Effective Date: 05/03/2018

Soliris® (eculizumab injection)

FDA approval: 3/16/2007
HCPCS: J1300
Benefit: Medical

I. Policy Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested medication is provided when all the below criteria are met:
   a. Patient must be vaccinated against meningococcal infection at least 2 weeks prior to eculizumab treatment
   b. Documented diagnosis of PNH (flow cytometric confirmation of at least 10% PNH type III red cells)
      1. Had at least 1 transfusion in 24 months preceding eculizumab
      2. OR documented history of major adverse thrombotic vascular events from thromboembolism
      3. Platelets >30,000 prior to eculizumab therapy
   c. Or documented diagnosis of atypical hemolytic uremic syndrome (aHUS)
   d. Diagnosis of refractory gMG
      i. Patient must be vaccinated against meningococcal infection according to the most current Advisory Committee on Immunization Practice (ACIP) recommendations for patients with complement deficiencies at least 2 weeks prior to eculizumab treatment.
      ii. Prescribed by a neurologist.
      iii. Documented diagnosis of refractory, anti-AChR antibody positive MG identified by:
         1. Lab record or chart notes indicating positive anti-AChR antibody and 1 of the following:
            a. Positive edrophonium test
            b. History of clinical response to oral cholinesterase inhibitors (Ex. pyridostigmine)
            c. Electrophysiological evidence of abnormal neuromuscular transmission by repetitive nerve stimulation (RNS) or single-fiber electromyography (SFEMG).
         iv. Patients must NOT have a history of:
            1. Thymectomy within 12 months
2. Thymoma
3. Other neoplasms of the thymus

v. Must demonstrate profound muscle weakness throughout the body resulting in one or more of the following:
   1. Slurred speech
   2. Impaired swallowing and choking
   3. Double vision
   4. Upper and lower extremity weakness
   5. Disabling fatigue
   6. Shortness of breath due to respiratory muscle weakness
   7. Episodes of respiratory failure

vi. Failure of corticosteroids and at least 2 or more immunosuppressive agents (Ex. azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus)

vii. Trial and failure of 3 of the following:
   1. Cyclophosphamide
   2. Rituximab
   3. Chronic intravenous immunoglobulin (IVIG)
   4. Chronic plasma exchange (PLEX)

B. Quantity Limitations, Authorization Period, and Renewal Criteria
   a. PHN and UHS
      i. Quantity Limit:
         1. FDA approved dosing
      ii. Initial authorization period: 1 year
      iii. Authorization will be reviewed at least annually to assess improvement on therapy
         1. Serum LDH levels may assist in monitoring hemolysis during and after treatment with Soliris
         2. In the setting of unchanged transfusion requirements or persistent thromboembolism events, discontinuation of Soliris may be considered
      iv. Renewal authorization period: 1 year
   b. Refractory gMG
      i. Quantity Limit:
         1. FDA approved dosing
      ii. Initial authorization period: 6 months
      iii. Authorization will be reviewed at least every 6 months to assess improvement on therapy
      iv. Renewal authorization period: 6 months

C. Soliris is considered investigational when used for all other conditions, including but not limited to:
   a. Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS), or typical hemolytic uremic syndrome
   b. Antibody mediated rejection (transplant)
   c. Guillain-Barre syndrome
   d. Thrombotic thrombocytopenic purpura (TTP)
   e. Systemic lupus erythematosus (SLE)
   f. Multifocal motor neuropathy
   g. Renal transplant rejection
   h. Hemolytic cold agglutinin disease
   i. Catastrophic antiphospholipid antibody syndrome

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j. Antineutrophil cytoplasmic autoantibody (ANCA) vasculitis
k. Dense deposit disease or C3 nephropathy
l. Non-exudative (dry) macular degeneration
m. Neuromyelitis optica

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

II. Therapeutic Considerations:

A. FDA Approved Indication:
   a. For the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
   b. For the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
   c. For the treatment of patients with refractory generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

B. Background Information:
   a. Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare, 1-2 cases per million, potentially life threatening disease characterized by a genetic mutation that causes complement induced intravascular hemolytic anemia (due to the destruction of red blood cells in the blood stream), red urine, and thrombosis
   b. 40-50% of patients develop thrombosis, (main cause of complications and death in PNH)
   c. Eculizumab is a recombinant humanized IgG monoclonal antibody that binds to complement protein C5, inhibiting its enzymatic cleavage, blocking formation of the terminal complement complex, preventing cell lysis
   d. Myasthenia gravis (MG) is the most common disorder of neuromuscular transmission with a prevalence of 25-142 per million world-wide, with about 85% of patients having positive antibodies to AChR. Refractory generalized myasthenia gravis (gMG) affects about 10% of patients with MG.
      a. These patients have typically failed to respond to conventional treatments and require repeated rescue treatment and/or experience frequent myasthenic crises.
      b. The American Academy of Neurology defines refractory MG as:
         i. a post-intervention status that is, “unchanged or worse after corticosteroids and at least 2 other immunosuppressive agents when used for an adequate dose for an adequate duration, with persistent symptoms or side effects that limit functioning, as defined by patient and physician”.
      c. Along with relevant signs and symptoms, a clinical diagnosis can be confirmed by laboratory testing including: a positive serological antibody test, a positive edrophonium test, and electrophysiologic testing.
         i. A serological test positive for anti-AChR antibody confirms MG in a patient with appropriate symptoms and clinical findings as the assay is very specific and present in roughly 80% of patients with generalized MG.
         ii. Edrophonium is an anticholinesterase inhibitor with rapid onset and short duration, by prolonging ACh in the neuromuscular junction, improved strength may be seen in patients with MG. An edrophonium test is considered positive.
when improvement in strength is seen following IV administration of edrophonium.

iii. Electrophysiologic testing such as RNS and SFEMG aim to identify abnormal transmission in the neuromuscular junction. RNS depletes the immediate stores of ACh at the neuromuscular junction. SFEMG is the most sensitive test for detecting abnormal neuromuscular transmission as it measures muscle fiber action potentials generated by the same motor neuron.

e. Guidelines
   a. American Society of Hematology (ASH-2010) eculizumab is recommended. Well tolerated long term (> 8 years) with continued improvement in PNH symptoms, reduction in transfusion requirements, and higher proportion of transfusion independent patients than previously seen
   b. The 2016 American Academy of Neurology’s (AAN) international consensus guidance for management of myasthenia gravis recommend that the goal for treatment is so that the patient has no symptoms or functional limitations from MG but has some weakness on examination of some muscles.
      i. Pyridostigmine should be part of the initial treatment in most patients with MG.
      ii. Corticosteroids or immunosuppressive therapy should be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine.
      iii. Immunosuppressive agents that can be used in MG include: azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus.
      iv. Nonsteroidal immunosuppressive agents should be used alone when corticosteroids are contraindicated or refused.
      v. Patients with refractory MG should be referred to an expert in MG.
      vi. Additionally, patients with refractory MG can be treated with chronic IVIG (intravenous immunoglobulin) and chronic PLEX (plasma exchange), cyclophosphamide, rituximab in addition to the previously mentioned immunosuppressive agents.
         1. Although rituximab has evidence of efficacy, a formal consensus was not reached by the committee.
      vii. At the time of guideline recommendation, no recommendations were made for the use of eculizumab for refractory MG.

C. Efficacy:
   *Please refer to most recent prescribing information.

D. Medication Safety Considerations:

   Boxed Warning: Yes
   Serious meningococcal infections

   *Please refer to most recent prescribing information.

E. Dosing and Administration:

   a. PNH: 600 mg weekly for the 1st 4 weeks, then 900mg for 5th dose (one week later), then 900mg every 2 weeks thereafter
   b. aHUS: 900mg weekly for the 1st 4 weeks, then 1200mg for 5th dose (one week later), then 1200mg every 2 weeks thereafter

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c. Refractory gMG: 900mg weekly for the 1st 4 weeks, then 1200mg for 5th dose (one week later), then 1200mg every 2 weeks thereafter

F. How Supplied:
300mg single-use vials

References: