Utilization Review Policy 194A

POLICY: Soliris® (eculizumab injection, for intravenous use – Alexion)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 01/17/2024

COVERAGE CRITERIA FOR: UCare Medicaid and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

OVERVIEW

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

- **Atypical hemolytic uremic syndrome** (aHUS), to inhibit complement-mediated thrombotic microangiopathy.
  Limitation of Use. Soliris is not indicated for the treatment of patients with Shiga toxin *Escherichia coli*-related hemolytic uremic syndrome.
- **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.

The Soliris prescribing information has a Boxed Warning about serious meningococcal infections.[1] Soliris is only available through a restricted access program, Soliris Risk Evaluation and Mitigation Strategy (REMS).[1]

The safety and effectiveness of Soliris for the treatment of gMG, NMOSD, and PNH in pediatric patients have not been established.[1] 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

Hemolytic uremic syndrome (HUS) is defined as the triad of non-immune hemolytic anemia, thrombocytopenia, and acute renal failure, in which the underlying lesions are mediated by systemic thrombotic microangiopathy.[2] aHUS should be distinguished from a more common condition referred to as typical HUS.[3] aHUS is a sub-type of HUS in which thrombotic microangiopathy is the consequence of endothelial damage in the microvasculature of the kidneys and other organs due to a dysregulation of the activity of the complement system. The typical form is caused by infection with certain strains of *E. coli* bacteria that produce toxic substances called Shiga-like toxins; Soliris is not indicated for the treatment of Shiga toxin *E. coli*-related hemolytic uremic syndrome.[1-3]

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 MG is muscle weakness that worsens after periods of activity and improves after periods of rest. Acquired MG results from the binding of autoantibodies to components of the neuromuscular junction, most commonly the AChR.[5] Soliris was studied in patients with gMG with anti-AChR antibodies with a Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV and a Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score ≥ 6.[1]

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 resulting in 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 respond 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 uses, corticosteroids, azathioprine, mycophenolate mofetil, and rituximab are treatments prescribed as preventative therapy.

PNH is a rare, genetic disorder of hematopoietic stem cells.[12,13] The mutation in the X-linked gene phosphatidylinositol glycan class A (PIGA) results in a deficiency in the glycosylphosphatidylinositol (GPI) protein, which is responsible for anchoring other protein moieties to the surface of the erythrocytes. Loss of anchoring of these proteins causes cells to hemolyze and leads to complications such as hemolytic anemia, thrombosis, and peripheral blood cytopenias. 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 cell lineages.[12,14] Prior to the availability of complement inhibitors, only supportive measures, in terms of managing the cytopenias and controlling thrombotic risk were available. Supportive measures include platelet transfusion, immunosuppressive therapy for patients with bone marrow failure, use of erythropoietin for anemias, and aggressive anticoagulation.

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 used in MG 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.[15] 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 gMG who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with anti-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-AChR antibody-positive MG.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Soliris. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is provided in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation

and diagnosis of patients treated with Soliris as well as the monitoring required for adverse events and long-term efficacy, approval requires Soliris to be prescribed by or in consultation with a physician who specializes in the condition being treated. All reviews will be forwarded to a Physician Medical Director for evaluation.

Documentation: Documentation is required for use of Soliris as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information. Subsequent coverage reviews for a patient who has previously met the documentation requirements and related criteria in the *Complement Inhibitors – Soliris Advanced Clinical Evaluation Medical Policy*, and who is requesting reauthorization, the criteria utilized do NOT require re-submission of documentation for reauthorization, except for the criterion requiring documentation of a continued benefit from Soliris therapy.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Soliris is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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4. Atypical Hemolytic Uremic Syndrome. Approve for 1 year if the patient meets the following (A and B):

A) Patient does not have Shiga toxin *Escherichia coli*-related hemolytic uremic syndrome; AND

B) The medication is being prescribed by or in consultation with a nephrologist.

Dosing. Approve if the dose meets ONE of the following (A or B):

A) For patients ≥ 18 years of age, the dose is administered intravenously and meets ONE of the following (i or ii):

- **i.** The dose is ≤ 900 mg weekly for the first 4 weeks; OR
- **ii.** The dose is ≤ 1,200 mg every 2 weeks thereafter.

B) For patients < 18 years of age, the dose is administered intravenously and meets ONE of the following (i, ii, iii, iv, or v):

- **i.** ≥ 40 kg: 900 mg weekly x 4 doses, 1,200 mg at week 5; then 1,200 mg every 2 weeks; OR
- **ii.** 30 kg to < 40 kg: 600 mg weekly x 2 doses, 900 mg at week 3; then 900 mg every 2 weeks; OR
- **iii.** 20 kg to < 30 kg: 600 mg weekly x 2 doses, 600 mg at week 3; then 600 mg every 2 weeks; OR
- **iv.** 10 kg to < 20 kg: 600 mg weekly x 1 dose, 300 mg at week 2; then 300 mg every 2 weeks; OR
- **v.** 5 kg to < 10 kg: 300 mg weekly x 1 dose, 300 mg at week 2; then 300 mg every 3 weeks.

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5. Generalized Myasthenia Gravis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, vi, and vii):

- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient has confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis **[documentation required]**; AND
- **iii.** Patient meets both of the following (a and b):
  - **i.** Myasthenia Gravis Foundation of America classification of II to IV; AND
  - **ii.** Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 6; AND

iv. Patient meets one of the following (a or b):
- **i.** Patient previously received or is currently receiving pyridostigmine; OR
- **ii.** Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND

v. Patient meets one of the following (a or b):
- **i.** Patient previously received or is currently receiving two different immunosuppressant therapies for ≥ 1 year; OR
- **ii.** Patient had inadequate efficacy, a contraindication, or significant intolerance to two different immunosuppressant therapies; AND
  Note: Examples of immunosuppressant therapies tried include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, and cyclophosphamide.

vi. Patient has evidence of unresolved symptoms of generalized myasthenia gravis; AND
Note: Evidence of unresolved symptoms of generalized myasthenia gravis includes difficulty swallowing, difficulty breathing, and a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility).

vii. The medication is being prescribed by or in consultation with a neurologist.

B) Patient is Currently Receiving Soliris. Approve for 1 year if the patient meets the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient is continuing to derive benefit from Soliris, according to the prescriber.
  Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis, improvements in speech, swallowing, mobility, and respiratory function.
- **iii.** The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve if the dose is administered intravenously and meets ONE of the following (A or B):
A) The dose is ≤ 900 mg weekly for the first 4 weeks; OR
B) The dose is ≤ 1,200 mg every 2 weeks thereafter.

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6. Neuromyelitis Optica Spectrum Disorder. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 year if the patient meets the following (i, ii, iii, iv, and v):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Diagnosis was confirmed by a positive blood serum test for anti-aquaporin-4 antibody **[documentation required]**; AND
- **iii.** Patient is currently receiving or has previously tried two of the following systemic therapies (a, b, c, or d):
  - **a.** Azathioprine; OR
  - **b.** Corticosteroid; OR
  - **c.** Mycophenolate mofetil; OR
  - **d.** Rituximab; AND
    Note: An exception to the requirement for a trial of a systemic therapy can be made if the patient has already tried Enspryng (satralizumab-mwge subcutaneous injection) or Uplizna (inebilizumab-cdon intravenous infusion) for neuromyelitis optica spectrum disorder (NMOSD). Patients who have already tried Enspryng or Uplizna for NSOMD are not required to try another systemic agent.
- **iv.** Patient has a history of at least one relapse in the last 12 months or two relapses in the last 2 years; AND
- **v.** The medication is being prescribed by or in consultation with a neurologist.

B) Patients is Currently Receiving Soliris. Approve for 1 year if the patient meets the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Diagnosis was confirmed by positive blood serum test for anti-aquaporin-4 antibody; AND
- **iii.** According to the prescriber, patient has had clinical benefit from the use of Soliris; AND
  Note: Examples of clinical benefit include reduction in relapse rate, reduction in symptoms (e.g., pain, fatigue, motor function), and a slowing progression in symptoms.
- **iv.** The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve if the dose is administered intravenously and meets ONE of the following (A or B):
A) The dose is ≤ 900 mg weekly for the first 4 weeks; OR
B) The dose is ≤ 1,200 mg every 2 weeks thereafter.

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7. **Paroxysmal Nocturnal Hemoglobinuria.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, and iii):
   - **i.** Patient is ≥ 18 years of age; AND
   - **ii.** Diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on at least two cell lineages **[documentation required]**; AND
   - **iii.** The medication is being prescribed by or in consultation with a hematologist; OR

   B) Patient is Currently Receiving Soliris. Approve for 1 year if the patient meets the following (i, ii, and iii):
   - **i.** Patient is ≥ 18 years of age; AND
   - **ii.** Patient is continuing to derive benefit from Soliris, according to the prescriber; AND
     Note: Examples of derived benefit include stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis.
   - **iii.** The medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve if the dose is administered intravenously and meets ONE of the following (A or B):
   A) The dose is ≤ 600 mg weekly for the first 4 weeks; OR
   B) The dose is ≤ 900 mg every 2 weeks thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Soliris is not recommended in the following situations:

1. **Concomitant Use with Empaveli > 4 Weeks.** Concomitant use of Soliris with Empaveli is not recommended. However, to reduce the risk of hemolysis from abrupt treatment discontinuation in a patient switching from Soliris to Empaveli, patient should use both therapies for 4 weeks; after which, Soliris is discontinued and patient is continued on Empaveli monotherapy.

2. **Concomitant Use with a Rituximab Product, a Neonatal Fc Receptor Blocker, Enspryng (satralizumab-mwge subcutaneous injection), Fabhalta (iptacopan capsule), Ultomiris (ravulizumab-cwzy 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,

Note: Examples of Neonatal Fc receptor blockers are: Vyvgart (efgartigimod alfa-fcab intravenous infusion), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection), and Rystiggo [rozanolixizumab-noli subcutaneous infusion).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Conditions Not Recommended for Approval:** The conditions were combined and the title was changed to "**Concurrent Use with Another Complement Inhibitor, a Rituximab Product, Enspryng (satralizumab-mwge subcutaneous injection), or Vyvgart (efgartigimod alfa-fcab intravenous infusion)**". Vyvgart and Ultomiris subcutaneous were added to this condition.	08/31/2022
Selected Revision	**Generalized Myasthenia Gravis:** Revised the Myasthenia Gravis Activities of Daily Living (MG-ADL) score to ≥ 6 to align with the prescribing information; previously it was MG-ADL ≥ 5.	05/31/2023
Early Annual Revision	**Generalized Myasthenia Gravis:** Initial therapy, for the criterion regarding evidence of unresolved symptoms of generalized myasthenia gravis, the examples of evidence of unresolved symptoms of generalized myasthenia gravis were moved to a Note. **Conditions Not Recommended for Approval:** Criterion regarding concomitant use of Soliris with another complement inhibitor, a rituximab product, Enspryng, Ultomiris, Uplizna, or Vyvgart was revised to include other neonatal Fc receptor blockers (Vyvgart Hytrulo, Rystiggo). Examples of neonatal Fc receptor blockers (including Vyvgart) were added as a Note. In addition, Empaveli was removed from this statement and added as a separate criterion: Concomitant use with Empaveli > 4 weeks.	09/20/2023
Selected revision	**Conditions Not Recommended for Approval:** Criterion regarding concomitant use with other agents was revised to include Fabhalta and Zilbrysq.	01/17/2024