Generic Name: N/A

Therapeutic Class or Brand Name: Complement C5 Inhibitor Agents

Applicable Drugs: Bkemv (eculizumab-aeeb), Epysqli (eculizumab-aagh), Piasky (crovalimab-akkz), Soliris (eculizumab), Ultomiris (ravulizumab-cwvz), Veopoz (pozelimab-bbfg)

Preferred: N/A

Non-preferred: N/A

Date of Origin: 7/10/2026

Date Last Reviewed / Revised: 7/10/2026

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through IV are met)

I. Documented diagnosis of one of the following A through E, and the patient must meet the criteria under the applicable diagnosis:

A. Atypical hemolytic uremic syndrome (aHUS)

i. Thrombotic thrombocytopenic purpura (TTP) has been excluded by an ADAMTS13 activity level of greater than or equal to 10%.

ii. Shiga toxin-producing Escherichia coli hemolytic uremic syndrome (STEC-HUS) has been ruled out via negative stool PCR, culture, or immunoassay.

iii. Patient has a documented diagnosis of thrombotic microangiopathy (TMA), as evidenced by documentation of pretreatment laboratory findings showing all of the following 1 through 3:

1. Microangiopathic hemolytic anemia (MAHA), characterized by the following:

a. Hemoglobin level less than 10 g/dL

b. Serum lactate dehydrogenase (LDH) level greater than 1.5 times the upper limit of normal

c. Documented undetectable or severely low haptoglobin level

d. Presence of schistocytes (fragmented red blood cells) on a peripheral blood smear

e. Negative Coombs test

2. Documented thrombocytopenia (platelet count less than 150 × 10^9/L or greater than 25% decrease from baseline).

3. Documentation of acute end-organ damage (e.g., renal impairment).

iv. Treatment must be prescribed by or in consultation with a hematologist or nephrologist.

B. CD55-deficient protein-losing enteropathy (PLE) (i.e., CHAPLE disease)
    i. Clinical diagnosis of CHAPLE disease and confirmed CD55 loss-of-function mutation by genetic testing.
    ii. Documentation showing hypoalbuminemia (defined as serum albumin concentration of less than or equal to 3.2 g/dL).
    iii. Documentation of one or more of the following signs or symptoms within the last six months:
        1. Abdominal pain
        2. Diarrhea
        3. Peripheral edema
        4. Facial edema
        5. Infection with concomitant hypogammaglobulinemia
        6. New thromboembolic event
    iv. Treatment must be prescribed by or in consultation with a hematologist, gastroenterologist, or specialist in rare genetic diseases.

C. Generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor (AChR) antibody positive
    i. Documented positive serologic test for anti-AChR antibodies.
    ii. Documented Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy.
    iii. Documented Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score greater than or equal to 6 at initiation of therapy. See Appendix Table 1 for MG-ADL scale criteria.
    iv. Documented treatment failure or contraindication after a trial of pyridostigmine in combination with another therapy.
    v. Documented treatment failure or contraindication to a trial of at least two immunosuppressive therapies (ISTs) for 6–12 months each (e.g., azathioprine, mycophenolate mofetil, corticosteroids, cyclosporine, methotrexate, tacrolimus) OR a trial of at least one traditional IST *plus* the requirement of chronic plasmapheresis/plasma exchange (PLEX) (e.g., maintenance dependence for greater or equal to 6 months) or intravenous immunoglobulin (IVIg).
    vi. Patient has not failed a previous course of a complement C5 inhibitor therapy [e.g., Bkemv (eculizumab-aeeb), Epysqli (eculizumab-aagh), Soliris (eculizumab), or Ultomiris (ravulizumab-cwvz)].
    vii. Patient is not receiving the requested product in combination with any of the following for treatment of the same indication:

a. B-cell depletion therapy [e.g., Uplizna (inebilizumab)]

b. FcRn blocker [e.g., Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), Rystiggo (rozanolixizumab-noli)]

c. Immune globulin (e.g., Hizentra, Privigen, Gammagard)

viii. Treatment must be prescribed by or in consultation with a neurologist or neuromuscular specialist.

D. Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

i. Diagnosis of neuromyelitis optica spectrum disorder (NMOSD) with documentation of one of the following core clinical characteristics 1 through 6:

1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome (e.g., episode of otherwise unexplained hiccups, nausea, or vomiting)
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

ii. Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies.

iii. Exclusion of alternative diagnoses (e.g., multiple sclerosis, cancer, and chronic infections).

iv. Patient has not failed a previous course of a complement C5 inhibitor therapy for treatment of NMOSD [e.g., Bkemv (eculizumab-aeeb), Epysqli (eculizumab-aagh), Soliris (eculizumab), or Ultomiris (ravulizumab-cwvz)].

v. Documented treatment failure or contraindication to rituximab therapy.

vi. Patient is not receiving the requested product in combination with any of the following for treatment of the same indication:

1. Anti-IL6 therapy [e.g., Actemra (tocilizumab), Enspryng (satralizumab)].
2. B-cell depletion therapy [e.g., rituximab, Uplizna (inebilizumab)].
3. Disease modifying therapies FDA approved for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab)].

vii. Treatment must be prescribed by or in consultation with a neurologist experienced in demyelinating disorders.

E. Paroxysmal nocturnal hemoglobinuria (PNH)

i. Flow cytometry confirmation: Documented diagnosis of PNH confirmed by high-sensitivity peripheral blood flow cytometry demonstrating a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) on red blood cells (RBCs) and white blood cells (WBCs), showing one of the following 1 or 2:

1. A PNH granulocyte or monocyte clone size of greater than or equal to 10%.
2. A total PNH RBC clone size of greater than or equal to 5%.

ii. Patient must demonstrate objective evidence of high disease activity, defined by meeting one of the following criteria 1 through 3:

1. Serum lactate dehydrogenase (LDH) level greater than or equal to 1.5 times the upper limit of normal (ULN), accompanied by at least one classic PNH symptom (e.g., severe fatigue, hemoglobinuria, abdominal pain, dyspnea, or severe anemia).
2. Documented history of a major adverse vascular or thrombotic event (arterial or venous) attributable to underlying PNH, regardless of current LDH levels.
3. Documented history of requiring at least 1 packed red blood cell (pRBC) transfusion within the past 12 months due to PNH-induced anemia.

iii. Patient is not receiving the requested product in combination with any of the following for treatment of the same indication:

1. Complement C3 inhibitor [e.g., Empaveli (pegcetacoplan)]
2. Complement factor B inhibitor [e.g., Fabhalta (iptacopan)]

iv. Treatment must be prescribed by or in consultation with a hematologist, oncologist, or immunology specialist.

II. Documented complete meningococcal vaccine series was administered at least 2 weeks prior to the requested first dose of the complement C5 inhibitor OR prescriber has explicitly stated that the clinical risk of delaying treatment outweighs the risk of developing a meningococcal infection, and the patient will receive immediate vaccination alongside a mandatory minimum of 2 weeks of prophylactic antibacterial drug therapy (antibiotic prophylaxis) starting concurrently with the first dose of the C5 inhibitor.

III. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

IV. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, there must be documented failure, intolerance, or contraindication to a preferred product.

EXCLUSION CRITERIA

- Coadministration with another complement C5 inhibitor.
- Patients with active or unresolved *Neisseria meningitidis* infection.
- Generalized myasthenia gravis (gMG): Treatment of MGFA class I and V.
- Medication-specific exclusion criteria as listed in Appendix Table 2.

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Requested quantities not exceeding limits listed in Appendix Table 2.

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** 1 year, with an updated letter of medical necessity or progress notes showing that current medical necessity criteria are met and that the medication is effective. Indication-specific re-authorization criteria listed in Appendix Table 3.

APPENDIX

- Table 1. MG-ADL Scoring Template

Grade	0	1	2	3	Score
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	
				Total Score:	

Wolfe GI, Herbelin L, Nations SP, Foster B, Bryan WW, Barohn RJ. Neurology 1999;52(7):1487-9

- Table 2. FDA indications, drug-specific criteria, and quantity limits for complement C5 inhibitors.

COMPLEMENT C5 INHIBITORS: INJECTABLE AND INFUSION AGENTS

Bkemv (eculizumab-aeeb)
• Indications:
  ○ PNH, Age ≥ 18 years old
  ○ aHUS, Adults and pediatrics (weight-based dosing)
  ○ gMG and AChR antibody positive, Age ≥ 18 years old
  ○ NMOSD and AQP4 antibody positive, Age ≥ 18 years old
• Quantity limits:
  ○ PNH
  ▪ 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter
  ○ gMG, NMOSD
  ▪ 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter
  ○ aHUS
  ▪ Adults: 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter
  ▪ Pediatrics:

• 40 kg and over: 900 mg weekly for the first 4 weeks; 1,200 mg at week 5; then 1,200 mg every 2 weeks • 30 kg to less than 40 kg: 600 mg weekly for the first 2 weeks; 900 mg at week 3; then 900 mg every 2 weeks • 20 kg to less than 30 kg: 600 mg weekly for the first 2 weeks; 600 mg at week 3; then 600 mg every 2 weeks • 10 kg to less than 20 kg: 600 mg single dose at week 1; 300 mg at week 2; then 300 mg every 2 weeks • 5 kg to less than 10 kg: 300 mg single dose at week 1; 300 mg at week 2; then 300 mg every 3 weeks • Others: o Bkemv is available only through a restricted program called BKEMV REMS o Bkemv is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
Epysqli (eculizumab-aagh) • Indications: o PNH, Age ≥ 18 years old o aHUS, Adults and pediatrics (weight-based dosing) • Quantity limits: o PNH ▪ 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter o aHUS ▪ Adults: 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter ▪ Pediatrics: • 40 kg and over: 900 mg weekly for four doses; 1,200 mg at week 5; then 1,200 mg every 2 weeks • 30 kg to less than 40 kg: 600 mg weekly for two doses; 900 mg at week 3; then 900 mg every 2 weeks • 20 kg to less than 30 kg: 600 mg weekly for two doses; 600 mg at week 3; then 600 mg every 2 weeks • 10 kg to less than 20 kg: 600 mg single dose for one dose; 300 mg at week 2; then 300 mg every 2 weeks • 5 kg to less than 10 kg: 300 mg single dose for one dose; 300 mg at week 2; then 300 mg every 3 weeks • Others: o Epysqli is available only through a restricted program called the Epysqli REMS o Epysqli is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
Piasky (crovalimab-akkz) • Indications: o PNH, Age ≥ 13 years old and body weight ≥ 40 kg • Quantity limits: o Patients weighing ≥ 40 kg to < 100 kg

- Loading dose
  - Day 1: 1,000 mg IV
  - Days 2, 8, 15, and 22: 340 mg SUBQ
- Maintenance dose
  - Day 29 and every 4 weeks thereafter: 680 mg SUBQ

- Patients weighing ≥ 100 kg
  - Loading dose
    - Day 1: 1,500 mg IV
    - Days 2, 8, 15, and 22: 340 mg SUBQ
  - Maintenance dose
    - Day 29 and every 4 weeks thereafter: 1,020 mg SUBQ

- Others:
  - Piasky is available only through a restricted program called the Piasky REMS

Soliris (eculizumab)

- Indications:
  - PNH, Age ≥ 18 years old
  - aHUS, Adults and pediatrics (weight-based dosing)
  - gMG and AChR antibody positive, Adults and pediatrics (weight-based dosing)
  - NMOSD and AQP4 antibody positive, Age ≥ 18 years old
- Quantity limits:
  - PNH: 600 mg weekly for the first 4 weeks, followed by 900 mg for the fifth dose 1 week later, then 900 mg every 2 weeks thereafter
  - aHUS, gMG
    - Adults: 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter
    - Pediatrics:
      - 40 kg and over: 900 mg weekly for the first 4 weeks; 1,200 mg at week 5; then 1,200 mg every 2 weeks
      - 30 kg to less than 40 kg: 600 mg weekly for the first 2 weeks; 900 mg at week 3; then 900 mg every 2 weeks
      - 20 kg to less than 30 kg: 600 mg weekly for the first 2 weeks; 600 mg at week 3; then 600 mg every 2 weeks
      - 10 kg to less than 20 kg: 600 mg single dose at week 1; 300 mg at week 2; then 300 mg every 2 weeks
      - 5 kg to less than 10 kg: 300 mg single dose at week 1; 300 mg at week 2; then 300 mg every 3 weeks
  - NMOSD: 900 mg weekly for the first 4 weeks, followed by 1,200 mg for the fifth dose 1 week later, then 1,200 mg every 2 weeks thereafter
- Others:
  - Soliris is available only through a restricted program called the Ultomiris and Soliris REMS.
  - Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Ultomiris (ravulizumab-cwvz)

- Indications:

○ PNH, Age ≥ 1 month ○ aHUS, Age ≥ 1 month ○ gMG and AChR antibody positive: Age ≥ 1 month ○ NMOSD and AQP4 antibody positive: Age ≥ 1 month • Quantity limits: ○ PNH, aHUS ▪ 5 kg to less than 10 kg: Loading dose 600 mg; Maintenance dose 300 mg every 4 weeks ▪ 10 kg to less than 20 kg: Loading dose 600 mg; Maintenance dose 600 mg every 4 weeks ▪ 20 kg to less than 30 kg: Loading dose 900 mg; Maintenance dose 2,100 mg every 8 weeks ▪ 30 kg to less than 40 kg: Loading dose 1,200 mg; Maintenance dose 2,700 mg every 8 weeks ○ PNH, aHUS, gMG, or NMOSD ▪ 40 kg to less than 60 kg: Loading dose 2,400 mg; Maintenance dose 3,000 mg every 8 weeks ▪ 60 kg to less than 100 kg: Loading dose 2,700 mg; Maintenance dose 3,300 mg every 8 weeks ▪ 100 kg or greater: Loading dose 3,000 mg; Maintenance dose 3,600 mg every 8 weeks ○ The under-40 kg weight category is labeled for PNH or aHUS only (not gMG or NMOSD). • Others: ○ Ultomiris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Ultomiris REMS, prescribers must enroll in the program. ○ Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).
Veopoz (pozelimab-bbfg) • Indications: ○ CD55-deficient protein-losing enteropathy (CHAPLE disease), Age ≥ 1 year • Quantity limits: ○ Day 1 (loading dose): Administer a single 30 mg/kg dose by intravenous infusion after dilution ○ Day 8 and thereafter (maintenance dosage): Inject 10 mg/kg as a subcutaneous injection once weekly starting on Day 8 (maximum maintenance dosage: 800 mg once weekly)
AChR: anti-acetylcholine receptor, aHUS: atypical hemolytic uremic syndrome, AQP4: anti-aquaporin-4, gMG: generalized myasthenia gravis, IV: intravenous, NMOSD: neuromyelitis optica spectrum disorder, PNH: paroxysmal nocturnal hemoglobinuria, REMS: Risk Evaluation and Mitigation Strategy, STEC-HUS: Shiga toxin-producing Escherichia coli related hemolytic uremic syndrome, SUBQ: subcutaneous

- Table 3. Indication-specific re-authorization criteria for complement C5 inhibitors

FDA Labeled Indication-Specific Re-Authorization Criteria
Atypical hemolytic uremic syndrome (aHUS) • Re-authorization criteria: ○ Documentation demonstrating a clinically meaningful improvement from baseline (e.g., reduced plasma exchange requirements, reduced dialysis dependence, increased platelet count, stabilization of hemoglobin, or decreased evidence of hemolysis).
CD55-deficient protein-losing enteropathy (PLE) (i.e., CHAPLE disease) • Re-authorization criteria: ○ Documentation demonstrating a clinically meaningful improvement from baseline (e.g., normalization of serum albumin, reduction of peripheral or facial edema, reduction in abdominal pain or diarrhea, or reduced thrombosis risk).
Generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor (AChR) antibody positive • Re-authorization criteria: ○ Documentation demonstrating a clinically meaningful improvement from baseline (e.g., improvement in MG-ADL score, reduction in signs and symptoms of myasthenia gravis, or reduction of rescue therapy use).
Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive • Re-authorization criteria: ○ Documentation demonstrating a clinically meaningful improvement from baseline (e.g., absence of relapses, reduced relapse frequency, decreased relapse severity, or reduced use of rescue therapy).
Paroxysmal nocturnal hemoglobinuria (PNH) • Re-authorization criteria: ○ Documentation demonstrating a clinically meaningful improvement from baseline (e.g., increased or stable hemoglobin levels, reduced transfusion requirements, improvement in hemolysis, decreased lactate dehydrogenase (LDH) levels, or increased reticulocyte count).

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