Soliris® (eculizumab)
(Intravenous)

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I. Length of Authorization

PNH and aHUS: Coverage will be provided for twelve months and may be renewed.

gMG and NMOSD: Initial coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

Loading Doses:

3 vials Days 1, 8, 15, & 22; then 4 vials Day 29

Maintenance Dose:

4 vials every 14 days

B. Max Units (per dose and over time) [Medical Benefit]:

Indication	Loading Doses	Maintenance Dose
PNH	60 billable units Days 1, 8, 15, & 22; then 90 billable units Day 29	90 billable units every 14 days
aHUS, gMG, NMOSD	90 billable units Days 1, 8, 15, & 22; then 120 billable units Day 29	120 billable units every 14 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient does not have a systemic infection; AND
- Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of therapy and revaccinated according to current medical guidelines for vaccine use *(If urgent Soliris therapy is indicated in an unvaccinated patient, administer meningococcal*

vaccine(s) as soon as possible and provide patients with two weeks of antibacterial drug prophylaxis.); **AND**

- Prescriber is enrolled in the Soliris Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
- Will not be used in combination with other complement-inhibitor therapy (i.e., ravulizumab); **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH) †

- Patient is 18 years or older; **AND**
- Diagnosis must be accompanied by detection of PNH clones of at least 10% by flow cytometry diagnostic testing; **AND**
    - Demonstrate the presence of at least 2 different glycosylphosphatidylinositol (GPI) protein deficiencies (e.g. CD55, CD59, etc.) within at least 2 different cell lines (granulocytes, monocytes, erythrocytes); **AND**
- Patient has one of the following indications for therapy:
    - Presence of a thrombotic event
    - Presence of organ damage secondary to chronic hemolysis
    - Patient is pregnant and potential benefit outweighs potential fetal risk
    - Patient is transfusion dependent
    - Patient has high LDH activity (defined as ≥1.5 x ULN) with clinical symptoms
- Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, and packed RBC transfusion requirement; **AND**
- Patient had an inadequate response, or has a contraindication or intolerance, to ravulizumab-cwvz [Ultomiris™]

Atypical Hemolytic Uremic Syndrome (aHUS) †

- Patient is 2 months or older; **AND**
- Thrombotic Thrombocytopenic Purpura (TTP) has been ruled out by evaluating ADAMTS-13 level (ADAMTS-13 activity level > 10%); **AND**
- Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS) has been ruled out; **AND**
- Other causes have been ruled out such as coexisting diseases or conditions (e.g. bone marrow transplantation, solid organ transplantation, malignancy, autoimmune disorder, drug-induced, malignant hypertension, HIV infection, etc.), *Streptococcus pneumoniae* or Influenza A (H1N1) infection, or cobalamin deficiency; **AND**
- Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), serum creatinine/eGFR, platelet count, and plasma exchange/infusion requirement; **AND**

- Patient had an inadequate response, or has a contraindication or intolerance, to ravulizumab-cwvz [Ultomiris™]

Generalized Myasthenia Gravis (gMG) †

- Patient is 18 years or older; **AND**
- Patient has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV disease; **AND**
- Patient has a positive serologic test for anti-acetylcholine receptor (AchR) antibodies; **AND**
- Physician has assessed the baseline Quantitative Myasthenia Gravis (QMG) score; **AND**
- Patient has a MG-Activities of Daily Living (MG-ADL) total score of ≥6; **AND**
- Patient has failed treatment over at least 1 year with at least 2 immunosuppressive therapies (e.g. azathioprine, cyclosporine, mycophenolate, etc), or has failed at least 1 immunosuppressive therapy and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG)

Neuromyelitis Optica Spectrum Disorder (NMOSD) †

- Patient is 18 years or older; **AND**
- Patient was found to be seropositive for aquaporin-4 (AQP4) IgG antibodies; **AND**
- Patient has a history of at least 2 relapses in the last 12 months OR 3 relapses in the last 24 months, with at least 1 relapse in the last 12 months; **AND**
- Patient has an Expanded Disability Status Score (EDSS) of ≤ 7 (consistent with the presence of at least limited ambulation with aid); **AND**
- Patient is receiving concurrent corticosteroid therapy of 20 mg per day or less and those receiving immunosuppressive therapy (e.g. azathioprine, glucocorticoids, mycophenolate, etc) are on a stable dose regimen; **AND**
- Patient has not received therapy with rituximab or mitoxantrone in the last 3 months; **AND**
- Patient has not received intravenous immune globulin (IVIG) in the last 3 weeks.

† FDA Approved Indication(s)

IV. Renewal Criteria

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: serious meningococcal infections (septicemia and/or meningitis), infusion reactions, serious infections, thrombotic microangiopathy complications (TMA), etc.; **AND**
- Disease response indicated by one or more of the following:
  - PNH
    - Decrease in serum LDH from pretreatment baseline

- Stabilization/improvement in hemoglobin level from pretreatment baseline
- Decrease in packed RBC transfusion requirement from pretreatment baseline

- aHUS
  - Decrease in serum LDH from pretreatment baseline
  - Stabilization/improvement in serum creatinine/eGFR from pretreatment baseline
  - Increase in platelet count from pretreatment baseline
  - Decrease in plasma exchange/infusion requirement from pretreatment baseline
- gMG
  - Improvement of at least 3-points from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score
  - Improvement of at least 5-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score
- NMOSD
  - Stabilization/improvement of neurologic symptoms as evidenced by a decrease in acute relapses, EDSS, hospitalizations or plasma exchange treatments

V. Dosage/Administration

Indication	Dose*
Paroxysmal nocturnal hemoglobinuria (PNH)	Loading dose: – 600 mg intravenously every 7 days for the first 4 weeks, followed by 900 mg intravenously for the fifth dose 7 days later Maintenance dose: – 900 mg intravenously every 14 days
Atypical hemolytic uremic syndrome (aHUS)	**Adults** Loading dose: – 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later Maintenance dose: – 1200 mg intravenously every 14 days **Patients < 18 years** 5 kg - <10 kg: – 300 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 3 weeks 10 kg - <20 kg: – 600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 2 weeks 20 kg -<30 kg: – 600 mg weekly x 2 doses, 600 mg at week 3, then 600 mg every 2 weeks 30 kg - <40 kg: – 600 mg weekly x 2 doses, 900 mg at week 3, then 900 mg every 2 weeks ≥ 40 kg: – 900 mg weekly x 4 doses, 1200 mg at week 5, then 1200 mg every 2 weeks

Generalized Myasthenia Gravis (gMG) and Neuromyelitis Optica Spectrum Disorder (NMOSD)	Loading dose: – 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later Maintenance dose: – 1200 mg intravenously every 14 days

Dose Adjustment for aHUS (adult and pediatric patients), gMG (adult patients), and NMOSD (adult patients) in case of Plasmapheresis, Plasma Exchange or Fresh Frozen Plasma Infusion

Type of Plasma Intervention	Most Recent Soliris Dose	Supplemental Soliris With Each Plasma Intervention	Timing of Supplemental Soliris Dose
Plasmapheresis or plasma exchange (PE)	300 mg	300 mg per each plasmapheresis or PE	Within 60 minutes after each plasmapheresis or PE
	≥ 600 mg	600 mg per each plasmapheresis or PE	
Fresh frozen plasma infusion (FFP)	≥ 300 mg	300 mg per each infusion of FFP	60 minutes prior to each infusion of FFP

**Doses should be administered at the above intervals, or within two days of these time points.*

VI. Billing Code/Availability Information

Jcode:

J1300 – Injection, eculizumab, 10 mg; 1 billable unit = 10 mg

NDC:

Soliris 300 mg/30 mL single-use vials for injection: 25682-0001-xx

VII. References

1. Soliris [package insert]. Boston, MA; Alexion Pharmaceuticals, Inc; June 2019. Accessed July 2019.
2. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Borowitz MJ, Craig FE, DiGiuseppe JA, Illingworth AJ, Rosse W, Sutherland DR, Wittwer CT, Richards SJ. Cytometry B Clin Cytom. 2010 Jul;78(4):211-30. doi: 10.1002/cyto.b.20525.
3. Effect of eculizumab on hemolysis and transfusion requirements in patients with paroxysmal nocturnal hemoglobinuria. Hillmen P; Hall C; Marsh JC; Elebute M; Bombara MP; Petro BE; Cullen MJ; Richards SJ; Rollins SA; Mojcik CF; Rother RP. N Engl J Med 2004 Feb 5;350(6):552-9.

4. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. Hillmen P; Young NS; Schubert J; Brodsky RA; Socie G; Muus P; Roth A; Szer J; Elebute MO; Nakamura R; Browne P; Risitano AM; Hill A; Schrezenmeier H; Fu CL; Maciejewski J; Rollins SA; Mojcik CF; Rother RP; Luzzatto L. N Engl J Med. 2006 Sep 21;355(12):1233-43.
5. Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinuria. Brodsky RA; Young NS; Antonioli E; Risitano AM; Schrezenmeier H; Schubert J; Gaya A; Coyle L; de Castro C; Fu CL; Maciejewski JP; Bessler M; Kroon HA; Rother RP; Hillmen P. Blood. 2008 Feb 15;111(4):1840-7. Epub 2007 Nov 30.
6. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood. 2005 Dec 1. 106(12):3699-709.
7. 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 Jan;31(1):15-39.
8. Taylor CM, Machin S, Wigmore SJ, et al. Clinical practice guidelines for the management of atypical haemolytic uraemic syndrome in the United Kingdom. Br J Haematol. 2010 Jan;148(1):37-47.
9. 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.
10. Cheong HI, Kyung Jo S, Yoon SS, et al. Clinical Practice Guidelines for the Management of Atypical Hemolytic Uremic Syndrome in Korea. J Korean Med Sci. 2016 Oct;31(10):1516-1528.
11. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis-Executive Summary. Neurology. 2016 Jul 26; 87(4): 419-25.
12. Howard JF. REGAIN: A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Eculizumab in Subjects With Refractory Generalized Myasthenia Gravis (gMG). Presented at the 14th International Congress on Neuromuscular Diseases (ICNMD), Toronto, July 7, 2016.
13. Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 2014; 261:1.
14. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. N Engl J Med 2019.
15. National Government Services, Inc. Local Coverage Article: Eculizumab (Soliris®) - Related to LCD L33394 (A54548). Centers for Medicare & Medicaid Services, Inc. Updated 11/22/2017 with effective dates 12/01/2017. Accessed July 2019.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D59.3	Hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]

ICD-10	ICD-10 Description
G36.0	Neuromyelitis optica [Devic]
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): 6; K	**NCD/LCD or Article Document (s):** A54548
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A54548&bc=gAAAAAAAAAAA	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC