

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) [NDC Unit]:

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) [HCPCS Unit]:

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 ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **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**

Universal Criteria ¹

- Patient does not have an unresolved, serious systemic infection (e.g., *Neisseria meningitidis*, etc.); **AND**
- Will not be used in combination with another complement-inhibitor therapy (i.e., ravulizumab, etc.); **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH) † Φ ^{1,2-6,9}

- 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 $\geq 1.5 \times$ ULN) with clinical symptoms; **AND**
- Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, and packed RBC transfusion requirement

Atypical Hemolytic Uremic Syndrome (aHUS) † Φ ^{1,7,8,10}

- Patient is at least 2 months of age; **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

Generalized Myasthenia Gravis (gMG) † Φ 1,11,12

- 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 had an inadequate response after a minimum one year trial with either:
 - Two (2) or more immunosuppressive therapies (e.g. azathioprine, cyclosporine, mycophenolate, etc.); **OR**
 - One (1) immunosuppressive therapy **AND** required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG)

Neuromyelitis Optica Spectrum Disorder (NMOSD) † Φ 1,13-15

- Patient has a confirmed diagnosis based on the following:
 - Patient was found to be seropositive for aquaporin-4 (AQP4) IgG antibodies; **AND**
 - Patient has at least one core clinical characteristic §; **AND**
 - Alternative diagnoses have been excluded (e.g., multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); **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 ≤ 7.0 (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; **AND**
- Patient had an inadequate response, or has a contraindication or intolerance, to rituximab **OR** inebilizumab; **AND**
- Patient will not concomitantly receive therapy with any of the following:
 - IL6-inhibitor (e.g., satralizumab); **OR**
 - Anti-CD20-directed antibody (e.g., rituximab); **OR**
 - Anti-CD19-directed antibody (e.g., inebilizumab)

§ Core Clinical Characteristics of NMOSD ¹⁵

- Optic neuritis
- Acute myelitis

- Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
- Acute brainstem syndrome
- Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
- Symptomatic cerebral syndrome with NMOSD-typical brain lesions

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

IV. Renewal Criteria ^{1,2-6}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant 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	<u>Loading dose:</u>

hemoglobinuria (PNH)	<ul style="list-style-type: none"> – 600 mg intravenously every 7 days for the first 4 weeks, followed by 900 mg intravenously for the fifth dose 7 days later <p><u>Maintenance dose:</u></p> <ul style="list-style-type: none"> – 900 mg intravenously every 14 days
Atypical hemolytic uremic syndrome (aHUS)	<p>Adults</p> <p><u>Loading dose:</u></p> <ul style="list-style-type: none"> – 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later <p><u>Maintenance dose:</u></p> <ul style="list-style-type: none"> – 1200 mg intravenously every 14 days <p>Patients < 18 years</p> <p><u>5 kg - <10 kg:</u></p> <ul style="list-style-type: none"> – 300 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 3 weeks <p><u>10 kg - <20 kg:</u></p> <ul style="list-style-type: none"> – 600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 2 weeks <p><u>20 kg - <30 kg:</u></p> <ul style="list-style-type: none"> – 600 mg weekly x 2 doses, 600 mg at week 3, then 600 mg every 2 weeks <p><u>30 kg - <40 kg:</u></p> <ul style="list-style-type: none"> – 600 mg weekly x 2 doses, 900 mg at week 3, then 900 mg every 2 weeks <p><u>≥ 40 kg:</u></p> <ul style="list-style-type: none"> – 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)	<p><u>Loading dose:</u></p> <ul style="list-style-type: none"> – 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later <p><u>Maintenance dose:</u></p> <ul style="list-style-type: none"> – 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

<u>Type of Plasma Intervention</u>	<u>Most Recent Soliris Dose</u>	<u>Supplemental Soliris With Each Plasma Intervention</u>	<u>Timing of Supplemental Soliris Dose</u>
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

HCPCS code:

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 2020.
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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.
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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.
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12. Howard JF Jr, Utsugisawa K, Benatar M, 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. Lancet Neurol. 2017 Dec;16(12):976-986.
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. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.
16. National Government Services, Inc. Local Coverage Article: Billing and Coding: Eculizumab (A54548). Centers for Medicare & Medicaid Services, Inc. Updated 11/01/2019 with effective dates 11/07/2019. Accessed July 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D59.3	Hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
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), Local Coverage Articles (LCAs), 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/LCA/LCD):

Jurisdiction(s): 6; K	NCD/LCA/LCD Document (s): A54548
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<https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A54548&bc=gAAAAAAAAAAAA>

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