Overview

Useful For
Monitoring for compliance of methadone treatment for analgesia or drug rehabilitation

Assessing compliance with rehabilitation programs by urine measurement of 2-ethylidene-1,5-dimethyl-1,3,3-diphenylpyrrolidine

Method Name
Gas Chromatography-Mass Spectrometry (GC-MS) Confirmation with Quantitation

NY State Available
Yes

Specimen

Specimen Type
Urine

Advisory Information
1. For situations where chain of custody is required, a Chain-of-Custody Kit (T282) is available. For chain-of-custody testing, order MTDNX / Methadone Confirmation, Chain of Custody, Random, Urine.

2. Additional drug panels and specific requests are available. Call 800-533-1710 or 507-266-5700.

3. If urine creatinine is required or adulteration of the sample is suspected, order ADULT / Adulterants Survey, Random, Urine.

Specimen Required
Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic, 10-mL urine tube

Specimen Volume: 10 mL

Collection Instructions:
1. Collect a random urine specimen.

2. No preservative.

Forms
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

<table>
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<th>Gross hemolysis</th>
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Document generated March 25, 2020 at 7:47am CDT
Test Definition: MTDNU
Methadone Confirmation, U

| Gross icterus | OK |

Specimen Stability Information

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<th>Temperature</th>
<th>Time</th>
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<tr>
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<td></td>
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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 with the primary metabolite being 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 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 presence of methadone in urine strongly suggests adulteration of the urine specimen by direct addition of methadone to the specimen.

Reference Values

Negative

Cutoff concentrations:

METHADONE BY GC-MS

<100 ng/mL
**Test Definition: MTDNU**

**Methadone Confirmation, U**

2-ETHYLIDENE-1,5-DIMETHYL-3,3-DIPHENYL PYRROLIDINE 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 greater than 0.60.(7)

An EDDP:methadone ratio less than 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**


**Performance**

**Method Description**

Confirmation is performed by gas chromatography-mass spectrometry, solid phase extraction.(Unpublished Mayo method)

**PDF Report**
Test Definition: MTDNU
Methadone Confirmation, U

No

Day(s) and Time(s) Test Performed
Tuesday through Friday

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

G0480 (if appropriate)

LOINC® Information

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