I. Length of Authorization

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

gMG: 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]:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Loading Doses</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNH</td>
<td>60 billable units Days 1, 8, 15, &amp; 22; then 90 billable units Day 29</td>
<td>90 billable units every 14 days</td>
</tr>
<tr>
<td>aHUS, gMG</td>
<td>90 billable units Days 1, 8, 15, &amp; 22; then 120 billable units Day 29</td>
<td>120 billable units every 14 days</td>
</tr>
</tbody>
</table>

III. Initial Approval Criteria

Site of care specialty infusion program requirements are met (refer to Moda Site of Care Policy).

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: 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

**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): **AND**

Patient had an inadequate response, or has a contraindication or intolerance, to rituximab

† 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 (septicaemia and/or meningitis), infusion reactions, serious infections, thrombotic microangiopathy complications (TMA), etc.: **AND**
• Disease response indicated by one or more of the following:
  o **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
  o **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
  o **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

**V. Dosage/Administration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal nocturnal hemoglobinuria (PNH)</td>
<td>Loading dose:</td>
</tr>
<tr>
<td></td>
<td>– 600 mg intravenously every 7 days for the first 4 weeks, followed by 900 mg intravenously for the fifth dose 7 days later</td>
</tr>
<tr>
<td></td>
<td>Maintenance dose:</td>
</tr>
<tr>
<td></td>
<td>– 900 mg intravenously every 14 days</td>
</tr>
</tbody>
</table>
## 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

<table>
<thead>
<tr>
<th>Weight Range</th>
<th>Loading Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 kg - &lt;10 kg</td>
<td>600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 3 weeks</td>
</tr>
<tr>
<td>10 kg - 20 kg</td>
<td>600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 2 weeks</td>
</tr>
<tr>
<td>20 kg - 30 kg</td>
<td>600 mg weekly x 2 doses, 600 mg at week 3, then 600 mg every 2 weeks</td>
</tr>
<tr>
<td>30 kg - &lt;40 kg</td>
<td>600 mg weekly x 2 doses, 900 mg at week 3, then 900 mg every 2 weeks</td>
</tr>
<tr>
<td>≥ 40 kg</td>
<td>900 mg weekly x 4 doses, 1200 mg at week 5, then 1200 mg every 2 weeks</td>
</tr>
</tbody>
</table>

### Generalized Myasthenia Gravis (gMG)

**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) and gMG (adult patients) in case of Plasmapheresis, Plasma Exchange or Fresh Frozen Plasma Infusion

<table>
<thead>
<tr>
<th>Type of Plasma Intervention</th>
<th>Most Recent Soliris Dose</th>
<th>Supplesmental Soliris With Each Plasma Intervention</th>
<th>Timing of Supplemental Soliris Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmapheresis or plasma exchange (PE)</td>
<td>300 mg</td>
<td>300 mg per each plasmapheresis or PE</td>
<td>Within 60 minutes after each plasmapheresis or PE</td>
</tr>
<tr>
<td></td>
<td>≥ 600 mg</td>
<td>600 mg per each plasmapheresis or PE</td>
<td></td>
</tr>
<tr>
<td>Fresh frozen plasma infusion (FFP)</td>
<td>≥ 300 mg</td>
<td>300 mg per each infusion of FFP</td>
<td>60 minutes prior to each infusion of FFP</td>
</tr>
</tbody>
</table>

*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


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.


Appendix 1 – Covered Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D59.3</td>
<td>Hemolytic-uremic syndrome</td>
</tr>
<tr>
<td>D59.5</td>
<td>Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]</td>
</tr>
<tr>
<td>G70.00</td>
<td>Myasthenia gravis without (acute) exacerbation</td>
</tr>
<tr>
<td>G70.01</td>
<td>Myasthenia gravis with (acute) exacerbation</td>
</tr>
</tbody>
</table>

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):** 5, 8

**NCD/LCD Document (s):** L34741


**Jurisdiction(s):** 6: K

**NCD/LCD or Article Document (s):** A54548


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