Reference number(s)
1632-A

Standard Medicare Part B Management Soliris and Biosimilars

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Soliris	eculizumab
Bkemv	eculizumab-aeeb
Epysqli	eculizumab-aagh

Indications

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

FDA-approved Indications[1,12,13]

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 patients 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.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

- 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.

Compendial Uses[11]

- Antibody mediated heart transplant rejection
- Antibody mediated renal transplant rejection
- Complement C3 glomerulopathy (C3G) post-kidney transplant

Limitation 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 will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

- For initial requests:
  - 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 benefit from therapy.

Coverage Criteria

Paroxysmal Nocturnal Hemoglobinuria (PNH)[1,2,6-9,12,13]

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

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

- 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)[1,3,12,13]

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

- 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)[1,4,10,12,13]

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

- The member is 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)[1,5]

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

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

- The member is anti-aquaporin-4 (AQP4) antibody positive.
- The 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.

Antibody Mediated Heart Transplant Rejection[11]

Authorization of 6 months may be granted for treatment of antibody mediated heart transplant rejection.

Antibody Mediated Renal Transplant Rejection[11]

Authorization of 6 months may be granted for treatment of antibody mediated renal transplant rejection.

Complement C3 Glomerulopathy (C3G) Post-Kidney Transplant[11]

Authorization of 6 months may be granted for treatment of complement C3 glomerulopathy (C3G) post-kidney transplant.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from 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).

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Atypical Hemolytic Uremic Syndrome (aHUS)

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with requested medication.
- The member is receiving benefit from 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 for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from 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 for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy (e.g., reduction in number of relapses as compared to baseline).
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Antibody Mediated Heart Transplant Rejection

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy.

Antibody Mediated Renal Transplant Rejection

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Complement C3 Glomerulopathy (C3G) Post-Kidney Transplant

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The member is receiving benefit from therapy.

Dosage And Administration

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

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Soliris, Bkemv, and Epysqli.
- The available compendium
  - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
  - Micromedex DrugDex
  - American Hospital Formulary Service- Drug Information (AHFS-DI)
  - Lexi-Drugs
  - Clinical Pharmacology
- Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy.
- Guidelines for the Diagnosis and Monitoring of Paroxysmal Nocturnal Hemoglobinuria and Related Disorders by Flow Cytometry.
- International consensus guidance for management of myasthenia gravis.
- An international consensus approach to the management of atypical hemolytic uremic syndrome in children.
- International consensus guidance for management of myasthenia gravis: 2020 update.
- International consensus diagnostic criteria for neuromyelitis optica spectrum disorders.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Soliris, Bkemv, and Epysqli are covered in addition to the following:

- Antibody mediated heart transplant rejection
- Antibody mediated renal transplant rejection
- Complement C3 glomerulopathy (C3G) post-kidney transplant

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Support for using percentage of PNH cells or percentage of GPI-AP deficiency poly-morphonuclear cells can be found in the guidelines for diagnosis of PNH (Borowitz et al and Preis et al). Flow cytometry is the gold standard for assessing the percentage of GPI-AP deficient poly-morphonuclear cells. Classic PNH is defined as greater than 50% of GPI-AP deficient PMNs. It is also possible to diagnose PNH by assessing the percentage of PNH cells. Most clinical trials for the complement inhibitors required at least 10% PNH cells, but the trials associated with Ultomiris only required 5% PNH cells. Therefore, the baseline requirement for all complement inhibitor programs will be at least 5%.

Currently there are no treatment guidelines or literature supporting the concomitant use of complement inhibitors (e.g., Empaveli, Fabhalta, Piasky, Ultomiris) for the treatment of PNH.

Currently there are no treatment guidelines or literature supporting the concomitant use of complement inhibitors (e.g., Ultomiris) for the treatment of aHUS

Support for Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of greater than or equal to 5 can be found in the trials associated with Vyvgart and Vyvgart Hytrulo. Most clinical trials of myasthenia gravis agents required a MG-ADL of greater than or equal to 6, however, to align myasthenia gravis programs the baseline requirement will be greater than or equal to 5. MG-ADL is a scale that assesses the impact of myasthenia gravis on daily functions. This scale was used as an assessment tool to evaluate response to myasthenia gravis treatment from baseline in the clinical trials.

Support for the trial of immunosuppressive agents and IVIG before initiating therapy with eculizumab (Soliris) can be found in the 2020 update to the international consensus guidance for management of myasthenia gravis. The recommendations indicate that eculizumab should be considered in the treatment of severe, refractory myasthenia gravis (after trials of other immunotherapies have been unsuccessful in meeting treatment goals).

Currently there are no treatment guidelines or literature supporting the concomitant use of complement inhibitors (e.g., Soliris, Ultomiris, Zilbrysq) or neonatal Fc receptor blockers (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

Support for the list of core clinical characteristics of NMOSD can be found in the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder (Wingerchuk et al). There are six clinical characteristics cited in the diagnostic criteria:

- 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

Currently there are no treatment guidelines or literature supporting the concomitant use with other biologics for the treatment of NMOSD.

Support for antibody mediated heart transplant rejection can be found in several small studies and case reports. In a study by Kittleson et al, the addition of eculizumab to treatment of heart transplant recipients

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

with cardiogenic shock and high suspicion of antibody mediated rejection (AMR) did not significantly improve survival or other outcomes in a small retrospective study, but eculizumab was used at the discretion of treating physicians and administered to sicker patients. In heart transplant recipients with AMR and hemodynamic compromise resistant to standard therapy (plasmapheresis and thymoglobulin), the addition of bortezomib, eculizumab, and consolidation with total lymphoid irradiation was associated in 3 of 4 patients with survival, reduced donor specific antibodies (DSA), improved cardiac function, and no recurrence of AMR in survivors at time of publication, in a very small pilot study by Mokshagundam et al. In case reports of heart transplant recipients, eculizumab stabilized graft function in 3 patients with severe acute antibody mediated rejection (AMR) who received eculizumab after at least 5 plasmapheresis and IV immune globulin treatments (Tomeczkowicz et al), produced complete complement inhibition and left ventricular ejection fraction (LVEF) normalization as one of the initial treatments in 1 patient (Yerly et al), improved graft function in 2 heart transplant recipients with biopsy-negative rejection and presumed refractory AMR (Murphy et al), and improved LVEF and heart failure symptoms to allow retransplantation in 1 patient with chronic AMR attributed to DSAs (Kearney et al).

Support for antibody mediated renal transplant rejection can be found in several small studies. In a study by Tan et al, eculizumab treatment alone or in combination with plasmapheresis and/or IV immune globulin improved graft function and histologic factors in a case series of solitary kidney transplant recipients with active antibody-mediated rejection (AMR) within the first 30 days posttransplant, and no graft losses occurred during the median follow up of 13 months. Eculizumab alone compared with plasmapheresis and IV immune globulin (standard of care) did not prevent progression to chronic AMR or transplant glomerulopathy in a small, open-label, randomized trial (Heo et al) in kidney transplant recipients with biopsy-proven AMR; however, no patient lost their graft and DSA titers were reduced in both groups. In a study (Norville et al) of electronic health records of kidney transplant recipients, treatment with eculizumab improved graft survival and patient survival rates compared with published reported incidences in a cohort of patients with AMR also receiving plasmapheresis and IV immunoglobulin. When evaluated with regard to splenectomy, treatment with eculizumab plus splenectomy improved outcomes compared with eculizumab or splenectomy alone in a retrospective study (Orandi et al) of incompatible live donor kidney transplant recipients with early severe AMR; all patients also received plasmapheresis and IV immune globulin.

Support for Complement C3 glomerulopathy (C3G) post-kidney transplant can be found in a few small studies. In a study by Gonzalez Suarez et al, adult kidney transplant recipients with post-transplant complement C3 glomerulopathy (C3G), rates of allograft loss were lower with eculizumab than with therapeutic plasma exchange or rituximab, including in the subgroup of patients with C3 glomerulonephritis (C3GN), in a systematic review and analyses of cohort studies and case series. Pooled sample sizes were small, and data in patients with dense deposit disease was limited. In retrospective evaluations, eculizumab, with or without other therapies, resulted in complete or partial remission in some patients with C3G recurrence; however, some eculizumab-treated patients also developed graft loss (Mirioglu et al) or kidney failure (Caravaca-Fontan et al).

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

References

1. Soliris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2025.
2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. Hematology. 2011; 21-29.
3. 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: January 1, 2016.
4. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021;96(3):114-122.
5. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85:177-189.
6. 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.
7. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
8. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.
9. 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.
10. Barnett C, Herbelin L, Dimachkie MM, Barohn RJ. Measuring Clinical Treatment Response in Myasthenia Gravis. Neurol Clin. 2018 May;36(2):339-353.
11. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, CO. Available at: http://www.micromedexsolutions.com. Accessed March 14, 2025.
12. Bkemv [package insert]. Thousand Oaks, CA: Amgen Inc.; October 2024.
13. Epysqli [package insert]. Republic of Korea: Samsung Bioepis Co., Ltd.; November 2024.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.