

## **Clinical Policy: Eculizumab (Soliris)**

Reference Number: CP.PHAR.97

Effective Date: 03.01.12

Last Review Date: 02.21

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Eculizumab (Soliris<sup>®</sup>) is a complement inhibitor.

### **FDA Approved Indication(s)**

Soliris is indicated for the treatment of:

- Patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
- Patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)
- Adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive
- Adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive

Limitation(s) of use: Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS).

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Soliris is **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Paroxysmal Nocturnal Hemoglobinuria (must meet all):**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with a hematologist;
3. Age  $\geq$  18 years;
4. Flow cytometry shows detectable GPI-deficient hematopoietic clones or  $\geq$  10% PNH cells;
5. Member meets one of the following (a or b):
  - a. History of  $\geq$  1 red blood cell transfusion in the past 24 months and (i or ii):
    - i. Documentation of hemoglobin  $<$  7 g/dL in members without anemia symptoms;
    - ii. Documentation of hemoglobin  $<$  9 g/dL in members with anemia symptoms;
  - b. History of thrombosis;
6. Soliris is not prescribed concurrently with Ultomiris<sup>®</sup>;

7. Dose does not exceed 600 mg per week for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter.

**Approval duration: 6 months**

**B. Atypical Hemolytic Uremic Syndrome (must meet all):**

1. Diagnosis of aHUS (i.e., complement-mediated HUS);
2. Prescribed by or in consultation with a hematologist or nephrologist;
3. Age  $\geq 2$  months;
4. Member has signs of TMA as evidenced by all of the following (a, b, and c):
  - a. Platelet count  $\leq 150 \times 10^9/L$ ;
  - b. Hemolysis such as an elevation in serum lactate dehydrogenase (LDH);
  - c. Serum creatinine above the upper limits of normal or member requires dialysis;
5. Documentation that member does not have either of the following:
  - a. A disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13 (ADAMTS13) deficiency;
  - b. STEC-HUS;
6. Soliris is not prescribed concurrently with Ultomiris;
7. Dose does not exceed 900 mg per week for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter.

**Approval duration: 6 months**

**C. Generalized Myasthenia Gravis (must meet all):**

1. Diagnosis of gMG;
2. Prescribed by or in consultation with a neurologist;
3. Age  $\geq 18$  years;
4. Myasthenia Gravis-Activities of Daily Living (MG-ADL) score  $\geq 6$  at baseline;
5. Myasthenia Gravis Foundation of America Clinical Classification (MGFA) Class II to IV;
6. Member has positive serologic test for anti-AChR antibodies;
7. Failure of a corticosteroid (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
8. Failure of a cholinesterase inhibitor (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
9. Failure of two immunosuppressive therapies (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
10. Dose does not exceed 900 mg per week for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter.

**Approval duration: 6 months**

**D. Neuromyelitis Optica Spectrum Disorder (must meet all):**

1. Diagnosis of NMOSD;
2. Prescribed by or in consultation with a neurologist;
3. Age  $\geq 18$  years;
4. Member has positive serologic test for anti-AQP4 antibodies;
5. Member has experienced at least one relapse within the previous 12 months;
6. Member meets one of the following (a or b):

- a. History of at least two relapses during the previous 12 months;
- b. History of three relapses during the previous 24 months;
7. Baseline expanded disability status scale (EDSS) score of  $\leq 7$ ;
8. Failure of rituximab (Ruxience<sup>™</sup> is preferred) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for rituximab*
9. Soliris is not prescribed concurrently with rituximab, Enspryng<sup>™</sup>, or Uplizna<sup>®</sup>;
10. Dose does not exceed 900 mg per week for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter.

**Approval duration: 6 months**

**E. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Paroxysmal Nocturnal Hemoglobinuria and Atypical Hemolytic Uremic Syndrome (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a or b):
  - a. PNH:
    - i. Improved measures of intravascular hemolysis (e.g., normalization of LDH);
    - ii. Reduced need for red blood cell transfusions;
    - iii. Increased or stabilization of hemoglobin levels;
    - iv. Less fatigue;
    - v. Improved health-related quality of life;
    - vi. Fewer thrombotic events;
  - b. aHUS:
    - i. Improved measures of intravascular hemolysis (e.g., normalization of LDH);
    - ii. Increased or stabilized platelet counts;
    - iii. Improved or stabilized serum creatinine or estimated glomerular filtration rate (eGFR);
    - iv. Reduced need for dialysis;
3. Soliris is not prescribed concurrently with Ultomiris;
4. If request is for a dose increase, new dose does not exceed (a or b):
  - a. For PNH: 900 mg every 2 weeks;
  - b. For aHUS: 1,200 mg every 2 weeks.

**Approval duration: 6 months**

**B. Generalized Myasthenia Gravis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;

2. Member is responding positively to therapy as evidenced by a 2-point reduction in MG-ADL total score;
3. If request is for a dose increase, new dose does not exceed 1,200 mg every 2 weeks.

**Approval duration: 6 months**

**C. Neuromyelitis Optica Spectrum Disorder (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy – including but not limited to improvement or stabilization in any of the following parameters:
  - a. Frequency of relapse;
  - b. EDSS;
  - c. Visual acuity;
3. Soliris is not prescribed concurrently with rituximab, Enspryng, or Uplizna;
4. If request is for a dose increase, new dose does not exceed 1,200 mg every 2 weeks.

**Approval duration: 6 months**

**D. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.  
**Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B.** STEC-HUS;
- C.** Antiphospholipid syndrome (D68.61);
- D.** Unspecified nephritic syndrome with other morphologic changes (N05.8).

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

AchR: acetylcholine receptor  
ADAMTS13: a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13  
aHUS: atypical hemolytic uremic syndrome  
AQP-4: aquaporin-4  
EDSS: Expanded Disability Status Scale  
FDA: Food and Drug Administration

gMG: generalized myasthenia gravis  
LDH: lactate dehydrogenase  
MG-ADL: Myasthenia Gravis-Activities of Daily Living  
MGFA: Myasthenia Gravis Foundation of America Clinical Classification  
PNH: paroxysmal nocturnal hemoglobinuria  
STEC-HUS: Shiga toxin E. coli related hemolytic uremic syndrome

TMA: thrombotic microangiopathy

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Corticosteroids</b>		
betamethasone	Oral: 0.6 to 7.2 mg PO per day	7.2 mg/day
dexamethasone	Oral: 0.75 to 9 mg/day PO	9 mg/day
methylprednisolone	Oral: 12 to 20 mg PO per day; increase as needed by 4 mg every 2-3 days until there is marked clinical improvement or to a maximum of 40 mg/day	40 mg/day
prednisone	Oral: 15 mg/day to 20 mg/day; increase by 5 mg every 2-3 days as needed. Maximum: 60 mg/day	60 mg/day
<b>Cholinesterase Inhibitors</b>		
pyridostigmine (Mestinon <sup>®</sup> , Regonol <sup>®</sup> )	Oral immediate-release: 600 mg daily in divided doses (range, 60-1500 mg daily in divided doses) Oral sustained release: 180-540 mg QD or BID IV or IM: 2 mg every 2-3 hours	See regimen
neostigmine (Bloxivert <sup>®</sup> )	Oral: 15 mg TID. The daily dosage should be gradually increased at intervals of 1 or more days. The usual maintenance dosage is 15-375 mg/day (average 150 mg) IM or SC: 0.5 mg based on response to therapy	See regimen
<b>Immunosuppressants</b>		
azathioprine (Imuran <sup>®</sup> )	Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day	3 mg/kg/day
mycophenolate mofetil (Cellcept <sup>®</sup> )*	Oral: Dosage not established. 1 gram BID has been used with adjunctive corticosteroids or other non-steroidal immunosuppressive medications	2 g/day
cyclosporine (Sandimmune <sup>®</sup> )*	Oral: initial dose of cyclosporine (Non-modified), 5 mg/kg/day in 2 divided doses	5 mg/kg/day
Rituxan <sup>®</sup> (rituximab), Ruxience <sup>™</sup> (rituximab-pvvr), Truxima <sup>®</sup> (rituximab- abbs)* <sup>†</sup>	IV: 375 mg/m <sup>2</sup> once a week for 4 weeks; an additional 375 mg/m <sup>2</sup> dose may be given every 1 to 3 months afterwards  <b>NMOSD</b> IV: 375 mg/m <sup>2</sup> per week for 4 weeks as induction, followed by 375 mg/m <sup>2</sup> biweekly every 6 to 12 months	See regimen

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

\*Off-label

†Prior authorization is required for rituximab products

#### Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): unresolved serious *Neisseria meningitidis* infection, patients who are not currently vaccinated against *Neisseria meningitidis*, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection
- Boxed warning(s): serious meningococcal infections

#### Appendix D: General Information

- Soliris is only available through a REMS (Risk Evaluation and Mitigation Strategy) program due to the risk of life-threatening and fatal meningococcal infection. Patients should be vaccinated with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of Soliris and revaccinated according to current medical guidelines for vaccine use. Patients should be monitored for early signs of meningococcal infections, evaluated immediately if infection is suspected, and treated with antibiotics if necessary.
- The Advisory Committee on Immunization Practices (ACIP)'s recommendations regarding the meningococcal vaccine are found here:  
<http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html>
- Examples of positive response to therapy include:
  - PNH: improved measures of intravascular hemolysis (e.g., normalization of lactate dehydrogenase [LDH]), reduced need for red blood cell transfusions, less fatigue, improved health-related quality of life, fewer thrombotic events;
  - aHUS: decreased need for plasma therapy (plasma exchange or plasma infusion), decreased need for dialysis, increased glomerular filtration rate, normalization of platelet counts and/or LDH levels;
  - gMG: a 2-point reduction in MG-ADL total score is considered a clinically meaningful improvement. The scale can be accessed here:  
<https://myasthenia.org/Portals/0/ADL.pdf>;
  - NMOSD: stabilization or reduction in EDSS total score. EDSS ranges from 0 (no disability) to 10 (death).
- The MGFA classification has some subjectivity in it when it comes to distinguishing mild (Class II) from moderate (Class III) and moderate (Class III) from severe (Class IV). Furthermore, it is insensitive to change from one visit to the next.
- AQP-4: AQP-4-IgG-seropositive status is confirmed with the use of commercially available cell-binding kit assay (Euroimmun).
- Ultomiris is a humanized monoclonal antibody to complement component C5 that was engineered from Soliris. It is virtually identical to Soliris but has a longer half-life that allows for less frequent dosing intervals.
- Coverage is excluded for the following indications. The use of Soliris for these indications is considered investigational due to lack of conclusive, evidence-based data with randomized controlled trials. As such, alternative therapies for these indications include:
  - Antiphospholipid syndrome: anticoagulation therapy (e.g., vitamin K antagonists)

- Unspecified nephritic syndrome with other morphologic changes: immunosuppression (e.g., prednisone, mycophenolate mofetil)

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
PNH	IV infusion: 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	900 mg/dose
aHUS	IV infusion: 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter	1,200 mg/dose
gMG, NMOSD	IV infusion: 900 mg every 7 days for the first 4 weeks, followed by a single dose of 1,200 mg 7 days after the fourth dose, and then 1,200 mg every 2 weeks thereafter	1,200 mg/dose

**VI. Product Availability**

Single-dose vial: 300 mg/30 mL

**VII. References**

1. Soliris Prescribing Information. New Haven, CT: Alexion Pharmaceuticals, Inc.; June 2019. Available at: [www.soliris.net](http://www.soliris.net). Accessed October 20, 2020.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Blood* 2005; 106(12):3699-3709. doi:10.1182/blood-2005-04-1717.
3. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. *Cytometry Part B (Clinical Cytometry)*. 2010; 78B: 211–230.
4. CDC. Meningococcal ACIP Vaccine Recommendations. Advisory Committee for Immunization Practices (ACIP). *MMWR* 2017. Available at <http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html>. Accessed October 27, 2019.
5. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. 2016; 31: 15-39.
6. Howard JF, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicenter study. *Lancet Neurol*. 2017; 16(12): 976-986.
7. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidelines for the management of myasthenia gravis. *Neurology*. 2016; 87: 419-425.
8. Muppidi S. The myasthenia gravis-specific activities of daily living profile. *Ann N Y Acad Sci*. 2012; 1274:114-119.
9. Pittock SJ, et al. Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *NEJM*. May 2019. DOI:10.1056.
10. Canaud G, Kamar N, Anglicheau D, et al. Eculizumab improves posttransplant thrombotic microangiopathy due to antiphospholipid syndrome recurrence but fails to prevent chronic vascular changes. *Am J Transplant*. 2013;13(8):2179-2185.

11. Lebreton C, Bacchetta J, Dijoud F, et al. C3 glomerulopathy and eculizumab: A report on four paediatric cases. *Pediatr Nephrol.* 2017;32(6):1023-1028.
12. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. *European Journal of Neurology.* 2010; 17: 1019–1032.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1300	Injection, eculizumab 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Removed requirement of <i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae type b</i> (Hib) infections. Modified initial and approval duration to 6 months and 12 months respectively. Removed age requirements. Added max dose to continued approval criteria	03.17	04.17
1Q18 Annual Review Policies combined for Centene Medicaid and Commercial lines of business. Medicaid: For PNH, removed conditions constituting severe PNH that are not objective/specific. Modified requirement for 4 transfusions in last 12 months to 1 transfusion in the last 24 months per the inclusion criteria of the second pivotal trial for approval. For aHUS, removed requirements for specific clinical presentation as a specialist is required to be involved in the care. Removed requirement for causes of aHUS to be ruled out as this is non-specific and under the purview of the provider. For PNH and aHUS, removed contraindication for <i>Neisseria meningitidis</i> infection as this is covered by the REMS program. Commercial: For PNH, added prescriber requirement. Removed requirement for baseline platelet count $\geq 30,000$ /microliter (a clinical trial inclusion criterion). Modified requirement for “history of major adverse vascular events from thromboembolism” to “history of thrombosis”. For aHUS, added prescriber requirement. Both: Added age requirements per prescribing information. Added nephrologist as a prescriber option for aHUS. Removed criteria surrounding meningococcal vaccination as this is covered by the Soliris REMS program. Added STEC-HUS as an indication not covered. Modified all approval durations to 6 months.	11.13.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added generalized myasthenia gravis indication and criteria for approval.	12.12.17	02.18
Added note to appendix B that prior authorization is required for Rituxan.	09.13.18	
1Q 2019 annual review: added HIM-Medical Benefit; no significant changes; references reviewed and updated.	10.12.18	02.19
Aligned criteria with Ultomiris policy; for PNH, allowed documentation of detectable GPI-deficient hematopoietic clones for flow cytometry; specified examples of positive response to therapy in Section II.A; references reviewed and updated.	02.19.19	05.19
Criteria added for new FDA indication: neuromyelitis optica spectrum disorder; references reviewed and updated.	08.13.19	11.19
1Q 2020 annual review: added HIM line of business; aHUS initial criteria and PNH/aHUS continued criteria updated to align with Ultomiris criteria; added antiphospholipid syndrome and unsp nephritic syndrome with other morphologic changes to Section III diagnoses not covered; references reviewed and updated. For NMOSD added redirection to rituximab product per SDC and prior clinical guidance.	01.15.20	02.20
For NMOSD: added requirement against concurrent use with rituximab, Enspryng, or Uplizna.	07.29.20	11.20
1Q 2021 annual review: for PNH and aHUS, added requirement against concurrent use with Ultomiris; for NMOSD, specified that Ruxience is the preferred rituximab product; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.20.20	02.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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