UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Complement Inhibitors – Eculizumab Products Utilization Management Medical Policy
- Bkemv® (eculizumab-aeeb intravenous infusion – Amgen)
- Epysqli® eculizumab-aagh intravenous infusion – Teva)
- Soliris® (eculizumab intravenous infusion – Alexion)

REVIEW DATE: 08/26/2026

OVERVIEW

Eculizumab, a complement C5 inhibitor, is indicated for the following uses:[1]

- **Atypical hemolytic uremic syndrome** (aHUS), to inhibit complement-mediated thrombotic microangiopathy.
  Limitation of Use. Eculizumab is not indicated for the treatment of patients with Shiga toxin *Escherichia coli*-related hemolytic uremic syndrome.
- **Generalized myasthenia gravis** (gMG), in adults and pediatric patients ≥ 6 years of age 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.

Bkemv and Epysqli are biosimilars to Soliris.[2,3]

The safety and effectiveness of eculizumab for the treatment of PNH or NMOSD in pediatric patients have not been established.[1] The safety and effectiveness of eculizumab in pediatric patients with aHUS is supported by evidence from four adequate and well-controlled clinical studies assessing the safety and effectiveness of eculizumab for the treatment of aHUS. The safety and effectiveness of eculizumab in pediatric patients for gMG is supported by evidence from an adequate and well-controlled trial in adults with additional pharmacokinetic and safety data in pediatric patients with gMG who are ≥ 12 years of age, and pharmacokinetic and safety data in other pediatric populations 6 to < 12 years of age.

For the gMG indication, eculizumab was studied in adults 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]

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.[4] aHUS should be distinguished from a more common condition referred to as typical HUS.[5] 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; eculizumab is not indicated for the treatment of Shiga toxin *E. coli*-related HUS.[1,4,5]

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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.[6] 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.[7]

NMOSD is a rare, relapsing, autoimmune disorder of the brain and spinal cord with optic neuritis and/or myelitis as predominate characteristic symptoms.[8,9] NMOSD often causes significant, permanent damage to vision and/or spinal cord function resulting in blindness or impaired mobility. Patients may experience pain, paralysis, loss of bowel and bladder control, loss of visual acuity, uncontrolled motor functions, and complications can cause death.

PNH is a rare genetic disorder of hematopoietic stem cells.[10,11] Variants in the X-linked phosphatidylinositol glycan class A (*PIGA*) gene result 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.[10,12]

Guidance for gMG

An international consensus guidance for the management of MG was published in 2016.[7] The consensus guidance recommends 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 this consensus guidance provided new recommendations for certain agents, including eculizumab.[13] Eculizumab should be considered in the treatment of severe, refractory, anti-AChR antibody-positive MG.

Pediatric patients with gMG. Cholinesterase inhibitors are used first-line for the symptomatic treatment of juvenile myasthenia gravis (JMG); pyridostigmine is the most widely used cholinesterase inhibitor for JMG.[14] There are no formal guidelines for the use of immunosuppressive therapy in JMG and current practice has been taken from adult guidelines and expert opinions based on individual experience. Prednisolone is accepted as the first-line immunosuppressive therapy in JMG. Second-line therapies or steroid-sparing agents include, but are not limited to, azathioprine, mycophenolate mofetil, tacrolimus, rituximab, cyclosporine, and cyclophosphamide.

Safety

Eculizumab has a Boxed Warning about serious meningococcal infections.[1] Soliris and biosimilars are only available through a restricted access program (Risk Evaluation and Mitigation Strategy [REMS]).

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POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of eculizumab. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. 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 eculizumab as well as the monitoring required for adverse events and long-term efficacy, approval requires eculizumab to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of eculizumab 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 BOTH of the following (A and B):
   - **A)** Patient does not have Shiga toxin *Escherichia coli*-related hemolytic uremic syndrome; AND
   - **B)** The medication is prescribed by or in consultation with a nephrologist.

   Dosing. Approve ONE of the following (A or B):
   Note: Eculizumab is given as an intravenous infusion.
   - **A)** Patient is ≥ 18 years of age. 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, and then 1,200 mg every 2 weeks thereafter (maintenance); OR
   - **B)** Patient is < 18 years of age. Approve ONE of the following (i, ii, iii, iv, or v):
     - **i.** Patient weighs 5 kg to < 10 kg: 300 mg single dose at Week 1, followed by 300 mg at Week 2, and then 300 mg every 3 weeks (maintenance); OR
     - **ii.** Patient weighs 10 kg to < 20 kg: 600 mg single dose at Week 1, followed by 300 mg at Week 2, and then 300 mg every 2 weeks (maintenance); OR
     - **iii.** Patient weighs 20 kg to < 30 kg: 600 mg for the first 2 weeks, followed by 600 mg at Week 3, and then 600 mg every 2 weeks (maintenance); OR
     - **iv.** Patient weighs 30 kg to < 40 kg: 600 mg for the first 2 weeks, followed by 900 mg at Week 3, and then 900 mg every 2 weeks (maintenance); OR
     - **v.** Patient weighs ≥ 40 kg: 900 mg weekly for the first 4 weeks, followed by 1,200 mg at Week 5, and then 1,200 mg every 2 weeks (maintenance).

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2. **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 ALL of the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** If patient is ≥ 18 years of age, 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 ≥ 6; AND
     - **iii.** Patient has confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis; AND

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iv. Patient meets ONE of the following (a or b):
  a) Patient previously 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 previously 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 include corticosteroid, 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 prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Eculizumab. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
i. Patient is ≥ 6 years of age; AND
ii. According to the prescriber, patient is continuing to derive benefit from eculizumab.
  Note: Examples of benefit include reductions in exacerbations of myasthenia gravis, improvements in speech, swallowing, mobility, and respiratory function.
iii. The medication is prescribed by or in consultation with a neurologist.

Dosing. Approve ONE of the following (A or B):
Note: Eculizumab is given as an intravenous infusion.
A) Patient is ≥ 18 years of age. 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, and then 1,200 mg every 2 weeks thereafter (maintenance); OR
B) Patient is < 18 years of age. Approve ONE of the following (i, ii, iii, iv, iv, or v):
i. Patient weighs 5 kg to < 10 kg: 300 mg single dose at Week 1, followed by 300 mg at Week 2, and then 300 mg every 3 weeks (maintenance); OR
ii. Patient weighs 10 kg to < 20 kg: 600 mg single dose at Week 1, followed by 300 mg at Week 2, and then 300 mg every 2 weeks (maintenance); OR
iii. Patient weighs 20 kg to < 30 kg: 600 mg for the first 2 weeks, followed by 600 mg at Week 3, and then 600 mg every 2 weeks (maintenance); OR
iv. Patient weighs 30 kg to < 40 kg: 600 mg for the first 2 weeks, followed by 900 mg at Week 3, and then 900 mg every 2 weeks (maintenance); OR
v. Patient weighs ≥ 40 kg: 900 mg weekly for the first 4 weeks, followed by 1,200 mg at Week 5, and then 1,200 mg every 2 weeks (maintenance).

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3. 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 ALL of the following (i, ii, and iii):
i. Patient is ≥ 18 years of age; AND
ii. Diagnosis was confirmed by a positive blood serum test for anti-aquaporin-4 antibody; AND
iii. The medication is prescribed by or in consultation with a neurologist; OR
B) Patients is Currently Receiving Eculizumab. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient is ≥ 18 years of age; AND

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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 eculizumab; 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 prescribed by or in consultation with a neurologist.

Dosing. Approve eculizumab to be administered as an intravenous infusion at 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, and then 1,200 mg every 2 weeks thereafter (maintenance).

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4. **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 ALL of 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; AND
      iii. The medication is prescribed by or in consultation with a hematologist; OR
   B) Patient is Currently Receiving Eculizumab. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
      i. Patient is ≥ 18 years of age; AND
      ii. According to the prescriber, patient is continuing to derive benefit from eculizumab; AND
      Note: Examples of benefit include stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis, improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score.
      iii. The medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve eculizumab to be administered as an intravenous infusion at 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, and then 900 mg every 2 weeks thereafter (maintenance).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of eculizumab is not recommended in the following situations:

1. **Concomitant Use with Empaveli > 4 Weeks.** Concomitant use of eculizumab with Empaveli is not recommended.[1,2] However, to reduce the risk of hemolysis from abrupt treatment discontinuation in a patient switching from eculizumab to Empaveli, patient should use both therapies for 4 weeks; after which, eculizumab is discontinued and patient is continued on Empaveli monotherapy.

2. **Concomitant Use with Another Complement Inhibitor Except Voydeya (danicopan tablets).** There is no evidence to support concomitant use of eculizumab with another complement inhibitor, except Voydeya.[1,2]
   Note: Examples of complement inhibitors are Fabhalta (iptacopan capsules), PiaSky (crovalimab-akkz intravenous infusion or subcutaneous injection), and Ultomiris (ravulizumab-cwvz intravenous infusion).

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3. **Concomitant Use with a Rituximab Product, a Neonatal Fc Receptor Blocker, or Zilbrysq (zilucoplan subcutaneous injection)**. There is no evidence to support concomitant use of eculizumab with a rituximab product, a neonatal Fc receptor blocker, or Zilbrysq.[1]
   Note: Examples of Neonatal Fc receptor blockers are Imaavy (nipocalimab-aahu intravenous infusion), Rystiggo (rozanolixizumab-noli subcutaneous infusion), Vyvgart (efgartigimod alfa-fcab intravenous infusion), and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection).

4. **Concomitant Use with Enspryng (satralizumab-mwge subcutaneous injection) or Uplizna (inebilizumab-cdon intravenous infusion)**. There is no evidence to support concomitant use of eculizumab with Enspryng or Uplizna.[1]

5. 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	**Paroxysmal Nocturnal Hemoglobinuria, Patient is currently receiving Soliris:** "Improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score" was added to the Note of examples of benefit. **Conditions Not Recommended for Approval, Concomitant Use with a Rituximab Product, a Neonatal Fc Receptor Blocker, Enspryng (satralizumab-mwge subcutaneous injection), Fabhalta (iptacopan capsules), Ultomiris (ravulizumab-cwzy intravenous infusion or subcutaneous injection), Uplizna (inebilizumab-cdon intravenous infusion), or Zilbrysq (zilucoplan subcutaneous injection):** This criterion was separated into three criteria. The Note regarding neonatal Fc receptor blockers was moved to the relevant criterion. • **Concomitant Use with Another Complement inhibitor, Except Voydeya (danicopan tablets).** Fabhalta and Ultomiris were moved to a Note and PiaSky (crovalimab-akkz intravenous infusion or subcutaneous injection) was added to the Note. • **Concomitant Use with a Rituximab Product, or a Neonatal Fc Receptor Blocker, or Zilbrysq (zilucoplan subcutaneous injection).** **Concomitant Use with Enspryng (satralizumab-mwge subcutaneous injection) or Uplizna (inebilizumab-cdon intravenous infusion).**	09/25/2024
Selected Revision	• **Bkemv (biosimilar to Soliris):** This agent was added to the policy; the same criteria apply as that for Soliris. • **Policy Name Change:** The generic name replaced the brand name in the policy title: Complement Inhibitors – Eculizumab Products UM Medical.	02/26/2025
Selected Revision	**Epysqli (biosimilar to Soliris):** This agent was added to the policy; the same criteria apply as that for Soliris. **Generalized Myasthenia Gravis:** • Age requirement (for initial and continuation of therapy) was changed to "≥ 6 years of age"; previously it was "≥18 years of age". • Criterion that addresses the Myasthenia Gravis Foundation of America classification and Myasthenia Gravis Activities of Daily Living score was changed such that this requirement only applies to patients ≥ 18 years of age. • Corticosteroid was added to the Note of examples of immunosuppressant therapies.	03/19/2025
Annual Revision	**Atypical hemolytic uremic syndrome, dosing section:** Dosing recommendations were further clarified to align with the prescribing information. **Generalized myasthenia gravis, Neuromyelitis optica spectrum disorder, and Paroxysmal nocturnal hemoglobinuria, Dosing section:** Dosing recommendations were split for Initial Therapy and Patient is Currently Receiving Eculizumab. All dosing recommendations align with the prescribing information. **Conditions Not Recommended for Approval, Concomitant Use with a Rituximab Product, a Neonatal Fc Receptor Blocker, or Zilbrysq (zilucoplan subcutaneous injection):** Imaavy was added to the Note of examples of neonatal Fc receptor blockers.	08/06/2025
Annual Revision	**Atypical Hemolytic Uremic Syndrome, dosing section:** For each age/weight group, added the word "maintenance" to the end of the statement, to distinguish the maintenance doses from the induction dose. **Generalized Myasthenia Gravis, Neuromyelitis Optica Spectrum Disorder, and Paroxysmal Nocturnal Hemoglobinuria, dosing section:** Dosing recommendations for Initial Therapy and Patient is Currently Receiving Eculizumab were combined into one set of recommendations.	08/26/2026

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