Test Definition: ECUMP

Eculizumab Monitoring Panel, S

Overview

Useful For

Therapeutic drug monitoring of eculizumab

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
C5FX	C5 Complement, Functional, S	Yes	Yes
C5AG2	C5 Complement, Antigen, S	Yes, (Order C5AG)	Yes
INT86	ECUMP Interpretation	No	Yes

Method Name

C5AG2: Nephelometry

C5FX: Automated Liposome Lysis Assay

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Patient Preparation: Fasting preferred

Supplies: Aliquot Tube, 5 mL (T465)

Specimen Type: Serum

Collection Container/Tube: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1.5 mL

Collection Instructions:

1. Recommended timeframe for the blood collection is a trough, or immediately prior to next intravenous infusion.

2. Immediately after specimen collection, place the tube on wet ice.

3. Centrifuge and aliquot serum into plastic vial.

4. Freeze specimen within 30 minutes.

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

1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen	14 days	

Clinical and Interpretive

Clinical Information

Eculizumab (Soliris, Alexion Pharmaceuticals) is a humanized hybrid monoclonal antibody (IgG2/IgG4) that blocks complement C5 cleavage, thereby preventing the activation of the proinflammatory effects of C5a and the cytolytic effects of the membrane attack complex (MAC) formed by C5b-C9. It is FDA-approved for atypical hemolytic uremic syndrome(1) and paroxysmal nocturnal hemoglobinuria,(2) and it is also prescribed for other conditions such as C3 glomerulopathies.(3) The dosing regimen for an average adult may vary from 300 to 1,200 mg intravenously every 2 weeks during the maintenance stages, according to the condition for which the drug is prescribed. Therapy efficacy may be monitored by measuring efficiency of complement blockade.(4) Eculizumab will affect complement function assays that rely on the formation of the MAC to generate cell lysis. Although total complement (CH50) and soluble membrane attack complex (sMAC) have been recommended for eculizumab monitoring, the measurement of C5 function and C5 antigen more specifically indicate the impact of eculizumab on the complement system blockage and may help guide the next dose of the drug.

This panel measures the pharmacodynamics effects of eculizumab on the complement system.

Reference Values

C5 COMPLEMENT ANTIGEN

10.6-26.3 mg/dL

C5 COMPLEMENT FUNCTIONAL

29-53 U/mL

Interpretation

The panel will measure the pharmacodynamic effects of eculizumab on the complement system. Total complement (CH50) function, alternative pathway (AH50) function, and C5 function assays will be decreased to a similar extent in the presence of eculizumab. The function of C5 may be completely absent when eculizumab is present at therapeutic concentrations. C5 antigen, on the other hand, will be normal or elevated. C5 complement function drops on average 30% with 25 mcg/mL of eculizumab, and 70% with 50 mcg/mL. In the presence of 100 mcg/mL of eculizumab in serum, there is on average 20% residual C5 function.

Decreased C5 function in the presence of normal or elevated C5 antigen concentrations suggests eculizumab is partially blocking C5 activity.

Absent C5 function in the presence of normal or elevated C5 antigen concentrations suggests eculizumab is completely blocking C5 activity.

Normal C5 function in the presence of normal or elevated C5 antigen concentrations suggests eculizumab concentration is not sufficient to block C5 activity.

If C5 function and C5 antigen concentrations are all decreased, it may be due to a secondary consumption process, poor hepatic synthesis of complement proteins or C5 deficiency. Clinical correlation recommended. If indicated, resubmit samples to confirm results.

Cautions

As with all complement assays, proper sample handling is of utmost importance to ensure that the complement system is not activated before clinical testing

This panel of assays will not quantitate eculizumab concentrations.

If patient is on ravulizumab therapy, the best assay to monitor complement blockage is the alternative pathway (AH50). Test RAVUM / Ravulizumab Complement Blockage Monitoring, Serum offers appropriate interpretation for AH50 decreases in association with the expected ravulizumab drug concentration.

This panel will not measure the soluble membrane attack complex (sMAC).

Supportive Data

In a Mayo Clinic study with samples from individual subjects with normal complement activity defined by the total complement (CH50) assay and spiked with varying concentrations of eculizumab,(5) there was a significant decrease in CH50, alternative pathway function (AH50), and C5 functional results with eculizumab. Considering that the therapeutic target concentrations are expected to be above 50 mcg/mL, the results showed that eculizumab is partially blocking the complement cascade at 25 mcg/mL, with a complete blockage for C5 functional at 100 mcg/mL.

Clinical Reference

1. Wong EK, Goodship TH, Kavanagh D: Complement therapy in atypical haemolytic uraemic syndrome (aHUS). Mol Immunol. 2013;56:199-212

2. Rother RP, Rollins SA, Mojcik CF, Brodsky RA, Bell L: Discovery and development of the complement inhibitor eculizumab for the treatment of paroxysmal nocturnal hemoglobinuria. Nat Biotechnol. 2007;25:1256-1264

3. Zuber J, Le Quintrec M, Krid S, et al: Eculizumab for atypical hemolytic uremic syndrome recurrence in renal transplantation. Am J Transplant. 2012;12:3337-3354

4. Volokhina EB, van de Kar NC, Bergseth G, et al: Sensitive, reliable and easy-performed laboratory monitoring of

eculizumab therapy in atypical hemolytic uremic syndrome. Clin Immunol. 2015;160(2):237-243

5. Andreguetto B, Murray D, Snyder M, et al: The impact of eculizumab in complement assays. Mol Immunol. 2015;67:119-120

Performance

Method Description

Functional C5 complement

Component 5 (C5) complement activity is measured by mixing patient serum with a C5-deficient serum. The lytic activity of the serum mixture is tested against sensitized, labeled liposomes. If lysis occurs, the patient serum must be the source of the C5. The target liposomes are a commercial reagent.(Unpublished Mayo method)

C5 antigen

Anti-C5 reagent is added to patient serum and quantitated on a Dade Behring BN II analyzer by fixed-time kinetic nephelometry.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

2 days

Maximum Laboratory Time

14 days

Specimen Retention Time

14 days

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

86160

86161

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
ECUMP	Eculizumab Monitoring Panel, S	In Process

Result ID	Test Result Name	Result LOINC Value
C5FX	C5 Complement, Functional, S	60472-8
C5AG2	C5 Complement, Antigen, S	4505-4
INT86	ECUMP Interpretation	69048-7