Reference number
1632-A

STANDARD MEDICARE PART B MANAGEMENT

SOLIRIS (eculizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
B. Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
C. Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive
D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) positive.

Limitation of Use
Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. For initial requests:
   1. Paroxysmal nocturnal hemoglobinuria (PNH): flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency
   2. Generalized myasthenia gravis (gMG): Anti-acetylcholine receptor (AchR) antibody positive and use of two immunosuppressive therapies
   3. Neuromyelitis optica spectrum disorder (NMOSD): Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present
B. For continuation requests for PNH, aHUS, NMOSD: Chart notes or medical record documentation supporting benefit from therapy.

III. CRITERIA FOR INITIAL APPROVAL

A. Paroxysmal Nocturnal Hemoglobinuria (PNH)

Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) as demonstrated by either of the following:
   i. At least 5% PNH cells
   ii. At least 51% of GPI-AP deficient poly-morphonuclear cells
2. Flow cytometry is used to demonstrate GPI-APs deficiency

B. Atypical Hemolytic Uremic Syndrome (aHUS)

Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome (aHUS) that is not caused by Shiga toxin.

C. Generalized Myasthenia Gravis (gMG)

Authorization of 12 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:

1. The member is anti-acetylcholine receptor (AchR) antibody positive.
2. The member has had an inadequate response to at least two immunosuppressive therapies listed below:
   i. azathioprine
   ii. cyclosporine
   iii. mycophenolate mofetil
   iv. tacrolimus
   v. methotrexate
   vi. cyclophosphamide
   vii. rituximab

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 12 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

1. The member is anti-aquaporin-4 (AQP4) antibody positive.
2. The member exhibits one of the following core clinical characteristics of NMOSD:
   i. Optic neuritis
   ii. Acute myelitis
   iii. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
   iv. Acute brainstem syndrome
   v. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
   vi. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. **Paroxysmal Nocturnal Hemoglobinuria (PNH)**

Authorization for 12 months may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with Soliris.
2. The member is receiving benefit from therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

B. **Atypical Hemolytic Uremic Syndrome (aHUS)**
Authorization for 12 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with Soliris.
2. The member is receiving benefit from therapy (e.g., normalization of lactate dehydrogenase [LDH] levels, platelet counts).

C. **Neuromyelitis Optica Spectrum Disorder (NMOSD)**
Authorization for 12 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with Soliris.
2. The member is receiving benefit from therapy (e.g., reduction in number of relapses as compared to baseline).

D. **Generalized Myasthenia Gravis (gMG)**
Authorization for 12 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with Soliris.
2. The member is receiving benefit from therapy

V. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VI. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Soliris.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy.
4. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry.
5. International consensus guidance for management of myasthenia gravis
6. An international consensus approach to the management of atypical hemolytic uremic syndrome in children.
7. International consensus guidance for management of myasthenia gravis: 2020 update
8. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Soliris are covered.

VII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using percentage of PNH cells or percentage of GPI-AP deficiency poly-morphonuclear cells can be found in the guidelines for diagnosis of PNH (Borowitz et al and Preis et al). Flow cytometry is the gold standard for assessing the percentage of GPI-AP deficient poly-morphonuclear cells. Classic PNH is defined as greater than 50% of GPI-AP deficient PMNs. It is also possible to diagnose PNH by assessing the percentage of PNH cells. Most clinical trials for the complement inhibitors required at least 10% PNH cells, but the trials associated with Ultomiris only required 5% PNH cells. Therefore, the baseline requirement for all complement inhibitor programs will be at least 5%.

Support for the list of prerequisite therapies in generalized myasthenia gravis can be found in the guidelines for the management of MG (Narayanaswami et al). The guidelines support the use of azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide and rituximab as immunosuppressive therapies for gMG.

Support for the list of core clinical characteristics of NMOSD can be found in the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder (Wingerchuk et al). There are six clinical characteristics cited in the diagnostic criteria:

- 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 (figure 3)
- Symptomatic cerebral syndrome with NMOSD-typical brain lesions

VIII.REFERENCES

1. Soliris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; November 2020.
2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology.* 2011; 21-29.
3. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. Published online: January 1, 2016.
4. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology*. 2021;96(3):114-122.
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6. Borowitz MJ, Craig F, DiGiuseppe JA, et al. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry. *Cytometry B Clin Cytom*. 2010: 78: 211-230.
7. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
8. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.