Soliris® (eculizumab)
(Intravenous)

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I. Length of Authorization

- PNH and aHUS: Coverage will be provided for twelve (12) months and may be renewed.
- gMG and NMOSD: Initial coverage will be provided for six (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**

- Prescriber is enrolled in the Soliris Risk Evaluation and Mitigation Strategy (REMS) program; **AND**

Universal Criteria [1]

- Patient must be vaccinated against meningococcal disease at least two weeks prior to initiation of therapy and will continue to be 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**
- Patient does not have an unresolved, serious systemic infection (e.g., *Neisseria meningitidis*, etc.); **AND**
- Will not be used in combination with other immunomodulatory biologic therapies (i.e., efgartigimod, ravulizumab, pegcetacoplan, satralizumab, inebilizumab, etc.) *[Note: a 4-week run-in period is allowed when transitioning from eculizumab to pegcetacoplan]*; **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH) † Φ [1,2-6,9,16,23]

- 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 (e.g., granulocytes, monocytes, erythrocytes); **AND**
- Patient has laboratory evidence of significant intravascular hemolysis (i.e., LDH ≥1.5 x ULN) with symptomatic disease and at least one other indication for therapy from the following (regardless of transfusion dependence):
    - Patient has symptomatic anemia (i.e., hemoglobin < 7 g/dL or hemoglobin < 10 g/dL, in at least two independent measurements in a patient with cardiac symptoms
    - Presence of a thrombotic event related to PNH
    - Presence of organ damage secondary to chronic hemolysis (i.e., renal insufficiency, pulmonary insufficiency/hypertension)
    - Patient is pregnant and potential benefit outweighs potential fetal risk
    - Patient has disabling fatigue
    - Patient has abdominal pain (requiring admission or opioid analgesia), dysphagia, or erectile dysfunction; **AND**
- Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, packed RBC transfusion requirement, and history of thrombotic events; **AND**
- Patient had an inadequate response, contraindication, or intolerance to a trial of ravulizumab (Ultomiris®)

Atypical Hemolytic Uremic Syndrome (aHUS) † Φ [1,7,8,10,17]

- Patient is at least 2 months of age; **AND**
- Patient shows signs of thrombotic microangiopathy (TMA) (e.g., changes in mental status, seizures, angina, dyspnea, thrombosis, increasing blood pressure, decreased platelet count, increased serum creatinine, increased LDH, etc.); **AND**
- Thrombotic Thrombocytopenic Purpura (TTP) has been ruled out by evaluating ADAMTS-13 level (i.e., 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, Streptococcus pneumoniae sepsis or known genetic defect in cobalamin C metabolism, etc); **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, contraindication, or intolerance to a trial of ravulizumab (Ultomiris®)

Generalized Myasthenia Gravis (gMG) † Φ [1,11,12, 18-22]

- 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**
- Patient has had a thymectomy (*Note: Applicable only to patients with thymomas OR non-thymomatous patients who are 50 years of age or younger)*; **AND**
- Physician has assessed objective signs of neurological weakness and fatiguability on a baseline neurological examination (e.g., including, but not limited to, the Quantitative Myasthenia Gravis (QMG) score, etc.); **AND**
- Patient has a MG-Activities of Daily Living (MG-ADL) total score of ≥6; **AND**
- Patient will avoid or use with caution medications known to worsen or exacerbate symptoms of MG (e.g., certain antibiotics, beta-blockers, botulinum toxins, hydroxychloroquine, etc.); **AND**
- Patient had an inadequate response after a minimum one-year trial with two (2) or more immunosuppressive therapies (e.g., corticosteroids plus an immunosuppressant such as azathioprine, cyclosporine, mycophenolate, etc.); **OR**
    - Patient required chronic treatment with plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG) in addition to immunosuppressant therapy; **AND**

- Patient had an inadequate response, contraindication, or intolerance to a trial of ravulizumab (Ultomiris®)

- Patient had an inadequate response, or has a contraindication or intolerance, to efgartigimod alfa-fcab [Vyvgart™]

§ Myasthenia Gravis Foundation of America (MGFA) Disease Clinical Classification [19]:

- **Class I**: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
- **Class II**: Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - **IIa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - **IIb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- **Class III**: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - **IIIa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - **IIIb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- **Class IV**: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - **IVa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - **IVb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- **Class V**: Defined as intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb.

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 (i.e., 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); **AND**
    - Anti-CD20-directed antibody (e.g., rituximab); **AND**
    - 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); **Φ** Orphan Drug

IV. Renewal Criteria [1-6,23]

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: serious meningococcal infections (septicemia and/or meningitis), infusion reactions, serious infections, thrombotic microangiopathy complications (TMA), etc.; **AND**

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Patient has not developed severe bone marrow failure syndrome (i.e., aplastic anemia or myelodysplastic syndrome) OR experienced a spontaneous disease remission OR received curative allogeneic stem cell transplant**; AND**
- Disease response indicated by one or more of the following**:**
    - Decrease in serum LDH from pretreatment baseline Stabilization/improvement in hemoglobin level from pretreatment baseline
    - Decrease in packed RBC transfusion requirement from pretreatment baseline (i.e., reduction of at least 30%)
    - Reduction in thromboembolic events

Atypical Hemolytic Uremic Syndrome (aHUS)

- Disease response indicated by one or more of the following**:**
    - 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

Generalized Myasthenia Gravis (gMG)

- Patient experienced an improvement (i.e., reduction) of at least 3-points from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score; **OR**
- Patient experienced an improvement of at least 5-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Patient has stabilization and/or 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	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:

Disorder (NMOSD)	– 1200 mg intravenously every 14 days

Dose Adjustment for adult patients with aHUS (includes pediatric patients), gMG, and NMOSD 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

HCPCS Code:

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

NDC:

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

VII. References

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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: https://www.cms.gov/medicare-coverage-database/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
https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=54548&ver=20&bc=0	

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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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