

Overview

Useful For

Compliance monitoring of methadone

Assessment of methadone toxicity

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Container/Tube: Red top (Serum gel/SST are **not acceptable**)

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send a [Therapeutics Test Request](#) (T831) with the specimen.

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Minimum Volume

0.2 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	14 days	
	Ambient	14 days	
	Frozen	14 days	

Clinical & Interpretive**Clinical Information**

Methadone, a long-acting synthetic opioid analgesic, is an agonist at the mu receptor. It has several actions qualitatively similar to those of morphine, primarily involving the central nervous system and organs composed of smooth muscles. Analgesia, sedation, and detoxification or maintenance in opioid addiction can be achieved with therapeutic use of methadone hydrochloride. Methadone acts by binding to the mu-opioid receptor but also has some affinity for the N-methyl-D-aspartate receptor (NMDA) ionotropic glutamate receptor.

Methadone undergoes extensive biotransformation in the liver. Methadone is metabolized by cytochrome P450 (CYP) 3A4, CYP2B6, CYP2C19, and CYP2D6 enzymes. It is also a substrate for the P-glycoprotein efflux protein. The major inactive metabolite is a result of N-demethylation and cyclization, and forms 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidene (EDDP).

Substantial interindividual and intraindividual variabilities in metabolism and elimination have been noted. The half-life of methadone is highly variable and typically ranges from 7 to 59 hours; however, longer half-lives have been reported.

Reference Values

Not established

Interpretation

There is a significant overlap between the reported therapeutic and toxic concentrations of methadone in blood specimens.

Cautions

Methadone has a wide therapeutic index and dose-dependent toxicity. As a result, routine drug monitoring is not indicated in all patients.

Specimens collected in serum gel tubes are not acceptable because the drug can absorb on the gel and lead to falsely decreased concentrations.

Clinical Reference

1. Langman LJ, Bechtel LK, Meier BM, Holstege C: Clinical toxicology. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:832-887
2. Yaksh TL, Wallace MS: Chapter 18: Opioids, analgesia, and pain management. In: Brunton LL, Chabner BA, Knollmann BC, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 12th ed. McGraw-Hill Book Company; 2011
3. Baselt RC: Disposition of Toxic Drugs and Chemical in Man. 9th ed. Biomedical Publications; 2011:1021-1025

Performance**Method Description**

Liquid/liquid extraction of the serum sample followed by liquid chromatography-tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Performing Laboratory Location

Rochester

Fees & Codes**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 US Food and Drug Administration.

CPT Code Information

80358

G0480 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MDNS	Methadone and Metabolite, S	96602-8

Result ID	Reporting Name	LOINC®
36309	Methadone	3772-1
36310	EDDP	60071-8