Test Definition: MDNS

Methadone and Metabolites, Serum

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

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Red top (Serum gel/SST are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 1.0 mL
Collection Instructions: Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.

Forms

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

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container

Serum Red	Refrigerated (preferred)	28 days	
	Ambient	14 days	
	Frozen	28 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

Methadone:
Therapeutic: 100-400 ng/mL
Toxic: >2000 ng/mL

EDDP:
Not established

Cutoff concentrations by liquid chromatography tandem mass spectrometry:
Methadone: 10 ng/mL
EDDP: 5.0 ng/mL

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, Holstege CP. Clinical toxicology. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:chap 43
2. Yaksh TL, Wallace MS. 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:chap 18
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

Day(s) Performed
Tuesday, Thursday

Report Available
3 to 5 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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
80299

LOINC® Information

Test Definition: MDNS

Methadone and Metabolites, Serum

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

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