Ultomiris (ravulizumab)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Ultomiris (ravulizumab) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered a benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).
2. Ultomiris is indicated for the treatment of adults 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).

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review for new requests for treatment of:

A. For initial requests:
   1. Paroxysmal nocturnal hemoglobinuria: flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency
   2. Atypical hemolytic uremic syndrome: ADAMTS 13 level
   3. Generalized myasthenia gravis: anti-acetylcholine receptor (AchR) antibody positive, clinical classification of myasthenia gravis score, MG activities of daily living score, use of IVIG (if applicable), use of immunosuppressive therapies, prior chronic treatment with plasmapheresis or plasma exchange (if applicable)
   4. Neuromyelitis optica spectrum disorder: immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present
B. For continuation requests: Chart notes or medical record documentation supporting positive clinical response

Criteria for Initial Approval

A. Paroxysmal nocturnal hemoglobinuria

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

1. The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-Aps) as demonstrated by either of the following:
   a) At least 5% PNH cells
   b) At least 51% of GPI-AP deficient poly-morphonuclear cells
2. Flow cytometry is used to demonstrate GPI-Aps deficiency
3. For subcutaneous dosing: member must be 18 years of age or older

B. 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:

1. Absence of Shiga toxin
2. ADAMTS 13 activity level above 5%
3. For subcutaneous dosing: member must be 18 years of age or older

C. 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:

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 ≥6
4. Member has failed treatment over at least one year with at least two immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate, tacrolimus, methotrexate, cyclophosphamide, rituximab), OR member has failed at least one immunosuppressive therapy and required chronic plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (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)

D. Neuromyelitis Optica Spectrum Disorder (NMOSD)

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

1. Anti-aquaporin-4 (AQP4) antibody positive
2. The medication is being prescribed by, or in consultation with, a neurologist
3. Member exhibits one of the following core clinical characteristics of NMOSD:
   a) Optic neuritis

b) Acute myelitis
c) Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
d) Acute brainstem syndrome
e) Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
f) Symptomatic cerebral syndrome with NMOSD-typical brain lesions

4. Member has experienced a relapse that required rescue therapy in the last 12 months prior to initiating therapy
5. The member will not receive the requested drug concomitantly with any of the following:
   a) Other complement-inhibitors (i.e., eculizumab)
   b) Anti-CD20 therapy (i.e., rituximab)
   c) Anti-CD19 antibody (i.e., inebilizumab-cdon)
   d) IL-6 receptor antagonist (i.e., satralizumab-mwge)

Continuation of Therapy

A. Paroxysmal nocturnal hemoglobinuria
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and demonstrate a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).

B. Atypical hemolytic uremic syndrome (aHUS)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and demonstrate a positive response to therapy (e.g., normalization of lactate dehydrogenase [LDH] levels, platelet counts).

C. Generalized myasthenia gravis (gMG)
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and member demonstrates a positive response to therapy (e.g., improvement in MG-ADL score, changes compared to baseline in Quantitative Myasthenia Gravis (QMG) total score).

D. Neuromyelitis optica spectrum disorder (NMOSD)
Authorization of 12 months may be granted for continued treatment of neuromyelitis optica spectrum disorder (NMOSD) in anti-aquaporin-4 (AQP4) antibody positive adults requesting reauthorization when there is no evidence of unacceptable toxicity or disease progression while on the current regimen, they demonstrate a positive clinical response to therapy from baseline as demonstrated by a reduction in the number and/or severity of relapses, and the medication is being prescribed by, or in consultation with, a neurologist.

Ultomiris is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

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

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J1303 Injection, ravulizumab-cwvz, (Ultomiris), 10 mg

REFERENCES

- Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; September 2024.
- Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology.* 2011; 21-29.
- 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.
- 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.
- Preis M, Lowrey CH. Laboratory tests for paroxysmal nocturnal hemoglobinuria (PNH). Am J Hematol. 2014;89(3):339-341.
- 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.
- Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016;2016(1):208-216.
- Sanders D, Wolfe G, Benatar M et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2021; 96 (3) 114-122.
- Tuan Vu, Andreas Meisel, Renato Mantegazza, et al. Terminal Complement Inhibitor Ravulizumab in Generalized Myasthenia Gravis. NEJM Evid 2022; 1 (5)

POLICY HISTORY

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