MAYO CLINIC LABORATORIES

Test Definition: CLZ

Clozapine, Serum

Overview

Useful For

Monitoring patient compliance of clozapine treatment

An aid to achieving desired serum levels

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
Collection Instructions:
1. Collect specimen immediately before next scheduled dose.
2. Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.
Additional Information: Therapeutic range (trough level) applies to specimens collected immediately prior to next dose.

Forms

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

Specimen Minimum Volume

0.6 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	7 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Clozapine (Clozaril), a tricyclic dibenzodiazepine, is used for the symptomatic management of psychotic disorders and is considered an atypical antipsychotic drug. It is currently used primarily for the treatment of patients with schizophrenia or schizoaffective disorders who are at risk for recurrent suicidal behavior and who have encountered nonresponse or adverse, intolerable extrapyramidal side effects with more classical antipsychotics (chlorpromazine, haloperidol).

Although clozapine was developed about 30 years ago and the initial results were promising, the development of several fatal cases of agranulocytosis resulted in the discontinued use of this agent. Seizures, orthostatic hypotension, and an increased risk of fatal myocarditis have also been associated with the use of clozapine. The use of clozapine has regained interest for several reasons. Patients who did not respond to treatment with other antipsychotics improved when clozapine was administered. Also, agranulocytosis, which occurs in approximately 1% to 2% of patients, can be controlled with close hematologic monitoring. However, because of the significant risk of agranulocytosis and seizure associated with its use, clozapine should only be used in patients who have failed to respond adequately to treatment with appropriate courses of standard drug treatments, either because of insufficient effectiveness or the inability to achieve an effective dose because of intolerable adverse reactions from those drugs.

Treatment is usually started with dosages of 25 to 75 mg/day with a gradual increase to reach a final dose of 300 to 450 mg/day within approximately 2 weeks of the initiation of treatment. Once the desired effect is achieved, the dose may be gradually decreased to keep the patient on the lowest possible effective dose.

Patients being treated with clozapine should be closely monitored during treatment for adverse reactions. Treatment must include monitoring of white blood cell count and absolute neutrophil count. Clozapine treatment should be discontinued in patients failing to show an acceptable clinical response. In addition, the need for continuing treatment should be periodically reevaluated in patients exhibiting beneficial clinical responses.

Clozapine is metabolized to desmethylated and N-oxide derivatives. The desmethyl metabolite (norclozapine) has only limited activity, and N-oxide metabolite is inactive.

Reference Values

Clozapine
Therapeutic range: 350-600 ng/mL

Norclozapine
Therapeutic range: Not well established

Clozapine + Norclozapine
Therapeutic range: Not well established

Interpretation
The effectiveness of clozapine treatment should be based on clinical response and treatment should be discontinued in patients failing to show an acceptable clinical response.

Cautions
No significant cautionary statements

Clinical Reference
1. Volpicelli SA, Centorrino F, Puopolo PR, et al. Determination of clozapine, norclozapine, and clozapine-N-oxide in serum by liquid chromatography. ClinChem. 1993;39(8):1656-1659
2. Chung MC, Lin SK, Chang WH, Jann MW. Determination of clozapine and desmethylclozapine in human plasma by high-performance liquid chromatography with ultraviolet detection. J Chromatogr. 1993;613(1):168-173. doi:10.1016/0378-4347(93)80212-m
3. Perry PJ, Miller DD, Arndt SV, Cadoret RJ. Clozapine and norclozapine plasma concentrations and clinical response of treatment-refractory schizophrenia patients. Am J Psychiatry. 1991;148(2):231-235. doi:10.1176/ajp.148.2.231
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5. Fitton A, Heel RC. Clozapine. A review of its pharmacological properties, and therapeutic use in schizophrenia. Drugs. 1990;40(5);722-747. doi:10.2165/00003495-199040050-00007
6. Clozaril. Package insert: Novartis Pharmaceuticals; 05/2005
7. Mitchell PB. Therapeutic drug monitoring of psychotropic medications. Br J Clin Pharmacol. 2001;52(Suppl 1):45S-54S. doi:10.1046/j.1365-2125.2001.0520s1045.x
8. Hiemke C, Bergemann N, Clement HW, et al. Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology: Update 2017. Pharmacopsychiatry. 2018;51(1-02):9-62. doi:10.1055/s-0043-116492
9. Milone MC, Shaw LM. Therapeutic drugs and their management. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:420-453

Performance

Method Description
Deuterated stable isotope of clozapine is added to the serum sample as an internal standard. Protein is precipitated from the mixture by the addition of acetonitrile. Clozapine, norclozapine, and the internal standard are extracted from the resulting supernatant by an online extraction utilizing high-throughput liquid chromatography. This is followed by conventional liquid chromatography and analysis on a tandem mass spectrometer equipped with a heated nebulizer ion source.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Test Definition: CLZ

Clozapine, Serum

Report Available
3 to 5 days

Specimen Retention Time
2 weeks

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
80159

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CLZ	Clozapine, S	65632-2

Result ID	Test Result Name	Result LOINC® Value
33841	Norclozapine	10992-6
33842	Clozapine+Norclozapine Total	12375-2
33840	Clozapine	6896-5