MAYO CLINIC LABORATORIES

Test Definition: AMTRP

Amitriptyline and Nortriptyline, Serum

Overview

Useful For

Monitoring amitriptyline and nortriptyline serum concentrations during therapy

Evaluating potential amitriptyline and nortriptyline toxicity

May aid in evaluating patient compliance

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 mL Serum
Collection Instructions:
1. Collect specimen immediately before next scheduled dose (minimum 12 hours after last dose).
2. Within 2 hours of collection centrifuge and aliquot serum into a plastic vial. Serum **must be** separated from cells within 2 hours of collection.

Forms

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

Specimen Minimum Volume

Serum: 0.25 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	28 days	
	Ambient	7 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Amitriptyline is a tricyclic antidepressant that is metabolized to nortriptyline, which has similar pharmacologic activity. The relative blood levels of amitriptyline and nortriptyline are highly variable among patients. Amitriptyline is the drug of choice in treatment of depression when the side effect of mild sedation is desirable. Nortriptyline is used when its stimulatory side effect is considered to be of clinical advantage.

Nortriptyline is unique among the antidepressants in that its blood level exhibits the classical therapeutic window effect, as blood concentrations above or below the therapeutic window correlate with poor clinical response. Therefore, therapeutic monitoring to ensure that the blood level is within the therapeutic window is critical to accomplish successful treatment with this drug.

Amitriptyline displays major cardiac toxicity when the combined serum level of amitriptyline and nortriptyline is above 500 ng/mL, characterized by QRS widening (intraventricular conduction delay), which leads to ventricular tachycardia and asystole. In some patients, toxicity may manifest at lower concentrations.

Like amitriptyline, nortriptyline can cause major cardiac toxicity when the concentration is above 500 ng/mL, characterized by QRS widening, which leads to ventricular tachycardia and asystole. In some patients, toxicity may manifest at lower concentrations.

Reference Values

Amitriptyline and nortriptyline
Total therapeutic concentration: 80-200 ng/mL

Nortriptyline
Therapeutic concentration: 70-170 ng/mL
Note: Therapeutic ranges are for specimens collected at trough (ie, immediately before next scheduled dose). Levels may be elevated in non-trough specimens.

Interpretation

Most individuals display optimal response to amitriptyline when combined serum levels of amitriptyline and nortriptyline are between 80 and 200 ng/mL. Risk of toxicity is increased with combined levels are above 500 ng/mL.

Most individuals display optimal response to nortriptyline with serum levels between 70 and 170 ng/mL. Risk of toxicity is increased with nortriptyline levels above 500 ng/mL.

Some individuals may respond well outside of these ranges or may display toxicity within the therapeutic range; hence, interpretation should include clinical evaluation.

Therapeutic ranges are based on specimens collected at trough (ie, immediately before the next dose).

Cautions

This test cannot be performed on whole blood. Serum must be separated from cells within 2 hours of collection; if serum is not removed within this time, tricyclic antidepressant levels may be falsely elevated due to drug release from red blood cells.

Specimens that are obtained from gel tubes are not acceptable because the drug can absorb on the gel and lead to falsely decreased concentrations.

Clinical Reference

1. Wille SM, Cooreman SG, Neels HM, Lambert WE. Relevant issues in the monitoring and the toxicology of antidepressants. Crit Rev Clin Lab Sci. 2008;45(1):25-89
2. Thanacoody HK, Thomas SHL. Antidepressant poisoning. Clin Med (Lond). 2003;3(2):114-118
3. Hiemke C, Bergemann N, Clement HW, et al. Consensus guidelines for therapeutic drug monitoring in neuropsychopharmacology: Update 2017. Pharmacopsychiatry. 2018;51(1-02):e1. doi:10.1055/s-0037-1600991
4. Milone MC, Shaw LM. Therapeutic drugs and their management. In: Rifai N, Chiu RWK, Young I, Burnham C-AD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:420-453

Performance

Method Description

The tricyclic antidepressants are extracted from serum using a solvent to precipitate proteins. The supernatant is removed, and analysis is by liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday, Wednesday, Friday

Report Available

2 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 ID	Test Order Name	Order LOINC® Value
AMTRP	Amitriptyline and Nortriptyline, S	43106-4

Result ID	Test Result Name	Result LOINC® Value
63506	Amitriptyline	3333-2
36755	Nortriptyline	3872-9
36756	Amitriptyline and Nortriptyline	3335-7