Test Definition: ECULI

Eculizumab, Serum

Overview

Useful For

Assessing the response to eculizumab therapy when measured at trough, immediately before the next scheduled infusion

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

This assay **does not** differentiate between the originator and biosimilar products.

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 healthcare professionals 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 professional 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 Serum
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 a 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
Serum: 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
Drug and target:
Eculizumab 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.(1) The reference product for eculizumab is Soliris (Alexion Pharmaceuticals). Several biosimilars are US Food and Drug Administration (FDA)-approved, including eculizumab-aagh (Epysqli, Samsung Bioepis) and eculizumab-aeeb (Bkemv, Amgen).

Indications:
Eculizumab is FDA-approved for use in paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome

(aHUS), generalized myasthenia gravis and neuromyelitis optic spectrum disorder (NMOSD). All indications require meningococcal vaccination prior to therapy. Pediatric approval only applies to PNH and aHUS.(1) Eculizumab is administered as an intravenous (IV) infusion. The dosing regimen varies by indication. Eculizumab prescribed dosing for an average adult diagnosed with 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. 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.(1, 2) 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 high risk of recurrence.(3-7)

Pharmacokinetic highlights:
As an IV infusion, the bioavailability of the hybrid IgG2/IgG4 monoclonal antibody is estimated to be 100%. Eculizumab's half-life ranges from 8 to 15 days across studies, hence the administration every 2 weeks. Steady state is achieved after 4 to 5 half-lives, or approximately 4 to 6 weeks of therapy. Before then, serum concentrations tend to vary significantly. Higher clearance is observed in pediatric patients.

Immunogenicity:
The formation of anti-drug-antibodies (ADA) to eculizumab is uncommon (clinical trials suggest <2% detection) and not routinely investigated in clinical practice, as none of the detected antibodies were neutralizing nor influenced eculizumab's clinical response.(1) There are no clinical laboratory tests available to detect eculizumab ADA. Loss of efficacy is more often driven by underexposure, not formation of ADA.

Evidence for therapeutic drug monitoring:
There are two main uses for laboratory testing of eculizumab. The most used is the pharmacodynamic effect of eculizumab on complement blockage. Complement blockage studies can aid in determining if a therapeutic concentration of the drug has blocked the complement C5 function and subsequent production of sC5b-9.(8-10)

Measuring the concentration of eculizumab in serum is another use, most helpful when providers are considering personalized treatment decisions, such as therapy discontinuation or extending dose intervals beyond the standard every 2 weeks infusions, when patients are in remission states.(11-14) 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
>50 mcg/mL: Therapeutic concentration for atypical hemolytic uremic syndrome

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 to 100 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, it is okay to proceed with testing.

This assay is designed to quantify eculizumab, regardless of formulation. It is suitable for testing both the reference product and all US Food and Drug Administration/European Medicines Agency-approved biosimilars. It cannot differentiate between the originator and biosimilar products.

Clinical Reference

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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