Definition

Soliris is a monoclonal antibody that binds with high affinity to complement protein C5, which inhibits its cleavage to C5a and C5b and prevents the generation of the terminal complement complex C5b-9. In patients with paroxysmal nocturnal hemoglobinuria (PNH), eculizumab inhibits terminal complement mediated intravascular hemolysis and in patients with acquired hemolytic uremic syndrome, eculizumab inhibits complement-mediated thrombotic microangiopathy. The precise mechanism by which eculizumab exerts its therapeutic effect in neuromyelitis optica spectrum disorder (NMOSD) is unknown, but is presumed to involve inhibition of aquaporin-4 antibody induced terminal complement C5b-9 deposition.

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.

NMOSD: Initial authorization will be for no more than 6 months and reauthorization will be for no more than 12 months.
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>

I. 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 or 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**
  - 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
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)

Neuromyelitis Optica Spectrum Disorder (NMOSD) †

- Patient is 18 years or older; AND
- Submission of medical records (e.g. chart notes, laboratory values, etc.) to support the diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the following.
- Past medical history of one of the following:
  - 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; **AND**
- Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMP-IgG antibodies; **AND**
- Diagnosis of multiple sclerosis or other diagnoses have been ruled out; **AND**
- Patient has not failed a previous course of Soliris therapy; **AND**
- History of failure of, contraindication, or intolerance to rituximab therapy; **AND**
- **One** of the following:
  - History of at least two relapses during the previous 12 months prior to initiating Soliris
  - History of at least three relapses during the previous 24 months, at least one relapse occurring within the past 12 months prior to initiating Soliris; **AND**
  - Soliris is initiated and titrated according to the US FDA labeled dosing for NMOSD, up to maximum of 1200mg every 2 weeks; **AND**
  - Prescribed by a neurologist; **AND**
  - Patient is **not** receiving Soliris in combination with **any** of the following:
    a. Disease modifying therapies for the treatment of multiple sclerosis (e.g. Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.)
    b. Anti-IL6 therapy (e.g., Actemra (tocilizumab); **AND**

† FDA Approved Indication(s)

II. **Renewal Criteria**

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the criteria identified above; **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

  o **NMOSD**
    ▪ Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD
    ▪ Maintenance, reduction, or discontinuation of dose(s) of any baseline immunosuppressive therapy (IST) prior to starting Soliris. **Note:** Add on, dose escalation of IST, or additional rescue therapy will be considered as treatment and failure. **AND**
    ▪ Soliris is dosed according to the FDA labeled dosing for NMOSD: up to a maximum of 1200mg every 2 weeks; **and**
    ▪ Prescribed by a neurologist; **and**
    ▪ Patient is **not** receiving Soliris in combination with **any** of the following:
      a. Disease modifying therapies for the treatment of multiple sclerosis (e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.)
      b. Anti-IL6 therapy [e.g., Actemra (tocilizumab)] **AND**
    ▪ Reauthorization will be for no more than 12 months
III. **Dosage/Administration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose*</th>
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</table>
| **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 |
| 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 |
| **Atypical hemolytic uremic syndrome (aHUS)** | Loading dose:  
- 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)** | 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>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></td>
<td>≥ 600 mg</td>
<td>600 mg per each plasmapheresis or PE</td>
<td></td>
</tr>
</tbody>
</table>
**Fresh frozen plasma infusion (FFP)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Time</th>
</tr>
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<tbody>
<tr>
<td>≥ 300 mg</td>
<td>60 minutes prior to each infusion of FFP</td>
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</tbody>
</table>

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

**Limitations/Exclusions**

1. Soliris® (eculizumab) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.
2. Patients with unresolved serious Neisseria meningitidis infection
3. Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection.

**Applicable Procedure Codes**

- **J1300** Injection, eculizumab, 10 mg

**Applicable NDCs**

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

**Applicable Diagnosis Codes**

- **D59.3** Hemolytic-uremic syndrome
- **D59.5** Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
- **G36.0** Neuromyelitis Optica Spectrum Disorder (NMOSD)
- **G70.00** Myasthenia gravis without (acute) exacerbation
- **G70.01** Myasthenia gravis with (acute) exacerbation

**Revision History**

- **04/16/2020** Added two contraindications to Limitations/Exclusions per FDA Label:
  1. Patients with unresolved serious Neisseria meningitidis infection
  2. Patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Soliris treatment outweigh the risks of developing a meningococcal infection.

- **10/02/2019** Added the new indication for Neuromyelitis Optica Spectrum Disorder (NMOSD), added the criteria and it’s diagnosis code G36.0
IV. 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; Mojck 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; Mojck 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.


