

Market Applicability							
Market	DC	GA	KY	MD	NJ	NY	WA
Applicable	X	X	X	X	X	X	NA

## Soliris (eculizumab)

Override(s)	Approval Duration
Prior Authorization	1 year except as noted within the criteria below

Medications
Soliris (eculizumab)

### APPROVAL CRITERIA

Requests for initiation of therapy with Soliris (eculizumab) in **paroxysmal nocturnal hemoglobinuria (PNH)** may be approved if the following criteria are met:

- I. Individual has PNH as documented by flow cytometry, including the presence of (Parker 2005):
  - A. PNH type III red cell clone or measurable granulocyte or monocyte clone; **OR**
  - B. Glycosylphosphatidylinositol-anchored proteins (GPI-AP)-deficient polymorphonuclear cells (PMNs);

**AND**

- II. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab), unless the clinical record documents that the risks of delaying Soliris (eculizumab) outweigh the risk of meningococcal infection);

**AND**

- III. Individual has no evidence of an active meningococcal infection;

**AND**

- IV. Individual has (Hillmen 2006):
  - A. Lactate dehydrogenase is greater than 1.5 times the upper limit of normal; **OR**
  - B. One or more PNH-related sign or symptom (such as but not limited to anemia or history of a major adverse vascular event from thromboembolism).

**Initial Approval Duration:** 6 months

Requests for continued use of Soliris (eculizumab) in PNH may be approved if the following criteria are met:

- I. Individual has experienced a clinical response as shown by one of the following:
  - A. Stabilization of hemoglobin levels; **OR**
  - B. Reduction in number of transfusions required; **OR**
  - C. Improvement in hemolysis (for example, normalization or decrease of LDH levels).

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This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply. CRX-ALL-0488-20

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**Note:** If Soliris therapy is discontinued, individuals should be closely monitored for at least 8 weeks after cessation to detect hemolysis.

Requests for initiation of therapy with Soliris (eculizumab) in **neuromyelitis optica spectrum disorder** (NMOSD) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older with NMOSD; **AND**
- II. The diagnosis is confirmed by the presence of anti- aquaporin-4 (AQP4) antibodies;  
**AND**
- III. Individual has a history of at least 2 relapses in the last 12 months prior to initiation of therapy;  
**OR**
- IV. Individual has a history of at least 3 relapses in the last 24 months **AND** at least 1 relapse in the 12 months prior to initiation of therapy;  
**AND**
- V. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab), unless the clinical record documents the risks of delaying Soliris (eculizumab) outweigh the risk of meningococcal infection;  
**AND**
- VI. Individual has no evidence of an active meningococcal infection.

Requests for continued use of Soliris (eculizumab) in NMOSD may be approved if the following criteria are met:

- I. Individual has experienced a clinical response (for example, a reduction in the frequency of relapse).

Requests for initiation of therapy with Soliris (eculizumab) in **atypical hemolytic uremic syndrome** (aHUS) may be approved if the following criteria are met:

- I. Individual has a diagnosis of aHUS;  
**AND**
- II. The diagnosis of aHUS is supported by the absence of Shiga toxin-producing E. coli infection;  
**AND**
- III. Thrombotic thrombocytopenic purpura has been ruled out [for example, normal ADAMTS 13 activity and no evidence of an ADAMTS 13 inhibitor (Loirat 2011, 2016)],

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or if thrombotic thrombocytopenic purpura cannot be ruled out by laboratory and clinical evaluation, a trial of plasma exchange did not result in clinical improvement;

**AND**

IV. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab) (unless the clinical record documents that the risks of delaying Soliris (eculizumab) outweigh the risk of meningococcal infection);

**AND**

V. Individual has no evidence of an active meningococcal infection.

**Initial Approval Duration:** 12 weeks.

Requests for continued use of Soliris (eculizumab) in aHUS may be approved if the following criteria are met:

- I. There is clinical improvement after the initial trial (for example, increased platelet count or laboratory evidence of reduced hemolysis) until an individual becomes a candidate for physician-directed cessation as evidenced by the following (Merrill 2017):
  - A. Complete clinical remission has been achieved (that is, resolution of thrombocytopenia and mechanical hemolysis, and normalization or new baseline plateau of renal function) *and* improvement of precipitating illness is clinically apparent; **AND**
  - B. Duration of clinical remission has been stable for 2 months.

**Note:** Close monitoring after cessation is essential (for example: regular laboratory monitoring including complete blood count, peripheral smear, lactate dehydrogenase, renal function, and urine protein beginning the week of the held dose and weekly for 4 weeks, every 2 weeks for 1 month, and then monthly for 3 months at the discretion of the treating clinician).

Requests for resumption of Soliris (eculizumab) in aHUS may be approved if the following criteria are met (Fakhouri 2017):

- I. Individual experienced a relapse after discontinuation of therapy as defined by:
  - A. Reduction in platelet count to less than 150,000/mm<sup>3</sup> or greater than 25% from baseline; **OR**
  - B. Mechanical hemolysis (having 2 or more features of hemoglobin less than 10 g/dL, lactate dehydrogenase greater than 2 times upper limit of normal, undetectable haptoglobin, or presence of schistocytes on smear); **OR**
  - C. Acute kidney injury with serum creatinine increase greater than 15% from baseline levels.

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Applicable	X	X	X	X	X	X	NA

Requests for initiation of therapy with Soliris (eculizumab) in **generalized myasthenia gravis** (gMG) may be approved if the following criteria are met:

I. Individual is 18 years of age or older with the gMG;

**AND**

II. Individual has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV disease;

**AND**

III. Individual has a documented positive serologic test for binding anti-acetylcholine receptor antibodies (AChR-ab);

**AND**

IV. Individual has had an inadequate response to, is intolerant of, or has a contraindication to two or more immunosuppressive drug agents (such as, azathioprine, cyclosporine, or methotrexate) as monotherapy or in combination therapy for greater than or equal to 12 months;

**OR**

V. Individual has had an inadequate response to, is intolerant of, or has a contraindication to one or more immunosuppressive drug agents as monotherapy or in combination therapy and requires chronic plasma exchange or plasmapheresis or intravenous immunoglobulin therapy;

**AND**

VI. Individual has been immunized with a meningococcal vaccine at least 2 weeks prior to administration of the first dose of Soliris (eculizumab), unless the clinical record documents that the risk of delaying Soliris (eculizumab) outweighs the risk of meningococcal infection;

**AND**

VII. Individual has no evidence of an active meningococcal infection.

**Initial Approval Duration:** 26 weeks

Requests for continued use of Soliris (eculizumab) in gMG may be approved if the following criteria are met:

I. Individual has experienced a clinical response (for example, a reduction in signs or symptoms that impact daily function).

Requests for Soliris (eculizumab) may not be approved if the above criteria are not met and for all other indications.

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**Note:**

Soliris (eculizumab) has a black box warning for serious meningococcal infections. Life-threatening and fatal meningococcal infections have occurred in patients treated with Soliris (eculizumab) and meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Individuals should be immunized with meningococcal vaccines at least 2 weeks prior to initiating therapy unless the risks of delaying therapy outweigh the risk of developing a meningococcal infection. The FDA has required the manufacturer to develop a comprehensive risk management program that includes the enrollment of prescribers in the Soliris REMS Program. Additional information and forms for individuals, prescribers, and pharmacists may be found on the manufacturer's website: <http://www.solirisrems.com>.

State Specific Mandates		
State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

**Key References:**

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5. Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2006; 355(12):1233-1243.
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9. Fakhouri F, Fila M, Provot F, et al. Pathogenic variants in complement genes and risk of atypical hemolytic uremic syndrome relapse after eculizumab discontinuation. *Clin J Am Soc Nephrol*. 2017; 12:50-59.
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11. Sanders DB, Wolfe GI, Benatar M, et al for the Task Force of the Myasthenia Gravis Foundation of America (MGFA). International consensus guidance for management of myasthenia gravis. *Neurology* 2016; 87:419.
12. Lee JW, Fontbrune FS, et al. Ravulizumab vs Eculizumab in Adult Patients with PNH Naïve to Complement Inhibitors: The 301 Study. *Blood* 2018; prepublished online December 3, 2018; DOI 10.1182/blood-2018-09-876136.

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