MAYO CLINIC LABORATORIES

Test Definition: ECULI

Eculizumab, Serum

Overview

Useful For

Assessing the response to eculizumab therapy

Assessing the need for dose escalation

Evaluating the potential for dose de-escalation or discontinuation of therapy in remission states

Monitoring patients who need to be above a certain eculizumab concentration in order to improve the odds of a clinical response for therapy optimization

Method Name

Liquid Chromatography Tandem Mass Spectrometry, High-Resolution Accurate Mass (LC-MS/MS HRAM)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

Therapeutic drug monitoring of eculizumab may be useful when providers are considering personalized treatment decisions, such as therapy discontinuation of extended dose intervals when patients are in remission states.

For a panel that includes both eculizumab concentration and eculizumab complement blockage testing; order ECMP / Eculizumab Monitoring Panel, Serum.

Specimen Required

Patient Preparation: Suggest discontinuing natalizumab at least 4 weeks prior to testing for eculizumab quantitation in serum. Patient should consult the healthcare provider who prescribed this drug to determine if discontinuation is an option. If not, ok to proceed with testing while taking natalizumab**.**
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions:

1. Draw blood immediately before next scheduled dose.
2. Immediately after specimen collection, place the tube on wet ice.
3. After specimen has clotted on wet ice, centrifuge at 4 degrees C and aliquot serum into plastic vial.
4. Freeze specimen within 30 minutes of centrifugation. Specimen must be placed on dry ice if not frozen immediately.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Renal Diagnostics Test Request (T830)
-Coagulation Test Request (T753)
-Therapeutics Test Request (T831)

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Eculizumab (Soliris, Alexion Pharmaceuticals) is a humanized monoclonal IgG2/4 kappa antibody therapeutic directed against complement component 5 (C5). By association with C5, eculizumab inhibits the terminal complement pathway through simultaneous blockade of the generation of the potent prothrombotic and proinflammatory molecule, C5a, and the formation of membrane attack complex initiator, C5b.

Eculizumab is administered as an IV infusion. The dosing regimen prescribed for an average adult diagnosed with paroxysmal nocturnal hemoglobinuria (PNH) is 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, and 900 mg every 2 weeks thereafter. Eculizumab has been evaluated in patients with atypical hemolytic uremic syndrome (aHUS) through 2 prospective, open-label, single-arm studies (C08-002 and C08-003) as well as a single-arm retrospective study. In aHUS, it is prescribed for an average adult at 900 mg weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks thereafter. Eculizumab was generally well tolerated, and no significant adverse effects were attributed to drug treatment; some adverse reactions included upper respiratory tract infections and diarrhea in prospective and retrospective studies, hypertension, headache, and

leucopenia (C08-002/C08-003), and fever (C09-001R). Additional case reports suggest that eculizumab may prevent post transplantation recurrence of aHUS, even in those patients harboring *CFH/CFHR1* hybrid gene variants, who are at very high risk of recurrence. Further research is needed to determine the duration of eculizumab therapy in the context of the genetic background of aHUS cases and risk of disease relapse.

Therapeutic drug monitoring of eculizumab is helpful when providers are considering personalized treatment decisions, such as therapy discontinuation or extending dose intervals when patients are in remission states. In PNH, a minimum therapeutic concentration is expected to be above 35 mcg/mL. In aHUS, the therapeutic concentrations are expected to be above 50 to 100 mcg/mL of eculizumab. Complement blockage studies can aid in determining if a therapeutic concentration of the drug has blocked the complement function and subsequent production of sC5b-9. A panel that includes both eculizumab concentration and eculizumab complement blockage testing is available; see ECMP / Eculizumab Monitoring Panel, Serum.

Reference Values

Lower limit of quantitation =5.0 mcg/mL
>35 mcg/mL: Therapeutic concentration for paroxysmal nocturnal hemoglobinuria (PNH)
>50 mcg/mL: Therapeutic concentration for atypical hemolytic uremic syndrome (aHUS)

Interpretation

Minimum trough therapeutic concentrations (immediately before next infusion) of eculizumab are expected to be above 35 mcg/mL for paroxysmal nocturnal hemoglobinuria and above 50 mcg/mL for atypical hemolytic uremic syndrome.

Cautions

Patients in transition between eculizumab (ECULI / Eculizumab, Serum) and ravulizumab administration may have a skewed therapeutic level of the respective analytes reported under the relative orderable. Test results cannot be interpreted as absolute evidence for the presence or absence of malignant disease. This test should not form the sole basis for a diagnosis or treatment decisions.

Patients actively undergoing therapy with both natalizumab and eculizumab (extremely rare scenario) could present as assay interference. It is suggested patients discuss with their doctors the possibility of discontinuing natalizumab 4 weeks prior to testing. If discontinuation is not possible, ok to proceed with testing.

Clinical Reference

1. Ladwig PM, Barnidge DR, Willrich MA. Quantification of the IgG2/4 kappa monoclonal therapeutic eculizumab from serum using isotype specific affinity purification and microflow LC-ESI-Q-TOF mass spectrometry. J Am Soc Mass Spectrom. 2017;28(5):811-817
2. Willrich MA, Murray DL, Barnidge DR, et al. Quantitation of infliximab using clonotypic peptides and selective reaction monitoring by LC-MS/MS. Int Immunopharmacol. 2015;28(1):513-520
3. Ladwig PM, Barnidge DR, Willrich MA. Mass spectrometry approaches for identification and quantitation of therapeutic monoclonal antibodies in the clinical laboratory. Clin Vaccine Immunol. 2017;24(5):e00545-16

Performance

Method Description

Eculizumab is extracted from serum and measured by liquid chromatography high-resolution accurate-mass mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Wednesday

Report Available
3 to 9 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
ECULI	Eculizumab, S	90240-3

Result ID	Test Result Name	Result LOINC® Value
65676	Eculizumab, S	90240-3