Eculizumab Products (Soliris®, Bkemv™ [Eculizumab-aeeb], and Epysqli® [Eculizumab-aagh])

Some agents on this policy may require step therapy *See* "Step Therapy Requirements for Provider Administered Specialty Medications" Document at:
https://www.bcbst.com/docs/providers/Comm_BC_PAD_Step_Therapy_Guide.pdf

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Soliris is indicated for the treatment of:

- Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
- Generalized myasthenia gravis (gMG) in adult and pediatric patients six years of age or older who are anti-acetylcholine receptor (AChR) antibody positive.
- Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Bkemv and Epysqli are indicated for the treatment of:

- Paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.
- Atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
- Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive.

Limitations of Use:
Soliris, Bkemv, and Epysqli are not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- For initial requests:
  - Atypical hemolytic uremic syndrome: ADAMTS 13 level.

  - Paroxysmal nocturnal hemoglobinuria: Flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency.
  - Generalized myasthenia gravis:
    - Positive anti-acetylcholine receptor (AChR) antibody test.
    - Myasthenia Gravis Foundation of America (MGFA) clinical classification.
    - MG activities of daily living score.
    - Previous medications tried, including response to therapy. If therapy is not advisable, documentation of clinical reasons to avoid therapy.
  - Neuromyelitis optica spectrum disorder: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present.
- For continuation requests: Chart notes or medical record documentation supporting positive clinical response

COVERAGE CRITERIA

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

- The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) (e.g., at least 5% PNH cells, at least 51% of GPI-AP deficient poly-morphonuclear cells).
- Flow cytometry is used to demonstrate GPI-APs deficiency.
- Member has and exhibits clinical manifestations of disease (e.g., LDH > 1.5 ULN, thrombosis, renal dysfunction, pulmonary hypertension, dysphagia).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Piasky, Ultomiris) for the treatment of PNH (concomitant use with Voydeya is allowed).

Atypical Hemolytic Uremic Syndrome (aHUS)

Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome (aHUS) not caused by Shiga toxin when all of the following criteria are met:

- ADAMTS 13 activity level above 5%.
- Absence of Shiga toxin.
- The requested medication will not be used in combination with another complement inhibitor (e.g., Ultomiris) for the treatment of aHUS.

Generalized Myasthenia Gravis (gMG)

Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:

- Anti-acetylcholine receptor (AchR) antibody positive.
- Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV.
- MG activities of daily living (MG-ADL) total score of greater than or equal to 5.
- Meets one of the following:
  - Member has had an inadequate response or intolerable adverse event to at least two immunosuppressive therapies over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, tacrolimus).

  - Member has had an inadequate response or intolerable adverse event to at least one immunosuppressive therapy and intravenous immunoglobulin (IVIG) over the course of at least 12 months.
  - Member has a documented clinical reason to avoid therapy with immunosuppressive agents and IVIG.
- The requested medication will not be used in combination with another complement inhibitor (e.g., Ultomiris, Zilbrysq) or neonatal Fc receptor blocker (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

- Anti-aquaporin-4 (AQP4) antibody positive
- Member exhibits one of the following core clinical characteristics of NMOSD:
  - Optic neuritis
  - Acute myelitis
  - Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
  - Acute brainstem syndrome
  - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
  - Symptomatic cerebral syndrome with NMOSD-typical brain lesions
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

CONTINUATION OF THERAPY

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Piasky, Ultomiris) for the treatment of PNH (concomitant use with Voydeya is allowed).

Atypical Hemolytic Uremic Syndrome (aHUS)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Ultomiris) for the treatment of aHUS.

Generalized Myasthenia Gravis (gMG)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen
- The member demonstrates a positive response to therapy (e.g., improvement in MG-ADL score, MG Manual Muscle Test (MMT), MG Composite).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Ultomiris, Zilbrysq) or neonatal Fc receptor blocker (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., reduction in number of relapses).
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

MEDICATION QUANTITY LIMITS

Drug Name	Diagnosis	Maximum Dosing Regimen
Soliris (Eculizumab)	Atypical Hemolytic Uremic Syndrome (aHUS)	Route of Administration: Intravenous <18year(s) 5 - <10 kg Initial: 300mg weekly for 1 dose Maintenance: 300mg every 3 weeks, starting on week 2 10 - <20 kg Initial: 600mg weekly for 1 dose Maintenance: 300mg every 2 weeks, starting on week 2 20 - < 30 kg Initial: 600mg weekly for 2 doses Maintenance: 600mg every 2 weeks, starting on week 3 30 - < 40 kg Initial: 600mg weekly for 2 doses Maintenance: 900mg every 2 weeks, starting on week 3 ≥40kg Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5 ≥18 year(s) Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5
Soliris (Eculizumab)	Generalized Myasthenia Gravis (gMG)	Route of Administration: Intravenous ≥18 year(s) Initial: 900mg weekly for 4 doses

		Maintenance: 1200mg every 2 weeks, starting on week 5 <u><18 year(s)</u> ≥40kg Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5 30 - <40kg Initial: 600mg weekly for 2 doses Maintenance: 900mg every 2 weeks, starting on week 3 20 - <30kg Initial: 600mg weekly for 2 doses Maintenance: 600mg every 2 weeks, starting on week 3 10 - <20kg Initial: 600mg weekly for 1 dose Maintenance: 300mg every 2 weeks, starting on week 2 5 - <10kg Initial: 300mg weekly for 1 dose Maintenance: 300mg every 3 weeks, starting on week 2
Soliris (Eculizumab)	Neuromyelitis Optica Spectrum Disorder (NMOSD)	Route of Administration: Intravenous Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5
Soliris (Eculizumab)	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Route of Administration: Intravenous Initial: 600mg weekly for 4 doses Maintenance: 900mg every 2 weeks, starting on week 5
Bkemv (Eculizumab-aaeb) Epysqli (Eculizumab-aagh)	Atypical Hemolytic Uremic Syndrome (aHUS)	Route of Administration: Intravenous ≥18 year(s) Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5 <u><18 year(s)</u> ≥40kg Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5 30 - <40kg Initial: 600mg weekly for 2 doses Maintenance: 900mg every 2 weeks, starting on week 3 20 - <30kg

		Initial: 600mg weekly for 2 doses Maintenance: 600mg every 2 weeks, starting on week 3 10 - <20kg Initial: 600mg weekly for 1 dose Maintenance: 300mg every 2 weeks, starting on week 2 5 - <10kg Initial: 300mg weekly for 1 dose Maintenance: 300mg every 3 weeks, starting on week 2
Bkemv (Eculizumab-aaeb) Epysqli (Eculizumab-aagh)	Generalized Myasthenia Gravis (gMG)	Route of Administration: Intravenous Initial: 900mg weekly for 4 doses Maintenance: 1200mg every 2 weeks, starting on week 5
Bkemv (Eculizumab-aaeb) Epysqli (Eculizumab-aagh)	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Route of Administration: Intravenous Initial: 600mg weekly for 4 doses Maintenance: 900mg every 2 weeks, starting on week 5

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Soliris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2025.
2. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. Published online: April 11, 2015.
3. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology*. 2011; 21-29.
4. Sanders D, Wolfe G, Benatar M et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2021; 96 (3) 114-122 .
5. Jaretzki A, Barohn RJ, Ernstoff RM et al. Myasthenia Gravis: Recommendations for Clinical Research Standards. *Ann Thorac Surg*. 2000;70: 327-34.
6. Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *NEJM.* 2006;335:1233-43.

7. Howard JF, Utsugisawa K, Benatar M. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (REGAIN); a phase 3, randomized, double-blind, placebo-controlled, multicenter study. *Lancet Neurol*. 2017 Oct 20. http://dx.doi.org/10.1016/S1474-4422(17)30369-1Ingenix HCPCS Level II, Expert 2011.
8. Brodsky RA, Young NS, Antonioli E, et al. Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinuria. *Blood*. 2008;111(4):1840-1847.
9. Borowitz MJ, Craig F, DiGiuseppe JA, et al. Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry. *Cytometry B Clin Cytom*. 2010: 78: 211-230.
10. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
11. Lee JW, Sicre de Fontbrune F, Wong LL, et al. Ravulizumab (ALXN1210) vs eculizumab in adult patients with PNH naive to complement inhibitors: The 301 study. Blood. 2018 Dec 3; pii: blood-2018-09-876136.
12. Pittock SJ, Berthele A, Kim HJ, et al. Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. *N Engl J Med*. 2019 May 3. doi: 10.1056/NEJMoA1900866.
13. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders*. Neurology.* 2015; 85:177-189.
14. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.
15. Dezern AE, Borowitz MJ. ICCS/ESCCA consensus guidelines to detect GPI-deficient cells in paroxysmal nocturnal hemoglobinuria (PNH) and related disorders part 1 - clinical utility. Cytometry B Clin Cytom. 2018 Jan;94(1):16-22.
16. Barnett C, Herbelin L, Dimachkie MM, Barohn RJ. Measuring Clinical Treatment Response in Myasthenia Gravis. Neurol Clin. 2018 May;36(2):339-353.
17. Bkemv [package insert]. Thousand Oaks, CA: Amgen Inc.; October 2024.
18. Epysqli [package insert]. Republic of Korea: Samsung Bioepis Co., Ltd.; November 2024.

EFFECTIVE DATE 12/31/2025

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