AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Ultomiris (ravulizumab-cwvz)	Page:	1 of 4
Effective Date:	2/7/2025	Last Review Date:	2/7/2025
Applies to:	☒New Jersey		

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Ultomiris under the patient's prescription drug benefit.

Description:

FDA-Approved Indication

1. Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH). *(Reference NJ State Protocol for Paroxysmal Nocturnal Hemoglobinuria (PNH) Products).*
2. Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).
3. Ultomiris is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.
4. Ultomiris is indicated for the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

Limitations of Use: Ultomiris is 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.

Applicable Drug List:

Ultomiris

Policy/Guideline:

I. Documentation

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

A. Initial requests:

1. Atypical hemolytic uremic syndrome: ADAMTS 13 level
2. Generalized myasthenia gravis:
   i. Positive anti-acetylcholine receptor (AChR) antibody test
   ii. Myasthenia Gravis Foundation of America (MGFA) clinical classification
   iii. MG activities of daily living score
   iv. Previous medications tried, including response to therapy. If therapy is not advisable, documentation of clinical reasons to avoid therapy.
4. Neuromyelitis optica spectrum disorder: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present

B. Continuation requests:

1. Chart notes or medical record documentation supporting positive clinical response.

Criteria for Initial Approval:

A. Atypical hemolytic uremic syndrome

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

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

B. Generalized myasthenia gravis

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

1. Anti-acetylcholine receptor (AchR) antibody positive
2. Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
3. MG activities of daily living (MG-ADL) total score of greater than or equal to 5
4. Meets ONE of the following:
   i. 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)
   ii. 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
   iii. Member has a documented clinical reason to avoid therapy with immunosuppressive agents and IVIG
5. The requested medication will NOT be used in combination with another complement inhibitor (e.g., Soliris, Zilbrysq) or neonatal Fc receptor blocker (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

C. Neuromyelitis optica spectrum disorder

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

1. Anti-aquaporin-4 (AQP4) antibody positive
2. Member exhibits one of the following core clinical characteristics of NMOSD:
   i. Optic neuritis
   ii. Acute myelitis

iii. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
iv. Acute brainstem syndrome
v. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
vi. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

3. The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Criteria for Continuation of Therapy

A. Atypical hemolytic uremic syndrome

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

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

B. Generalized myasthenia gravis

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

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

C. Neuromyelitis optica spectrum disorder

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

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

Approval Duration and Quantity Restrictions:

Initial Approval: 6 months

Renewal Approval: 12 months

Quantity Level Limit:

Medication	Standard Limit
Ultomiris 245mg/3.5mL (70 mg/mL) single-dose prefilled cartridge for use only with supplied single-use on-body inj	8 single-dose prefilled cartridges per 28 days

References:

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2024.
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3. 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.
4. 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.
5. Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
6. 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.
7. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.
8. Sanders D, Wolfe G, Benatar M et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2021; 96 (3) 114-122.
9. Tuan Vu, Andreas Meisel, Renato Mantegazza, et al. Terminal Complement Inhibitor Ravulizumab in Generalized Myasthenia Gravis. NEJM Evid 2022; 1 (5).
10. 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.
11. Barnett C, Herbelin L, Dimachkie MM, Barohn RJ. Measuring Clinical Treatment Response in Myasthenia Gravis. Neurol Clin. 2018 May;36(2):339-353.
12. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015; 85:177-189.