I. Medication Description

Soliris (eculizumab) is an intravenous monoclonal antibody that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. It is indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and generalized myasthenia gravis in persons who are anti-acetylcholine receptor (AchR) antibody positive.

Eculizumab inhibits terminal complement-mediated intravascular hemolysis in PNH patients and complement-mediated thrombotic microangiopathy (TMA) in patients with aHUS. The precise mechanism by which eculizumab exerts its therapeutic effect in gMG patients is unknown, but is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction.

Soliris (eculizumab) is a monoclonal antibody designed to selectively block terminal complement component 5 (C5) activation. When C5 is activated it attracts and activates pro-inflammatory immune cells and causes cell death by triggering pore formation. By inhibiting the complement cascade at this late phase, normal processes to prevent disease in the complement cascade are preserved, but the over activation of inflammatory and cell destruction processes are inhibited.

Soliris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Soliris is provided for the following conditions when the listed criteria are met:

- Atypical hemolytic uremic syndrome (aHUS):
  - Medication is prescribed by (or in consultation with) a hematologist, nephrologist, and/or other appropriate specialist

- Generalized Myasthenia Gravis (gMG):
  - Member is 18 years of age or older AND
  - Medication is prescribed by (or in consultation with) a neurologist or other appropriate specialist AND
  - Member meets ALL of the following criteria (documentation must be provided):
    - Positive serologic test for anti-acetylcholine (AchR) antibodies AND
    - Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II-IV
- Myasthenia Gravis Activities of Daily Living (MG-ADL) total score equal to or greater than 6 AND
- Baseline Quantitative Myasthenia Gravis (QMG) score AND
- Member had an inadequate response or contraindication to pyridostigmine AND
- Member had an inadequate response or contraindication to corticosteroids AND
- Member had an inadequate response to at least TWO or more of the following medications in the previous 12 months (unless use is contraindicated or the severity of disease requires rapid improvement not attainable with immunosuppressive medications at the time of the request):
  - Azathioprine
  - Cyclosporine
  - Cyclophosphamide
  - Methotrexate
  - Mycophenolate mofetil
  - Tacrolimus AND
- In the previous 12 months, the member has had a progressive disease with an inadequate response (or contraindication) to the use of at least two courses of the following:
  - Immune Globulin (IVIG) OR
  - Plasma exchange
- Paroxysmal nocturnal hemoglobinuria (PNH):
  - Member is 18 years of age or older AND
  - Medication is prescribed by (or in consultation with) a hematologist and/or other appropriate specialist AND
  - Diagnosis is accompanied by detection of PNH clones by flow cytometry diagnostic test

IV. Quantity Limitations

Coverage is available as follows:
- aHUS or gMG full course treatment:
  - Maximum per infusion: 1200mg (120 billable units or 4 vials)
  - Maximum covered units when used for a full course treatment:
    - Initial/Loading Doses: 4800mg (480 billable units or 16 vials) over 5 weeks
    - Maintenance Dose: 2400mg (240 billable units or 8 vials) per each 28 days OR
- aHUS or gMG dose adjustments in case of concomitant plasmapheresis, plasma exchange, or fresh frozen plasma infusion:
  - Maximum per infusion: 600 mg (60 billable units or 2 vials) per each treatment
  - Quantity sufficient to accommodate FDA-approved dosing per type of treatment
- PNH:
  - Maximum per infusion: 900mg (90 billable units or 3 vials)
  - Maximum covered units:
    - Initial/Loading Doses: 3300mg (330 billable units or 11 vials) over 5 weeks
    - Maintenance Dose: 1800 mg (180 billable units or 6 vials) per each 28 days
V. Coverage Duration

Initial coverage is provided for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed in 12 month intervals based upon the following criteria:

- Absence of unacceptable toxicity from the drug **AND**
- Member displays improvement of symptoms or shows stabilization of the respective disease state:
  - **For the treatment of aHUS:**
    - Thrombotic microangiopathy (TMA) response and renal function maintained
  - **For the treatment of gMG:**
    - Improved MG-ADL total score or QMG total score
  - **For the treatment of PNH:**
    - A higher rate of stabilization of hemoglobin levels in the absence of transfusion, fewer packed red blood cell transfusions, less intravascular hemolysis, and improvement in quality of life

VII. Billing/Coding Information

- J1300: 1 unit = 10mg
- Available in 300mg single-use vials containing 30ml of 10mg/ml Soliris solution
- Pertinent diagnoses:
  - Hemolytic-uremic syndrome: D59.3
  - Myasthenia Gravis: G70.0
  - Paroxysmal Nocturnal Hemoglobinuria: D59.5

VIII. Summary of Policy Changes

- 6/15/12: addition of criteria for aHUS
- 3/15/13: removal of documentation of meningococcal vaccination requirement for approval for aHUS and PNH
- 3/15/14: maximum dosing clarified per diagnosis; REMS registration requirement removed from section III
- 3/15/15: no policy changes
- 6/15/15: no policy changes
- 7/1/15: formulary distinctions made
- 6/15/16: no policy changes
- 4/5/17: no policy changes
- 2/14/18: addition of criteria for gMG
- 5/1/18: no policy changes
IX. References

6. 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.
7. 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.
8. 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.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.