
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 (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum

Advisory Information

Therapeutic drug monitoring of eculizumab may be useful when assessing response to therapy is difficult or patients need to be above a certain therapeutic monoclonal antibody (mAb) concentration in order to improve the odds of a clinical response for therapy optimization, including potential dose de-escalation or discontinuation of therapy in remission states. Pharmacodynamic studies of complement blockage are also common, see ECUMP / Eculizumab Monitoring Panel, Serum for more information on related testing.

Specimen Required

Patient Preparation: Pembrolizumab/Keytruda must be discontinued at least 4 weeks prior to testing for eculizumab quantitation in serum.

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 1 mL

Collection Instructions:

1. Draw blood immediately before next scheduled dose.
2. Spin down within 2 hours of draw.

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)

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	Refrigerated (preferred)	28 days	
	Frozen	30 days	
	Ambient	4 days	

Clinical and Interpretive

Clinical Information

Eculizumab (Soliris, Alexion Pharmaceuticals), a humanized monoclonal IgG2/4 kappa antibody therapeutic directed against complement component C5, has been heralded as a breakthrough treatment for paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). 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. Since all 3 arms of the complement cascade converge at the point of C5 activation, targeted by eculizumab, this drug may have broad potential application and is being clinically evaluated in other disorders with complement overactivation. In PNH, eculizumab has become the standard of care, proving to be a safe and effective therapy with long-lasting effects, potentially enabling patients to become transfusion-independent and extending their survival.

Eculizumab is administered as an IV infusion, and the dosing regimen prescribed 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; then, 900 mg every 2 weeks thereafter. Eculizumab has been evaluated in aHUS patients 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 posttransplantation 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.

The drawbacks of eculizumab therapy are associated with its potentially life-threatening side-effects, variations in response profiles, and the cost of treatment. Patients treated with eculizumab are at an increased risk of susceptibility towards life-threatening infections such as *Neisseria meningitides*; to prevent such infections, vaccinations and, in some cases, prophylactic antibiotic treatment is recommended. A number of serious and potentially treatment-related adverse effects were observed including pyrexia, headache, abdominal distension, viral infection, renal impairment, and anxiety. It is important to note that there is variability among individuals towards eculizumab response, and some patients may not benefit from this therapy. This is potentially a life-long therapy with a high cost of administration. The cost of eculizumab may limit its use in routine clinical practice worldwide.

Therapeutic drug monitoring of eculizumab is typically not performed during treatment regimens due to the low toxicity of biologics. Measurement of therapy efficacy is usually based on clinical presentation and improvement of symptoms, although this landscape is changing, as it is recognized that patients undergoing life-long therapy with eculizumab who are in complete remission without significant evidence or pathogenic genetic variants leading to increased risk of relapse may benefit from dose de-escalation or discontinuing therapy.

Pharmacodynamic studies of complement blockage may also be recommended, see ECUMP / Eculizumab Monitoring Panel, Serum for more information.

Reference Values

Lower limit of quantitation =5.0 mcg/mL

>35 Therapeutic concentration for paroxysmal nocturnal hemoglobinuria (PNH)

>50 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 (PNH) and above 50 mcg/mL for aHUS.

Cautions

Patients actively undergoing therapy with both pembrolizumab and eculizumab (extremely rare scenario) should not have their therapeutic eculizumab level assessed using this test. If the patient has taken pembrolizumab in the past, they should wait for 4 weeks after therapy with pembrolizumab has ended before being tested for eculizumab quantitation using this method.

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 May;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. International immunopharmacology 2015 Sep;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 May 5;24(5)

Performance

Method Description

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

PDF Report

No

Day(s) and Time(s) Test Performed

Wednesday; 12:01 a.m.

Analytic Time

3 days

Maximum Laboratory Time

7 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. 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