 ng/mL because it will saturate all the binding sites of anti-Tramadol 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 less 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-Tramadol antibody-coupled particles and Tramadol-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.

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 particles should be centrifuged, filtered, or allowed to 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 Dipsticks
- Package insert

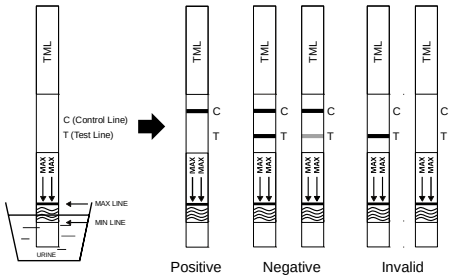
Materials Required But Not Provided

- Specimen collection container
- Timer

【DIRECTIONS FOR USE】

Allow the test, urine specimen, and/or controls to reach room temperature (15-30ºC) prior to testing.

1. Bring the pouch to room temperature before opening it. Remove the Test Dipstick from the sealed pouch or the closed canister 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 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 Tramadol concentration is below the detectable cut-off level (100 ng/mL).

***NOTE:** The shade of color in the test line region (T) may vary, but it should be considered 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 Tramadol concentration exceeds the detectable cut-off level (100 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 with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

【QUALITY CONTROL】

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

【LIMITATIONS】

1. The TML 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) is the preferred confirmatory method.[1,2]
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 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 Tramadol concentration is below the detectable level of 100ng/ml. Positive result means the concentration of Tramadol is above the level of 100ng/ml. The TML Rapid Test Dipstick has a sensitivity of 100ng/ml

【PERFORMANCE CHARACTERISTICS】

Accuracy

A comparison was conducted using the TML Rapid Test Dipstick (Urine) and GC/MS at 100 ng/mL cutoff. The following results were tabulated:

Method		GC/MS		Total Results
TML Rapid Test Dipstick	Results	Positive	Negative	
	Positive	82	12	94
	Negative	11	145	156
Total Results		93	157	250
% Agreement with GC/MS		88.2%	92.4%	90.8%

Analytical Sensitivity

A drug-free urine pool was spiked with Tramadol at the following concentrations: 0 ng/mL, 50 ng/mL, 75 ng/mL, 100 ng/mL, 125 ng/mL, 150 ng/mL and 300 ng/mL. The result demonstrates >99% accuracy at 50% above and 50% below the cut-off concentration of 100 ng/mL. The data are summarized below:

Tramadol Concentration (ng/mL)	Percent of Cut-off	n	Visual Result	
			Negative	Positive
0	0%	30	30	0
50	-50%	30	30	0
75	-25%	30	27	3
100	Cut-off	30	15	15
125	+25%	30	4	26
150	+50%	30	0	30
300	3X	30	0	30

Analytical Specificity

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

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
n-Desmethyl-cis-tramadol	200	o-Desmethyl-cis-tramadol	10,000
Cis-tramadol	100	Phencyclidine	100,000
Procyclidine	100,000	d,l-O-Desmethyl venlafaxine	50,000

Precision

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 Tramadol, 25% Tramadol above and below the cut-off, and 50% Tramadol above and below the 100 ng/mL cut-off were provided to each site. The following results were tabulated:

Tramadol Concentration (ng/mL)	n per Site	Site A		Site B		Site C	
		-	+	-	+	-	+
0	10	10	0	10	0	10	0
50	10	10	0	10	0	10	0
75	10	9	1	9	1	8	2
125	10	1	9	1	9	2	8
150	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 50 ng/mL and 150 ng/mL of Tramadol. The TML 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 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 Tramadol to 50 ng/mL and 150 ng/mL. The spiked, pH-adjusted urine was tested with the TML Rapid Test Dipstick (Urine) 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 Tramadol positive urine. The following compounds show no cross-reactivity when tested with the TML Rapid Test Dipstick (Urine) at a concentration of 100 μg/mL.

Non Cross-Reacting Compounds

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

【BIBLIOGRAPHY】

1. Dayer P, Collart L, Desmeules J. The pharmacology of tramadol. Division of Clinical Pharmacology and Pain Clinic, University Hospital, Geneva, Switzerland. Drugs [1994, 47 Suppl 1:3-7]
2. Lee CR, McTavish D, Sorkin EM. Tramadol. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute and chronic pain states. Adis International Limited, Auckland, New Zealand. Drugs [1993, 46(2):313-40]

Index of Symbols

	Attention, see instructions for use	Σ	Tests per kit	EC REP	Authorized Representative
IVD	For in vitro diagnostic use only		Use by		Do not reuse
30°C 2°C	Store between 2-30°C	LOT	Lot Number	REF	Catalog #
	Do not use if package is damaged				

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