

PHARMACY POLICY STATEMENT

Marketplace

DRUG NAME	Soliris (eculizumab)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Soliris is a C5 Complement inhibitor initially approved by the FDA in 2007. It is approved for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis, atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive, and neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. PNH is a rare hematopoietic stem cell disorder in which activation of the complement system destroys red blood cells.

aHUS is a type of thrombotic microangiopathy (TMA), a group of syndromes defined by the presence of hemolytic anemia, low platelets and organ damage due to microscopic blood clots in the capillaries. Unlike typical HUS, aHUS is usually genetic. The three main signs of aHUS are hemolytic anemia, thrombocytopenia, and acute kidney failure. Of note, the other type of TMA is called thrombotic thrombocytopenic purpura (TTP); Soliris is not used to treat TTP.

Soliris (eculizumab) will be considered for coverage when the following criteria are met:

Paroxysmal Nocturnal Hemoglobinuria (PNH)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a hematologist; AND
3. Member has a diagnosis of PNH as confirmed by flow cytometry; AND
4. Member has a lactate dehydrogenase (LDH) level >1.5x upper limit of normal (ULN); AND
5. Member has at least one PNH-related sign/symptom e.g., fatigue, hemoglobin <10 g/dL, thrombosis, pRBC transfusion, shortness of breath; AND
6. Member has tried and failed or is unable to try Ultomiris; AND
7. Member has received meningococcal vaccine.
8. **Dosage allowed/Quantity limit:** 600mg IV weekly x 4 weeks, then 900mg 1 week later, then 900mg every 2 weeks thereafter.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Clinical evidence of positive response to therapy such as increased hemoglobin level, decreased need for transfusions, normalized LDH levels, improved fatigue.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Atypical Hemolytic Uremic Syndrome (aHUS)

For **initial** authorization:

1. Medication is prescribed by or in consultation with a hematologist or nephrologist; AND
2. Member has a diagnosis of aHUS supported by ALL of the following:
 - a) Thrombocytopenia (platelet count $< 150 \times 10^9/L$),
 - b) Evidence of microangiopathic hemolytic anemia (MAHA) e.g., hemoglobin < 10 g/dL, elevated lactate dehydrogenase (LDH), low haptoglobin, presence of fragmented red blood cells or schistocytes on blood smear
 - c) Evidence of renal impairment (e.g., raised SCr or low eGFR); AND
3. Shiga toxin-producing E. coli related HUS (STEC-HUS) has been ruled out; AND
4. ADAMTS13 activity level is $> 10\%$ (to rule out TTP); AND
5. Member has tried and failed or is unable to try Ultomiris; AND
6. Member has received meningococcal vaccine.
7. **Dosage allowed/Quantity limit:**
Pediatrics: See weight-based dosing in package insert.
Adults: 900mg IV weekly x 4 weeks, then 1200mg 1 week later, then 1200mg every 2 weeks thereafter.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must demonstrate hematologic normalization as evidenced by increased platelet count or LDH maintained below upper limit of normal; AND
2. Improved or preserved kidney function.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Generalized Myasthenia Gravis (gMG)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a neurologist; AND
3. Member has a documented diagnosis of MGFA class II-IV myasthenia gravis (see Appendix); AND
4. Lab result in chart notes shows the member is seropositive for AChR antibodies; AND
5. Member has tried and failed at least 1 conventional therapy:
 - a) Pyridostigmine
 - b) Corticosteroid for at least 3 months
 - c) Non-steroid immunosuppressant (e.g., azathioprine) for at least 6 months; AND
6. Member has tried and failed or is unable to try Ultomiris (requires trial of IV Vyvgart); AND
7. Member has received meningococcal vaccine.
8. **Dosage allowed/Quantity limit:** 900 mg IV weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks thereafter.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must demonstrate improvement in activities of daily living, muscle strength, and/or health related quality of life; fewer exacerbations or hospitalizations, or reduced use of rescue medication.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Neuromyelitis Optica Spectrum Disorder (NMOSD)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a neurologist; AND
3. Member has a documented diagnosis of NMOSD and is seropositive for aquaporin-4 (AQP4) IgG antibodies; AND
4. Member had had 1 or more relapses within the past year; AND
5. Member has tried and failed at least one of the following for 6 months or longer: azathioprine, mycophenolate, rituximab (requires prior auth); AND
6. Member has received meningococcal vaccine.
7. **Dosage allowed/Quantity limit:** 900 mg IV weekly for the first 4 weeks, followed by 1200 mg for the fifth dose 1 week later, then 1200 mg every 2 weeks thereafter.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must document disease stabilization, symptom improvement, and/or reduced frequency of relapses.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Soliris (eculizumab) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
11/14/2017	New policy for Soliris created.
10/26/2019	New diagnosis of Neuromyelitis optica spectrum disorder (NMOSD) added.
10/15/2020	Revised criteria for NMOSD to align with other products. Only require at least 1 relapse in past year. Added trial of a standard therapy. Added trial of Enspryng. Reworded the criteria for meningitis vaccine. Removed the part about stable immunosuppressive therapy (just assessed for study purpose). Removed restrictions on prior Rituxan, mitoxantrone, IVIG (only applicable to the study design). Changed initial auth duration to 6 months. Edited the renewal criteria to be more appropriate. Also corrected the dose information error. Changed to nonpreferred drug status.
02/08/2021	gMG: Updated references. Added specialist requirement. Removed MG-ADL score. Amended prerequisite drugs to more closely match guidelines and literature. Removed clinical trial exclusion criteria. Reduced initial auth duration to 6 months. Revised renewal criteria
06/02/2021	aHUS: Updated references. Added specialist requirement. Revised diagnostic parameters. Removed list of restrictions from clinical trials. Stated Ultomiris as preferred. Amended dosing information. Revised renewal criteria. PNH: Updated references. Added age limit. Removed nephrology as specialist. Removed transfusion and organ damage requirements. Preference for Ultomiris. Amended dosing information. Reduced initial auth duration from 12 months to 6 months. Revised renewal criteria.
07/25/2023	Transferred to new template. PNH: Updated references. Added that they must be symptomatic. aHUS: Updated and added references. Corrected ADAMTS13 level cutoff. Changed "evidence of hemolysis" to evidence of MAHA. NMOSD: Added references. Removed requirement for trial of Enspryng.

MG: Added reference. Removed "severe, refractory" and added "MGFA class II-IV." Added MGFA appendix. Added trial of Ultomiris. Shortened and simplified list of conventional therapy trials.

APPENDIX:

MG Foundation of America (MGFA) Clinical Classification	
Class I	any ocular weakness; all other muscle strength is normal
Class II	mild weakness affecting other than ocular muscles; may also have ocular weakness at any level
Class III	moderate weakness affecting other than ocular muscles; may also have ocular weakness at any level
Class IV	severe weakness affecting other than ocular muscles; may also have ocular weakness at any level
Class V	defined by intubation, with or without mechanical ventilation

References:

- 2021 Georgia Code Title 33 – Insurance Chapter 20A - Managed Health Care Plans Article 2 - Patient's Right to Independent Review § 33-20A-31 Definitions. Justia US Law. Accessed April 25, 2023. <https://law.justia.com/codes/georgia/2021/title-33/chapter-20a/article-2/section-33-20a-31/>.
- Soliris [prescribing information]. Boston, MA: Alexion Pharmaceuticals Inc; 2020.
- Hillmen P, Young NS, Schubert J, et. al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Eng J Med*. 2006;355:1233-1243. Doi: 10.1056/NEJMMoa061648.
- Brodsky RA, Young NS, Antonioli E, et. al. Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinemia. *Blood*. 2008;111:1840-1847. Doi: 10.1182/blood-2007-06-094136.
- Sahin F, Akay OM, Ayer M, et al. Pesg PNH diagnosis, follow-up and treatment guidelines. *Am J Blood Res*. 2016;6(2):19-27. Published 2016 Aug 5.
- Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Hematology Am Soc Hematol Educ Program*. 2016;2016(1):208-216. doi:10.1182/asheducation-2016.1.208
- Devos T, Meers S, Boeckx N, et al. Diagnosis and management of PNH: Review and recommendations from a Belgian expert panel. *Eur J Haematol*. 2018;101(6):737-749. doi:10.1111/ejh.13166
- Patriquin CJ, Kiss T, Caplan S, et al. How we treat paroxysmal nocturnal hemoglobinuria: A consensus statement of the Canadian PNH Network and review of the national registry. *Eur J Haematol*. 2019;102(1):36-52. doi:10.1111/ejh.13176
- Bodó I, Amine I, Boban A, et al. Complement Inhibition in Paroxysmal Nocturnal Hemoglobinuria (PNH): A Systematic Review and Expert Opinion from Central Europe on Special Patient Populations. *Adv Ther*. 2023;40(6):2752-2772. doi:10.1007/s12325-023-02510-4
- Legendre CM, Licht C, Muus P, et. al. Terminal complement inhibitor eculizumab in atypical hemolytic-uremic syndrome. *N Eng J Med*. 2013;368:2169-2181. Doi: 10.1056/NEJMMoa1208981.
- Kato H, Nangaku M, Hataya H, et al. Clinical guides for atypical hemolytic uremic syndrome in Japan. *Clin Exp Nephrol*. 2016;20(4):536-543. doi:10.1007/s10157-016-1276-6
- 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(1):15-39. doi:10.1007/s00467-015-3076-8
- Pugh D, O'Sullivan ED, Duthie FA, Masson P, Kavanagh D. Interventions for atypical haemolytic uraemic syndrome. *Cochrane Database Syst Rev*. 2021;3(3):CD012862. Published 2021 Mar 23. doi:10.1002/14651858.CD012862.pub2
- Tseng MH, Lin SH, Tsai JD, et al. Atypical hemolytic uremic syndrome: Consensus of diagnosis and treatment in Taiwan. *J Formos Med Assoc*. 2023;122(5):366-375. doi:10.1016/j.jfma.2022.10.006
- Lee H, Kang E, Kang HG, et al. Consensus regarding diagnosis and management of atypical hemolytic uremic syndrome. *Korean J Intern Med*. 2020;35(1):25-40. doi:10.3904/kjim.2019.388
- Scully M, Goodship T. How I treat thrombotic thrombocytopenic purpura and atypical haemolytic uraemic syndrome. *Br J Haematol*. 2014;164(6):759-766. doi:10.1111/bjh.12718
- Howard Jr, James F., 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, multicentre study." *The Lancet Neurology* 16.12 (2017): 976-986.
- Dhillon, Sohita. "Eculizumab: A Review in Generalized Myasthenia Gravis." *Drugs* 78.3 (2018): 367-376.
- Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology*. 2016;87(4):419-425. doi:10.1212/WNL.0000000000002790

20. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021;96(3):114-122. doi:10.1212/WNL.00000000000011124
21. Alhaidar MK, Abumurad S, Soliven B, Rezania K. Current Treatment of Myasthenia Gravis. *J Clin Med*. 2022;11(6):1597. Published 2022 Mar 14. doi:10.3390/jcm11061597
22. Weinshenker B. Neuromyelitis Optica Spectrum Disorder. NORD (National Organization for Rare Disorders). <https://rarediseases.org/rare-diseases/neuromyelitis-optica/>. Published August 25, 2020. Accessed October 2, 2020.
23. Kessler RA, Mealy MA, Levy M. Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic. *Curr Treat Options Neurol*. 2016;18(1):2. doi:10.1007/s11940-015-0387-9
24. Mealy MA, Wingerchuk DM, Palace J, Greenberg BM, Levy M. Comparison of relapse and treatment failure rates among patients with neuromyelitis optica: multicenter study of treatment efficacy. *JAMA Neurol*. 2014;71(3):324-330. doi:10.1001/jamaneurol.2013.5699
25. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. *N Engl J Med*. 2019;381(7):614-625. doi:10.1056/NEJMoa1900866
26. Pardo S, Giovannoni G, Hawkes C, Lechner-Scott J, Waubant E, Levy M. Editorial on: Eculizumab in aquaporin4-positive neuromyelitis optica spectrum disorder. *Mult Scler Relat Disord*. 2019;33:A1-A2. doi:10.1016/j.msard.2019.07.001
27. Frampton JE. Eculizumab: A Review in Neuromyelitis Optica Spectrum Disorder [published correction appears in *Drugs*. 2020 Apr 21;:] [published correction appears in *Drugs*. 2020 Apr 22;:]. *Drugs*. 2020;80(7):719-727. doi:10.1007/s40265-020-01297-w
28. Pittock SJ, Fujihara K, Palace J, et al. Eculizumab monotherapy for NMOSD: Data from PREVENT and its open-label extension. *Mult Scler*. 2022;28(3):480-486. doi:10.1177/13524585211038291
29. Aungsumart S, Youngkong S, Dejthevaporn C, et al. Efficacy and safety of monoclonal antibody therapy in patients with neuromyelitis optica spectrum disorder: A systematic review and network meta-analysis. *Front Neurol*. 2023;14:1166490. Published 2023 Apr 4. doi:10.3389/fneur.2023.1166490
30. Wingerchuk DM, Zhang I, Kielhorn A, et al. Network Meta-analysis of Food and Drug Administration-approved Treatment Options for Adults with Aquaporin-4 Immunoglobulin G-positive Neuromyelitis Optica Spectrum Disorder. *Neurol Ther*. 2022;11(1):123-135. doi:10.1007/s40120-021-00295-8

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