

## Overview

### Useful For

Monitoring for compliance of methadone treatment for analgesia or drug rehabilitation

Urine measurement of 2-ethylidene-1,5-dimethyl-1,3,3-diphenylpyrrolidine is particularly useful for 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 under the control of personnel involved with testing the specimen at all times; 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) Confirmation with Quantitation

### NY State Available

Yes

## Specimen

### Specimen Type

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:** 20 mL

**Collection Instructions:** Collect 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 <20 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	
	Frozen	28 days	
	Ambient	14 days	

**Clinical and Interpretive**
**Clinical Information**

Methadone (dolophine) is a synthetic opioid, a compound that is structurally unrelated to the 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, to treat opioid abstinence syndrome, and to treat heroin addiction in the 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-1,3,3-diphenylpyrrolidine (EDDP).(1-4) The efficiency of this process is prone to wide inter- and intraindividual variability, due both 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

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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 who collected it, who handled it, and who 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

### Cutoff concentrations:

IMMUNOASSAY SCREEN

<300 ng/mL

METHADONE BY GC-MS

<100 ng/mL

2-ETHYLIDENE-1,5-DIMETHYL-3,3-DIPHENYLPYRROLIDINE BY GC-MS

<100 ng/mL

### Interpretation

The absolute concentration of methadone and its metabolites found in patient urine specimen can be highly variable and do 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 >0.60.(7)

An EDDP: methadone ratio <0.090 strongly suggests manipulation of the urine specimen by direct addition of methadone to the specimen.(6)

### 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. Chapter 23: Opioid analgesics. In Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 10th edition. Edited by HB Gutstein, H Akil. McGraw-Hill Book Company, 2001, pp 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;41:1153-1193
3. Ferrari A, Coccia CP, Bertolini A, Sternieri E: Methadone-metabolism, pharmacokinetics and interactions. Pharmacol Res 2004;50:551-559
4. Baselt RC: Disposition of Toxic Drugs and Chemicals in Man. Seventh edition. Foster City, CA, Chemical Toxicology Institute, 2005

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5. Principles of Forensic Toxicology. Second edition. AACCC Press, 2003, pp 385
  6. Galloway FR, Bellet NF: Methadone conversion to EDDP during GC-MS analysis of urine samples. J Anal Toxicol 1999;23:615-619
  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. Nader R, Horwath AR, Wittwer CT: Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. Sixth Edition. Elsevier 2018

## Performance

### Method Description

This test includes immunoassay and confirmation with quantification by gas chromatography-mass spectrometry (GC-MS).(Unpublished Mayo method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Monday, Wednesday, Friday; Varies

### Analytic Time

2 days

### Maximum Laboratory Time

5 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Rochester

## Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

### CPT Code Information

80358

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G0480 (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
MTDNX	Methadone Confirmation, CoC, U	In Process

Result ID	Test Result Name	Result LOINC Value
21105	Methadone Immunoassay Screen	70149-0
36208	EDDP-by GC-MS	58429-2
36209	Methadone-by GC-MS	16199-2
36210	Methadone Interpretation	69050-3
36211	Chain of Custody	77202-0