Effective Date **7/1/2024**
Coverage Policy Number **IP0549**

Eculizumab

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Related Coverage Resources

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Overview

This policy supports medical necessity review for eculizumab intravenous infusion (**Soliris®**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Eculizumab (Soliris) is considered medically necessary for the treatment of complement-mediated hemolytic uremic syndrome (atypical hemolytic uremic syndrome) when the individual meets ALL of the following criteria:

1. Diagnosis of thrombocytopenic purpura (TTP) has been excluded (for example, normal ADAMTS 13 activity) OR a trial of plasma exchange did not result in clinical improvement
2. Absence of Shiga toxin-producing escherichia coli (E. coli) infection
3. Has been vaccinated against meningococcal infection (at least 2 weeks prior to treatment, if not previously vaccinated), where and when clinically appropriate

4. Medication is prescribed by, or in consultation, with a hematologist and/or a nephrologist

Dosing. The recommended intravenous dose for Complement-mediated hemolytic uremic syndrome (atypical hemolytic uremic syndrome) is:

1. For individuals 18 years of age or older, **ONE** of the following:
   A. Induction: Up to 900 mg weekly for the first 4 weeks
   B. Maintenance: Up to 1,200 mg at week 5, then up to 1,200 mg every 2 weeks thereafter

2. For individuals less than 18 years of age, **ONE** of the following:
   A. 40 kg or more:
      i. Induction: 900 mg weekly for 4 doses
      ii. Maintenance: 1,200 mg at week 5, then 1,200 mg every 2 weeks
   B. 30 kg to less than 40 kg:
      i. Induction: 600 mg weekly for 2 doses
      ii. Maintenance: 900 mg at week 3, then 900 mg every 2 weeks
   C. 20 kg to less than 30 kg:
      i. Induction: 600 mg weekly for 2 doses
      ii. Maintenance: 600 mg at week 3, then 600 mg every 2 weeks
   D. 10 kg to less than 20 kg:
      i. Induction: 600 mg weekly for 1 dose
      ii. Maintenance: 300 mg at week 2, then 300 mg every 2 weeks
   E. 5 kg to less than 10 kg:
      i. Induction: 300 mg weekly for 1 dose
      ii. Maintenance: 300 mg at week 2, then 300 mg every 3 weeks

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Eculizumab (Soliris) is considered medically necessary for the treatment of generalized myasthenia gravis when the individual meets ALL of the following criteria:

1. 18 years of age or older
2. Documentation that the individual has confirmed anti-acetylcholine receptor antibody positive generalized myasthenia gravis
3. Myasthenia Gravis Foundation of America (MGFA) clinical classification class of II-IV (prior to starting therapy with Soliris) [See APPENDIX 1]
4. Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of 6 or higher (prior to starting therapy with Soliris) [See APPENDIX 2]
5. Documentation of **ONE** of the following:
   A. Is currently receiving pyridostigmine
   B. Failure, contraindication, or intolerance to pyridostigmine
6. Documentation of **ONE** of the following:
   A. Is currently receiving two different immunosuppressant therapies (for example, azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, cyclophosphamide, prednisone) for 1 year or longer
   B. Failure, contraindication, or intolerance to two different immunosuppressant therapies
7. Has objective evidence of unresolved symptoms of generalized myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (for example, double vision, talking, impairment of mobility)
8. The medication is prescribed by, or in consultation with a neurologist

Dosing. The recommended intravenous dose for Generalized Myasthenia Gravis is **ONE** of the following:

1. Induction: Up to 900 mg weekly for the first 4 weeks
2. Maintenance: Up to 1,200 mg at week 5, then up to 1,200 mg every 2 weeks thereafter

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Eculizumab (Soliris) is considered medically necessary for the treatment of neuromyelitis optica spectrum disorder (NMOSD) when the individual meets ALL of the following criteria:

1. 18 years of age or older
2. Neuromyelitis optica spectrum disorder diagnosis confirmed by blood serum test for anti-aquaporin-4 antibody positive
3. Has been vaccinated against meningococcal infection (at least 2 weeks prior to treatment, if not previously vaccinated) where and when clinically appropriate
4. Medication is prescribed by, or in consultation with a neurologist

Dosing. The recommended intravenous dose for Neuromyelitis Optica Spectrum Disorder (NMOSD) is **ONE** of the following:

1. Induction: Up to 900 mg weekly for the first 4 weeks
2. Maintenance: Up to 1,200 mg at week 5, then up to 1,200 mg every 2 weeks thereafter

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Eculizumab (Soliris) is considered medically necessary for the treatment of Paroxysmal nocturnal hemoglobinuria (PNH) when the individual meets ALL of the following criteria:

1. 18 years of age or older
2. Flow cytometry demonstrates one of the following:
    A. At least 10% PNH type III red cells
    B. Greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP)-deficient polymorphonuclear cells (PMNs)
3. At least one transfusion related to anemia secondary to PNH **OR** occurrence of a thromboembolic event
4. Has been vaccinated against meningococcal infection (at least 2 weeks prior to treatment, if not previously vaccinated) where and when clinically appropriate
5. Medication is prescribed by, or in consultation, with a hematologist

Dosing. The recommended intravenous dose for Paroxysmal nocturnal hemoglobinuria (PNH) is **ONE** of the following:

1. Induction: Up to 600 mg weekly for the first 4 weeks
2. Maintenance: Up to 900 mg at week 5, then up to 900 mg every 2 weeks thereafter

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy Criteria

Continuation of eculizumab (Soliris) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated by **ANY** of the following:

1. **Complement-mediated Hemolytic Uremic Syndrome (atypical hemolytic uremic syndrome):** Reduced hemolysis, improved thrombocytopenia or renal function
2. **Generalized Myasthenia Gravis:** Reductions in exacerbations of MG; improvements in speech, swallowing, mobility, and respiratory function, improvement in MG-ADL or QMG scores
3. **Neuromyelitis Optica Spectrum Disorder (NMOSD):** Reduction in relapse rate, reduction in symptoms (for example, pain, fatigue, motor function), or a slowing progression in symptoms
4. **Paroxysmal Nocturnal Hemoglobinuria (PNH):** Stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis

Authorization Duration

Initial approval duration:

- **Complement-mediated Hemolytic Uremic Syndrome (atypical hemolytic uremic syndrome):** up to 6 months
- **Generalized Myasthenia Gravis:** up to 6 months
- **Neuromyelitis Optica Spectrum Disorder (NMOSD):** up to 12 months
- **Paroxysmal Nocturnal Hemoglobinuria (PNH):** up to 6 months

Reauthorization approval duration:

- **Complement-mediated Hemolytic Uremic Syndrome (atypical hemolytic uremic syndrome):** up to 12 months
- **Generalized Myasthenia Gravis:** up to 12 months
- **Neuromyelitis Optica Spectrum Disorder (NMOSD):** up to 12 months
- **Paroxysmal Nocturnal Hemoglobinuria (PNH):** up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. Acute antibody mediated rejection
2. Chronic antibody-mediated rejection in recipients with persistently high B flow crossmatch after positive crossmatch kidney transplantation
3. Concomitant Use with a Rituximab Product, a Neonatal Fc Receptor Blocker, Enspryng (satralizumab-mwge subcutaneous injection), Fabhalta (iptacopan capsule), Ultomiris (ravulizumab-cwvz intravenous infusion or subcutaneous injection), Uplizna (inebilizumab-cdon intravenous infusion), or Zilbrysq (zilucoplan subcutaneous injection). There is no evidence to support concomitant use of Soliris with a rituximab product, a neonatal Fc receptor blocker, Enspryng, Fabhalta, Ultomiris, Uplizna, or Zilbrysq.

   Examples of Neonatal Fc receptor blockers are: Vyvgart (efgartigimod alfa-fcab IV infusion), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc SC injection), and Rystiggo (rozanolixizumab-noli SC infusion).
4. Geographic atrophy in age-related macular degeneration
5. Prevention of delayed graft function
6. Systemic lupus erythematosus
7. Stem cell transplant-associated thrombotic microangiopathy
8. Typical hemolytic uremic syndrome (HUS)

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1300	Injection, eculizumab, 10 mg

Background

OVERVIEW
Soliris, a complement inhibitor, is indicated for the following uses:[1]

- **Atypical hemolytic uremic syndrome** (aHUS), to inhibit complement-mediated thrombotic microangiopathy.
- **Generalized myasthenia gravis** (gMG), in adults who are anti-acetylcholine receptor (AChR) antibody positive.
- **Neuromyelitis optica spectrum disorder** (NMOSD), in adults who are anti-aquaporin-4 (AQP4) antibody positive.
- **Paroxysmal nocturnal hemoglobinuria** (PNH), to reduce hemolysis.

Soliris is not indicated for the treatment of patients with Shiga toxin *E. coli* related hemolytic uremic syndrome.[1] The safety and effectiveness of Soliris for the treatment of gMG, NMOSD, and PNH in pediatric patients have not been established. The safety and effectiveness of Soliris in pediatric patients for aHUS is supported by evidence from four adequate and well-controlled clinical studies assessing the safety and effectiveness of Soliris for the treatment of aHUS.

Disease Overview
Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs.[4] The hallmark of myasthenia gravis is muscle weakness that worsens after periods of activity and improves after periods of rest. Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often involved in the disorder; however, the muscles that control breathing and neck and limb movements may also be affected. Acquired MG results from the binding of autoantibodies to components of the neuromuscular junction, most commonly the acetylcholine receptor.[5]

NMOSD is a rare, relapsing, autoimmune disorder of the brain and spinal cord with optic neuritis and/or myelitis as predominate characteristic symptoms.[6] NMOSD often causes significant, permanent damage to vision and/or spinal cord function causing blindness or impaired mobility.[7] Patients may experience pain, paralysis, loss of bowel and bladder control, loss of visual acuity, uncontrolled motor functions, and complications can cause death. Uplizna™ (inebilizumab-cdon intravenous infusion) and Enspryng™ (satralizumab-mwge subcutaneous injection) are two other FDA-approved medications for treatment of NMOSD in adults who are anti-AQP4 antibody-positive.[8,9] For acute attacks, typical treatment is high-dose intravenous corticosteroids.[10,11] Plasma exchange may be effective in patients who suffer acute severe attacks that do not response to intravenous corticosteroids. For long-term control of the disease a variety of

immunosuppressive drugs are utilized as first-line therapy. While all are considered off-label use, corticosteroids, azathioprine, mycophenolate mofetil, and rituximab are treatments prescribed as preventative therapy.

PNH is a rare disorder involving bone marrow failure that manifests with hemolytic anemia, thrombosis, and peripheral blood cytopenias.[12] Due to the absence of two glycosylphosphatidylinositol (GPI)-anchored proteins, CD55 and CD59, uncontrolled complement activation leads to hemolysis and other PNH manifestations.[13] GPI anchor protein deficiency is often due to mutations in phosphatidylinositol glycan class A (PIGA), a gene involved in the first step of GPI anchor biosynthesis. PNH is a clinical diagnosis that should be confirmed with peripheral blood flow cytometry to detect the absence or severe deficiency of GPI-anchored proteins on at least two lineages.[14] Prior to the availability of Soliris, there was no specific therapy for PNH with only supportive management in terms of the cytopenias and control of thrombotic risk. Supportive measures used include platelet transfusion, immune suppressive therapy for patients with bone marrow failure, use of erythropoietin for anemias, and aggressive anticoagulation. Soliris is the treatment of choice for patients with severe manifestations of PNH. Bone marrow transplantation is the only cure for PNH but should be reserved for patients with a suboptimal response to Soliris. Other agents indicated for the management of PNH in adults include Empaveli™ (pegcetacoplan subcutaneous infusion), a complement C3 inhibitor, and Ultomiris® (ravulizumab intravenous infusion), a complement C5 inhibitor.[15,16]

Guidelines

An international consensus guidance for the management of MG was published in 2016.[5] The guidelines recommend pyridostigmine for the initial treatment in most patients with MG. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids or immunosuppressant therapy should be used in all patients with MG who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. It is usually necessary to maintain some immunosuppression for many years, sometimes for life. Plasma exchange and intravenous immunoglobulin can be used as short-term treatments in certain patients. A 2020 update to these guidelines provides new recommendations for methotrexate, rituximab, and Soliris.[17] All recommendations should be considered extensions or additions to recommendations made in the initial international consensus guidance. Oral methotrexate may be considered as a steroid-sparing agent in patients with generalized MG who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with muscle specific kinase antibody positive MG who have an unsatisfactory response to initial immunotherapy. Soliris should be considered in the treatment of severe, refractory, anti-acetylcholine receptor antibody positive generalized MG.

APPENDIX 1

[Myasthenia Gravis Foundation of America (MGFA) classification]

The Myasthenia Gravis Foundation of America (MGFA) classification is aimed at separating patients in groups based on disease severity and the localization of the symptoms, and does not have an evaluative purpose. The MGFA classes are pure ocular (class I), mild generalized (class II), moderate generalized (class III), severe generalized (class IV), and intubation/myasthenic crisis (class V). Within the generalized categories II, III, and IV, patients are subclassified as class A if their symptoms are predominantly generalized or class B if their symptoms are predominantly bulbar.[1] The MGFA also has a system to classify patients based on postintervention outcomes and includes remission, defined as 1 year or longer without signs or symptoms and without any symptomatic (pyridostigmine) treatment, and which can be divided in complete (no pharmacologic treatment at all) or pharmacologic remission. Minimal manifestation status is defined as minimal signs or symptoms (no specific time-frame was defined) and pyridostigmine use may be accepted.

Additionally, patients can be improved, unchanged, worse, experiencing an MG exacerbation, or have died of MG.[1] Because the original MGFA severity classification does not take into account those patients who are asymptomatic, many MG studies use a hybrid, whereby symptomatic patients are classified based on the I to V class system, and asymptomatic or oligosymptomatic patients are classified as remission or minimal manifestation status.[2]

APPENDIX 2
[Myasthenia Gravis Activities of Daily Living (MG-ADL)]
The Myasthenia Gravis Activities of Daily Living (MG-ADL) is a patient-reported outcome that combines 2 items on daily life activities—ability to brush teeth or comb hair, and limitations in the ability to rise from a chair—with 6 items reflecting other MG symptoms: diplopia, ptosis, chewing, swallowing, voice/speech problems, and respiratory symptoms.[3] Each item is scored between 0 and 3 and total scores range from 0 to 24, where higher scores indicate more disease severity. The main advantages of the MG-ADL are that it is very easy to use, and it is completely patient reported. A drawback is that it does not have a specific recall time frame (eg, 2 or 4 weeks) because it relies on comparing with the last visit, and that it is prone to floor effects.[4]

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