VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Complement Inhibitors – Soliris Utilization Management Medical Policy
- Soliris® (eculizumab intravenous infusion – Alexion)

REVIEW DATE: 05/04/2022

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.

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 dosing interval 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.

Automation: None.

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

FDA-Approved Indications

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1. Atypical Hemolytic Uremic Syndrome. Approve for 1 year if the patient meets the following criteria (A and B):
- **A)** Patient does not have Shiga toxin *E. 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 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.
  - **ii.** 30 kg to < 40 kg: 600 mg weekly x 2 doses, 900 mg at week 3; then 900 mg every 2 weeks.
  - **iii.** 20 kg to < 30 kg: 600 mg weekly x 2 doses, 600 mg at week 3; then 600 mg every 2 weeks.
  - **iv.** 10 kg to < 20 kg: 600 mg weekly x 1 dose, 300 mg at week 2; then 300 mg every 2 weeks.
  - **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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2. Generalized Myasthenia Gravis. Approve if the patient meets ONE of the following criteria (A or B):
- **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (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; AND
  - **iii.** Patient meets both of the following (a and b):
    - **a)** Myasthenia Gravis Foundation of America classification of II to IV; AND
    - **b)** Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 5; AND
  - **iv.** Patient meets one of the following (a or b):
    - **a)** Patient received or is currently receiving pyridostigmine; OR
    - **b)** Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND
  - **v.** Patient meets one of the following (a or b):
    - **a)** Patient received or is currently receiving two different immunosuppressant therapies for ≥ 1 year; OR
    - **b)** 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, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility); AND
  - **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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3. Neuromyelitis Optica Spectrum Disorder. Approve if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve for 1 year if the patient meets the following criteria (i, ii, iii, iv, and v):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Neuromyelitis optica spectrum disorder diagnosis was confirmed by a positive blood serum test for anti-aquaporin-4 antibody; 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. Patients who have already tried Enspryng or Uplizna for neuromyelitis optica spectrum disorder are not required to try another systemic agent.
- **iv.** Patient has a history of at least 1 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.** Neuromyelitis optica spectrum disorder 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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4. Paroxysmal Nocturnal Hemoglobinuria. Approve if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Paroxysmal nocturnal hemoglobinuria 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; 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.** 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 a rituximab product, Enspryng (satralizumab-mwge subcutaneous injection), Ultomiris (ravulizumab intravenous infusion), or Uplizna (inebilizumab-cdon intravenous infusion).** There is no evidence to support combining Soliris with rituximab, Enspryng, Ultomiris, or Uplizna.

2. **Concomitant Use with Empaveli (pegcetacoplan subcutaneous infusion) > 4 Weeks.** Concurrent use of Soliris with Empaveli is not recommended. However, to reduce the risk of hemolysis from abrupt treatment discontinuation, patients currently receiving Soliris and switching to Empaveli may receive these agents for no more than 4 weeks after starting Empaveli.

3. 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
Annual Revision	**Generalized Myasthenia Gravis:** For a patient who is currently receiving Soliris, age requirement of ≥ 18 years of age and specialist requirement were added as criteria. **Paroxysmal Nocturnal Hemoglobinuria:** For a patient who is currently receiving Soliris, age requirement of ≥ 18 years of age and specialist requirement were added as criteria. **Concomitant Use with a rituximab product, Enspryng™ (satralizumab-mwge subcutaneous injection), or Uplizna™ (inebilizumab-cdon intravenous infusion):** Ultomiris was added as a medication not allowed to be used in conjunction with Soliris. **Concomitant Use with Empaveli™ (pegcetacoplan subcutaneous infusion) > 4 Weeks:** This condition was added as a condition not recommended for approval.	06/02/2021
Selected Revision	**Generalized Myasthenia Gravis:** Wording in the requirements for a trial of pyridostigmine and immunosuppressant therapies was changed from "has tried and has contraindications, intolerance, or failed" to "has tried and has had inadequate efficacy, a contraindication, or significant intolerance to".	12/22/2021
Early Annual Revision	**Generalized Myasthenia Gravis:** Requirements for Myasthenia Gravis Foundation of America classification of II to IV and Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 5 were added to criteria.	05/04/2022