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. 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

Soliris must be requested by one of the following specialists:

- PNH – Hematologist; OR
- Atypical hemolytic uremic syndrome – Hematologist or Nephrologist; AND

- Patient does not have a systemic infection; AND

- Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of Soliris 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**

Coverage is provided in the following conditions:

**Paroxysmal Nocturnal Hemoglobinuria (PNH) †**

• Patient is 18 years or older; **AND**
• Diagnosis must be accompanied by detection of PNH clones by flow cytometry diagnostic testing; **AND**
  o 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:
  o Presence of a thrombotic event
  o Presence of organ damage secondary to chronic hemolysis
  o Patient is pregnant and potential benefit outweighs potential fetal risk
  o Patient is transfusion dependent
  o 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

**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)

† 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:
  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><strong>Paroxysmal nocturnal hemoglobinuria (PNH)</strong></td>
<td>Loading dose:&lt;br&gt;– 600 mg intravenously every 7 days for the first 4 weeks, followed by 900 mg intravenously for the fifth dose 7 days later&lt;br&gt;Maintenance dose:&lt;br&gt;– 900 mg intravenously every 14 days</td>
</tr>
<tr>
<td><strong>Atypical hemolytic uremic syndrome (aHUS)</strong></td>
<td>Adults&lt;br&gt; Loading dose:&lt;br&gt;– 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later&lt;br&gt;Maintenance dose:&lt;br&gt;– 1200 mg intravenously every 14 days&lt;br&gt;Patients &lt; 18 years&lt;br&gt; 5 kg - &lt;10 kg:&lt;br&gt;– 300 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 3 weeks&lt;br&gt;10 kg - &lt;20 kg:&lt;br&gt;– 600 mg weekly x 1 dose, 300 mg at week 2, then 300 mg every 2 weeks&lt;br&gt;20 kg - &lt;30 kg:&lt;br&gt;– 600 mg weekly x 2 doses, 600 mg at week 3, then 600 mg every 2 weeks&lt;br&gt;30 kg - &lt;40 kg:&lt;br&gt;– 600 mg weekly x 2 doses, 900 mg at week 3, then 900 mg every 2 weeks&lt;br&gt;≥ 40 kg:&lt;br&gt;– 900 mg weekly x 4 doses, 1200 mg at week 5, then 1200 mg every 2 weeks</td>
</tr>
<tr>
<td><strong>Generalized Myasthenia Gravis (gMG)</strong></td>
<td>Loading dose:&lt;br&gt;– 900 mg intravenously every 7 days for the first 4 weeks, followed by 1,200 mg intravenously for the fifth dose 7 days later&lt;br&gt;Maintenance dose:&lt;br&gt;– 1200 mg intravenously every 14 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Plasma Intervention</th>
<th>Most Recent Soliris Dose</th>
<th>Supplemental 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>≥ 600 mg</td>
<td>600 mg per each plasmapheresis or PE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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.

Limitations/Exclusions
Soliris® (eculizumab) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

<table>
<thead>
<tr>
<th>Procedure Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1300</td>
<td>Injection, eculizumab, 10 mg</td>
</tr>
</tbody>
</table>

Applicable NDCs

<table>
<thead>
<tr>
<th>NDC Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>25682-0001-xx</td>
<td>Soliris 300 mg/30 mL single-use vials for injection</td>
</tr>
</tbody>
</table>

Applicable Diagnosis Codes

<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>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>

Revision History

N/A

VI. 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.