Oscar Clinical Guideline: Soliris (eculizumab) (PG188, Ver. 2)

Soliris (eculizumab)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Soliris (eculizumab) is a recombinant humanized monoclonal antibody that specifically binds to the complement protein C5, inhibiting its cleavage into C5a and C5b and preventing the generation of the terminal complement complex C5b-9. Soliris (eculizumab) is FDA-approved for the following conditions:

1. Treatment of paroxysmal nocturnal hemoglobinuria (PNH)
2. Atypical hemolytic uremic syndrome (aHUS)
3. Anti-acetylcholine receptor antibody positive generalized myasthenia gravis (gMG) in adults
4. Anti-aquaporin-4 antibody positive neuromyelitis optica spectrum disorder (NMOSD) in adults.

By inhibiting terminal complement activity, Soliris (eculizumab) reduces intravascular hemolysis in PNH, complement-mediated thrombotic microangiopathy in aHUS, anti-AChR antibody-mediated neuromuscular damage in gMG, and complement-mediated injury to the central nervous system in NMOSD.

Definitions

"Acute Kidney Injury" refers to an acute condition in which there is a sudden decline in kidney function.

"**Anti-acetylcholine receptor (anti-AChR) antibodies**" are autoantibodies directed against the nicotinic acetylcholine receptor found at the neuromuscular junction.

"**Atypical hemolytic uremic syndrome (aHUS)**" is an ultra-rare, life-threatening genetic disorder caused by chronic, uncontrolled activation of the alternative complement pathway, resulting in complement-mediated thrombotic microangiopathy (TMA).

"Cholinesterase inhibitors" refer to a class of drugs that prevent the breakdown of acetylcholine, a neurotransmitter which plays a major role in memory and muscle movement and contraction.

"Expanded Disability Status Scale (EDSS)" is a clinical tool used in patients with multiple sclerosis (MS), to assess level of disability. The scale ranges from 0 to 10, with higher values associated with greater disability. See appendix, ***table 1***.

"Flow cytometry" is a tool used to rapidly assess the characteristics of a single cell using lasers in a buffered salt solution.

"**Generalized myasthenia gravis (gMG)**" is an autoimmune neuromuscular disease caused by antibodies that attack components of the neuromuscular junction (NMJ), impairing transmission between nerve and muscle, resulting in muscle weakness and fatigue.

"Immunomodulatory biologics" are large molecule drugs used to change one's immune response.

"Immunosuppressives," or immunosuppressive therapies, are any agent aimed at reducing the body's immune response, which may be used to treat conditions characterized by overactive immune systems, or to avoid rejection of bone marrow or organ transplant.

"**Myasthenia Gravis Activities of Daily Living (MG-ADL) score**" is a validated, 8-item patient-reported scale that assesses the impact of myasthenia gravis on daily functions.

"**Myasthenia Gravis Foundation of America (MGFA) Clinical Classification**" is a commonly used classification system that defines myasthenia gravis severity based on the degree and distribution of muscle weakness.

"**Neuromyelitis optica spectrum disorder (NMOSD)**" is a chronic inflammatory disorder of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting the optic nerves and spinal cord. The majority of patients have autoantibodies to aquaporin-4 (AQP4).

"**Paroxysmal nocturnal hemoglobinuria (PNH)**" refers to a rare, acquired, life-threatening disease of the blood characterized by complement-mediated hemolysis, thrombosis, and bone marrow failure.

"**Quantitative Myasthenia Gravis (QMG) score**" is a 13-item physician-administered scale that measures the severity of myasthenia gravis based on muscle weakness assessment.

"Relapse" refers to a deterioration or recurrence of a disease state after a temporary improvement.

"Thrombocytopenia" is a condition characterized by very low platelets in the blood.

"Thrombotic microangiopathy" refers to a group of rare disorders which is characterized by blood clots in small blood vessels, low platelet count, and the destruction of red blood cells.

"Thrombotic thrombocytopenic purpura" is a rare condition characterized by small blood clots in small blood vessels throughout the body, limiting or blocking the flow of blood to important areas of the body such as the heart, kidneys or brain.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Soliris (eculizumab)** medically necessary when ALL the following criteria are met for the applicable indication listed below:

1. Prescribed by, or in consultation with, a physician who specializes in the treatment of the specific condition:
    a. Atypical hemolytic uremic syndrome (aHUS) - hematologist or nephrologist; ***or***
    b. Generalized myasthenia gravis (gMG) - neurologist or neuromuscular disease specialist; ***or***
    c. Paroxysmal Nocturnal Hemoglobinuria (PNH) - hematologist; ***or***

d. Neuromyelitis Optica Spectrum Disorder (NMOSD) - neurologist or neuro-ophthalmologist; ***AND***

2. Will not be used concomitantly with other immunomodulatory biologic therapies (e.g., efgartigimod alfa, ravulizumab, rituximab, rozanolixizumab, zilucoplan, inebilizumab, etc.); ***AND***
3. Dosing is consistent with FDA-approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines based on indication, weight, and age; ***AND***
4. The member meets the medical necessity criteria for the applicable indication listed below:

<u>Atypical hemolytic uremic syndrome (aHUS)</u>

5. The member is at least 1 month of age; ***AND***
6. The member has a diagnosis of aHUS confirmed by ruling out:
    a. Thrombotic thrombocytopenic purpura (TTP), e.g., ADAMTS13 activity level above 5%; ***and***
    b. Shiga toxin E. coli-related HUS (STEC-HUS), e.g., STEC-test negative in members with a history of bloody diarrhea in the preceding 2-weeks; ***AND***
7. The member has documented presence of thrombotic microangiopathy, as evidenced by ALL of the following:
    a. Microangiopathic hemolytic anemia (e.g., anemia, increased LDH, decreased haptoglobin, increased indirect bilirubin, increased AST, elevated reticulocyte count, presence of schistocytes, helmet cells, and burr cells on peripheral blood smear)***; and***
    b. Thrombocytopenia, defined as a platelet count below 150,000/microliter***; and***
    c. Acute kidney injury (e.g., elevated serum creatinine, oliguria, presence of hematuria, proteinuria, pyuria, casts on urinalysis) or member requires dialysis.

<u>Generalized myasthenia gravis (gMG)</u>

5. The member is 18 years of age or older; ***AND***
6. The member has a confirmed diagnosis of generalized myasthenia gravis (gMG) **AND** documentation of **ALL** of the following:
    a. Positive serologic test for anti-acetylcholine receptor (anti-AChR) antibodies; ***and***
    b. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV (*see* Appendix*, **Table 1***); ***and***
    c. Baseline Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least (≥) 6; ***AND***
7. The member is unable to use, limited by toxicity, or has adequately tried and failed or experienced insufficient response to at least **TWO** standard therapies for gMG, such as:
    a. Cholinesterase inhibitors (eg, pyridostigmine); ***and/or***

b. Corticosteroids (e.g., prednisone) or inability to taper steroids below a reasonably acceptable level without return of symptoms; ***and/or***
c. Immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate mofetil, cyclophosphamide, tacrolimus).

<u>Neuromyelitis Optica Spectrum Disorder (NMOSD)</u>

5. The member is 18 years of age or older; ***AND***
6. The member has confirmed diagnosis of NMOSD, as evidenced by a positive serologic test for anti-aquaporin-4 (AQP4) antibodies; ***AND***
7. The member must have experienced at least **ONE** of the following:
    a. 2 or more relapses in the 12 months prior; ***or***
    b. 3 or more relapses in the 24 months prior, with at least 1 relapse occurring within the last 12 months; ***AND***
8. The member has an Expanded Disability Status Scale (EDSS) score of ≤ 7 (i.e., presence of at least limited ambulation with aid) (*see* Appendix*, **Table 2***); ***AND***
9. Soliris (eculizumab) will NOT be initiated during a NMOSD relapse episode.

<u>Paroxysmal Nocturnal Hemoglobinuria (PNH)</u>

5. The member is at least 1 month of age; ***AND***
6. Diagnosis of PNH confirmed by flow cytometry demonstrating a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) with EITHER of the following:
    a. at least 5% PNH cells (i.e., cells lacking GPI-AP expression); ***or***
    b. at least 51% of GPI-deficient poly-morphonuclear cells (e.g., neutrophils deficient in GPI-APs); ***AND***
7. The member has documentation of one or more of the following:
    a. Hemoglobin ≤ 9 g/dL with symptomatic anemia, or hemoglobin ≤ 7 g/dL; ***and/or***
    b. Absolute reticulocyte count ≥ 2 times the upper limit of normal; ***and/or***
    c. Thrombosis; ***and/or***
    d. Transfusion dependence (≥ 2 transfusions in the last 12 months).

<u>**If the above prior authorization criteria are met, Soliris (eculizumab) will be authorized for up to 6-months.**</u>

Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12-months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating **ALL** of the following criteria:

1. Prescribed by, or in consultation with, a physician who specializes in the treatment of the specific condition:
    a. Atypical hemolytic uremic syndrome (aHUS) - hematologist or nephrologist; ***or***
    b. Generalized myasthenia gravis (gMG) - neurologist or neuromuscular disease specialist; ***or***
    c. Neuromyelitis Optica Spectrum Disorder (NMOSD) - neurologist or neuro-ophthalmologist; ***or***
    d. Paroxysmal Nocturnal Hemoglobinuria (PNH) - hematologist; ***AND***
2. There is no unacceptable toxicity or adverse reaction to therapy, such as:
    a. Serious infections (e.g. serious respiratory or urinary tract infections); ***and/or***
    b. Severe hypersensitivity reactions; ***and/or***
    c. Severe immunosuppression; ***and/or***
    d. Other intolerable side effects or reactions; ***AND***
3. Will not be used concomitantly with other immunomodulatory biologic therapies (e.g., efgartigimod alfa, ravulizumab, rituximab, rozanolixizumab, zilucoplan, etc.); ***AND***
4. Dosing is consistent with FDA-approved labeling **OR** is supported by compendia or evidence-based published dosing guidelines based on indication, weight, and age; ***AND***
5. Ongoing therapy is required to maintain disease stability and control; ***AND***
6. Documentation of positive clinical response to therapy, such as ANY of the following:
    a. Atypical Hemolytic Uremic Syndrome (aHUS)
        i. Improvement or normalization of lactate dehydrogenase (LDH) levels and/or haptoglobin; ***and/or***
        ii. Improvement or normalization of platelet counts; ***and/or***
        iii. Improvement in serum creatinine from baseline and/or stabilization of renal function; ***and/or***
        iv. Reduction or absence of schistocytes or fragmented red blood cells on peripheral blood smear; ***and/or***
        v. Improvement in hemoglobin levels from baseline; ***or***
    b. Generalized Myasthenia Gravis
        i. Improvement in Myasthenia Gravis-Activities of Daily Living (MG-ADL) **OR** Quantitative Myasthenia Gravis (QMG) score from baseline; ***and/or***
        ii. Achievement of minimal symptom expression or pharmacological remission; ***and/or***

iii. Lack of relapses or reduced frequency/severity of relapses compared to baseline; ***or***

c. Neuromyelitis Optica Spectrum Disorder
   i. Reduction in the frequency and/or severity of relapses***; and/or***
   ii. Stabilization or improvement in disability scores***; and/or***
   iii. Absence of new lesions on MRI; ***or***

d. Paroxysmal Nocturnal Hemoglobinuria (PNH)
   i. Stabilization of hemoglobin levels; ***and/or***
   ii. Decreased transfusion requirements; ***and/or***
   iii. Reduced hemolysis; ***and/or***
   iv. Improvement in PNH symptoms; ***and/or***
   v. Improvement or normalization of lactate dehydrogenase (LDH) levels.

Experimental or Investigational / Not Medically Necessary

Soliris (eculizumab) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Antibody-mediated transplant rejection (excluding cardiac and renal transplants)
- Post-transplant recurrence of atypical hemolytic uremic syndrome (aHUS)
- Shiga toxin Escherichia coli-related hemolytic uremic syndrome (STEC-HUS)
- Thrombotic thrombocytopenic purpura (TTP)
- Concomitant use with other targeted immunomodulating biologics.
- Other complement-mediated diseases or conditions not listed above as medically necessary.
- Use in patients who have unresolved serious *Neisseria meningitidis* infection or are not adequately vaccinated against *Neisseria meningitidis.*

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour

96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
J1300	Injection, eculizumab, 10 mg
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
D59.3	Hemolytic-uremic syndrome
D59.30	Hemolytic-uremic syndrome, unspecified
D59.31	Infection-associated hemolytic-uremic syndrome
D59.32	Hereditary hemolytic-uremic syndrome
D59.39	Other hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria
G36.0	Neuromyelitis optica
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation
G70.2	Congenital and developmental myasthenia

Appendix

Table 1: Summary of Myasthenia Gravis Foundation of America (MGFA) Disease Clinical Classification

Class	*Description*
I	Ocular muscle weakness; All other muscles - normal strength
II	Mild generalized weakness

IIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
III	Moderate generalized weakness
IIIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
IV	Severe generalized weakness
IVa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IVb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
V	Intubation, with or without ventilation; Not for routine postoperative care

NOTE: The preceding table summarizes key aspects of the Myasthenia Gravis Foundation of America (MGFA) Disease Classifications. This is provided only for quick reference. For the exact definitions and details on the MGFA Disease Classifications, please refer to the original MGFA Classification document available at https://myasthenia.org/Portals/0/MGFA%20Classification.pdf.

Table 2: Expanded Disability Status Scale (EDSS)

Score	Description
0	Normal neurological examination, no disability in any functional system
1.0	No disability, minimal signs in one functional system
1.5	No disability, minimal signs in more than one functional system
2.0	Minimal disability in one functional system
2.5	Mild disability in one functional system or minimal disability in two functional systems
3.0	Moderate disability in one functional system, or mild disability in three or four functional systems. No walking impairment
3.5	Moderate disability in one functional system and more than minimal disability in

	several others. No walking impairment
4.0	Significant disability but self-sufficient and up and about some 12 hours a day. Able to walk without aid or rest for 500m
4.5	Significant disability but up and about much of the day. Able to work a full day. May otherwise have some limitation of full activity or require minimal assistance. Able to walk without aid or rest for 300m
5.0	Disability severe enough to impair full daily activities and ability to work a full day without special provisions. Able to walk without aid or rest for 200m
5.5	Disability severe enough to prevent full daily activities. Able to walk without aid or rest for 100m
6.0	Requires a walking aid – cane, crutch, etc. – to walk about 100m with or without resting
6.5	Requires two walking aids – pair of canes, crutches, etc. – to walk about 20m without resting
7.0	Unable to walk beyond approximately 5m even with aid. Essentially restricted to a wheelchair; though wheels a standard wheelchair and able to get in and out alone. Up and about in wheelchair some 12 hours a day
7.5	Unable to take more than a few steps. Restricted to a wheelchair and may need help getting in and out. Can wheel but cannot carry on in a standard wheelchair for a full day and may require a motorised wheelchair
8.0	Essentially restricted to a bed or chair or being pushed in wheelchair. May be out of bed much of the day. Retain many self-care functions. Generally has effective use of arms
8.5	Essentially restricted to a bed for much of the day. Has some effective use of arms, retains some self-care functions
9.0	Confined to bed. Can still communicate and eat
9.5	Confined to bed and totally dependent. Unable to communicate effectively or eat/swallow
10.0	Death due to MS

NOTE: The preceding table summarizes key aspects of the Expanded Disability Status Scale (EDSS). This is provided only for quick reference. For the exact definitions and details on the EDSS, please refer to the original EDSS document available at https://mstrust.org.uk/a-z/expanded-disability-status-scale-edss

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