

Clinical Policy: Eculizumab (Soliris)

Reference Number: LA.PHAR.97

Effective Date: 07.23.22

Last Review Date: 06.28.23

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

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

****Please note: This policy is for medical benefit****

Description

Eculizumab (Soliris®) 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 Louisiana Healthcare Connections 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 glycosylphosphatidylinositol (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 Empaveli™ or Ultomiris®, unless the member is in a 4-week period of cross-titration between Soliris and Empaveli;
*Provider must submit attestation of the presence or absence of concomitant Empaveli therapy
- 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 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 (MGFA) clinical classification of 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 at least one immunosuppressive therapy (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
- 10. Soliris is not prescribed concurrently with Ultomiris or Vyvgart™;
- 11. 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 (*RuxienceTM* and *Truxima[®]* are 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, EnspryngTM, or Uplizna[®];
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 (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to off-label use policy LA.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met 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 (a or b):

- a. PNH: Empaveli or Ultomiris;
 - b. aHUS: 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 Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Soliris for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy as evidenced by a 2-point reduction from baseline in MG-ADL total score;
3. Soliris is not prescribed concurrently with Ultomiris or Vyvgart;
4. 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 Louisiana Healthcare Connections benefit or member has previously met 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

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 policy LA.PMN.53
- 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

GPI: glycosylphosphatidylinositol
 LDH: lactate dehydrogenase
 MG-ADL: Myasthenia Gravis-Activities of Daily Living
 MGFA: Myasthenia Gravis Foundation of America
 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 require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--|---|-------------------------------------|
| Corticosteroids | | |
| 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 |
| Cholinesterase Inhibitors | | |
| pyridostigmine (Mestinon [®] , Regonol [®]) | 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 (Bloxiverz [®]) | 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 |
| Immunosuppressants | | |
| azathioprine (Imuran [®]) | Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day | 3 mg/kg/day |
| mycophenolate mofetil (Cellcept [®])* | Oral: Dosage not established. 1 gram BID has been used with adjunctive corticosteroids or other non-steroidal immunosuppressive medications | 2 g/day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|--|-----------------------------|
| cyclosporine (Sandimmune®)* | Oral: initial dose of cyclosporine (Non-modified), 5 mg/kg/day in 2 divided doses | 5 mg/kg/day |
| Rituxan® (rituximab), Riabni™ (rituximab-arrx), Ruxience™ (rituximab-pvvr), Truxima® (rituximab-abbs)*† | <p>gMG IV: 375 mg/m² once a week for 4 weeks; an additional 375 mg/m² dose may be given every 1 to 3 months afterwards</p> <p>NMOSD IV: 375 mg/m² per week for 4 weeks as induction, followed by 375 mg/m² biweekly every 6 to 12 months</p> | See regimen |

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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)
- In October 2021, the Institute for Clinical and Economic Review (ICER) published a final evidence report on the effectiveness and value of Soliris for the treatment of gMG. In adults with gMG positive for anti-AChR antibodies refractory to conventional therapy, there is:
 - Moderate certainty of a small or substantial net health benefit with high certainty of at least a small benefit for Soliris added to conventional therapy compared with conventional therapy alone (B+);
 - Insufficient evidence (I) to distinguish the net health benefits of rituximab from Soliris.
- The 2020 MGFA international consensus guidelines for gMG recommend that Soliris be considered after trials of other immunotherapies have been unsuccessful in meeting treatment goals. Soliris is a treatment option for severe, refractory, AChR antibody positive gMG.

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.; November 2020. Available at: www.soliris.net. Accessed November 3, 2022.
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.
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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.
13. Institute for Clinical and Economic Review. Eculizumab and efgartigimod for the treatment of myasthenia gravis: effectiveness and value: Effectiveness and value (final report). Published October 20, 2021. Available at: <https://icer.org/assessment/myasthenia-gravis>. Accessed November 3, 2022.

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 | LDH Approval Date |
|--------------------------------------|-------|-------------------|
| Converted corporate to local policy. | 04.22 | 07.23.22 |

| Reviews, Revisions, and Approvals | Date | LDH Approval Date |
|---|----------|-------------------|
| <p>For NMOSD, removed redirection to Enspryng; for gMG modified from two to one immunosuppressive therapy required, added requirement that Soliris is not prescribed concurrently with Ultomiris or Vyvgart.</p> <p>Template changes applied to other diagnoses/indications and continued therapy section.</p> <p>References reviewed and updated.</p> <p>Updated Appendix B</p> <p>Added verbiage this policy is for medical benefit only.</p> | 06.28.23 | |

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. LHCC 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.

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