Test Definition: MTDNX

Methadone Confirmation, Chain of Custody, Random, Urine

Overview

Useful For

Monitoring for compliance of methadone treatment for analgesia or drug rehabilitation

Assessing compliance with rehabilitation programs

Chain of custody is required whenever the results of testing could be used in a court of law. Its purpose is to protect the rights of the individual contributing the specimen by demonstrating that it was always under the control of personnel involved with testing the specimen; this control implies that the opportunity for specimen tampering would be limited.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
COCH	Chain of Custody Processing	No	Yes
ADLTX	Adulterants Survey, CoC, U	Yes	Yes

Testing Algorithm

Adulterants testing will be performed on all chain of custody urine samples as per regulatory requirements.

Method Name

Immunoassay/Gas Chromatography Mass Spectrometry (GC-MS)

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

This test is for situations that require the chain-of-custody process. For testing **not** requiring chain of custody, order MTDNU / Methadone Confirmation, Random, Urine

Specimen Required

Supplies: Chain of Custody Kit (T282)
Container/Tube: Chain-of-custody kit containing the specimen containers, seals, and documentation required.
Specimen Volume: 10 mL

Collection Instructions: Collect urine specimen in the container provided, seal, and submit with the associated documentation to satisfy the legal requirements for chain-of-custody testing.
Additional Information: Submitting less than 10 mL will compromise our ability to perform all necessary testing.

Forms

1. Chain of Custody Request is included in the Chain-of-Custody Kit (T282).
2. If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

2.5 mL

Reject Due To

Gross hemolysis	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Refrigerated (preferred)	28 days	
	Ambient	14 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Methadone (Dolophine) is a synthetic opioid, a compound that is structurally unrelated to natural opiates but is capable of binding to opioid receptors. These receptor interactions create many of the same effects seen with natural opiates, including analgesia and sedation. However, methadone does not produce feelings of euphoria and has substantially fewer withdrawal symptoms than opiates such as heroin.(1) Methadone is used clinically to relieve pain, treat opioid abstinence syndrome, and treat heroin addiction in an attempt to wean patients from illicit drug use.

Metabolism of methadone to inactive forms is the main form of elimination. Oral delivery of methadone makes it subject to first-pass metabolism by the liver and creates interindividual variability in its bioavailability, which ranges from 80% to 95%. The most important enzymes in methadone metabolism are cytochrome P450 (CYP) 3A4 and CYP2B6.(1-4) CYP2D6 appears to have a minor role, and CYP1A2 may possibly be involved.(1-5) Methadone is metabolized to a variety of metabolites, the primary metabolite is 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP).(1-4) The efficiency of this process is prone to wide inter- and intraindividual variability due to inherent differences in enzymatic activity as well as enzyme induction or inhibition by numerous drugs. Excretion of methadone and its metabolites (including EDDP) occurs primarily through the kidneys.(1,4)

Patients who are taking methadone for therapeutic purposes excrete both parent methadone and EDDP in their urine.

Clinically, it is important to measure levels of both methadone and EDDP. Methadone levels in urine vary widely depending on factors such as dose, metabolism, and urine pH.(5) EDDP levels, in contrast, are relatively unaffected by the influence of pH and are, therefore, preferable for assessing compliance with therapy.(5)

Some patients undergoing treatment with methadone have attempted to pass compliance testing by adding a portion of the supplied methadone to the urine.(6) This is commonly referred to as "spiking." In these situations, the specimen will contain large amounts of methadone and no or very small amounts of EDDP.(6) The absence of EDDP in the presence of methadone in urine strongly suggests adulteration of the urine specimen by direct addition of methadone to the specimen.

Chain of custody is a record of the disposition of a specimen to document the personnel who collected, handled, and performed the analysis. When a specimen is submitted in this manner, analysis will be performed in such a way that it will withstand regular court scrutiny.

Reference Values

Negative
Positive results are reported with a quantitative result.

Cutoff concentrations:

Immunoassay screen: 300 ng/mL

Gas chromatography mass spectrometry:
Methadone: 100 ng/mL
2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine: 100 ng/mL

Interpretation

The absolute concentration of methadone and its metabolites found in patient urine specimens can be highly variable and does not correlate with dose. However, the medical literature and our experience show that patients who are known to be compliant with their methadone therapy have ratios of 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP):methadone of greater than 0.60.(7)

An EDDP:methadone ratio less than

Cautions

Urine pH has a considerable effect on the ability to detect methadone, thus 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine is preferable for urine measurements.

Urine concentrations of methadone show very poor correlation to serum levels or the amount of drug administered.

Clinical Reference

1. Gutstein HB, Akil H. Opioid analgesics. In: Hardman JG, Limbird LE, eds. Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 10th ed. McGraw-Hill; 2001:569-619
2. Eap CB, Buclin T, Baumann P. Interindividual variability of the clinical pharmacokinetics of methadone: implications for the treatment of opioid dependence. Clin Pharmacokinet. 2002;41(14):1153-1193

3. Ferrari A, Coccia CP, Bertolini A, Sternieri E. Methadone-metabolism, pharmacokinetics and interactions. Pharmacol Res. 2004;50(6):551-559
4. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 7th ed. Chemical Toxicology Institute; 2005
5. Levine B. Principles of Forensic Toxicology. 2nd ed. AACC Press; 2003:385
6. Galloway FR, Bellet NF. Methadone conversion to EDDP during GC-MS analysis of urine samples. J Anal Toxicol. 1999;23(7):615-619
7. George S, Braithwaite RA. A pilot study to determine the usefulness of the urinary excretion of methadone and its primary metabolite (EDDP) as potential markers of compliance in methadone detoxification programs. J Anal Toxicol. 1999;23:81-85
8. Jutkiewicz EM, Traynor JR. Opioid analgesics. In: Brunton LL, Knollmann BC, eds. Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 14th Ed. McGraw-Hill Education; 2023
9. Langman LJ, Bechtel LK, Holstege CP. Clinical toxicology. In: Rifai N, Chiu RWK, Young I, Burnham C-AD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:chap 43

Performance

Method Description

This assay is based on the kinetic interaction of microparticles in a solution as measured by changes in light transmission. In the absence of sample drug, soluble drug conjugates bind to antibody-bound microparticles causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample drug, the absorbance increases. When a urine sample contains the drug in question, this drug competes with the drug derivative conjugate for microparticle-bound antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample. Sample drug content is determined relative to the value obtained for a known cutoff concentration of drug.(Package insert: EDDP Methadone Metabolite Enzyme Immunoassay. Roche (LIN-ZHI); V 3.0, 11/2023;)

Confirmation with quantification is performed by gas chromatography mass spectrometry (GC-MS).(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Tuesday, Thursday

Report Available

3 to 7 days

Specimen Retention Time

14 days

Performing Laboratory Location

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

G0480

80358 (if appropriate for select payers)

Clinical Toxicology CPT Code Client Guidance

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MTDNX	Methadone Confirmation, CoC, U	104626-7

Result ID	Test Result Name	Result LOINC® Value
21105	Methadone Immunoassay Screen	70149-0
36208	EDDP-by GC-MS	104627-5
36209	Methadone-by GC-MS	104628-3
36210	Methadone Interpretation	69050-3
36211	Chain of Custody	77202-0