Reference number(s)
2835-A

SPECIALTY GUIDELINE MANAGEMENT

ULTOMIRIS (ravulizumab-cwvz)

POLICY

I. 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. 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 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.

II. DOCUMENTATION

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

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:
      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. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

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

B. 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 of 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.

C. Generalized myasthenia gravis

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 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).

D. Neuromyelitis optica spectrum disorder

Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of 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.

IV. CONTINUATION OF THERAPY

A. Paroxysmal nocturnal hemoglobinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of 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 hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).
3. The requested medication will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Piasky, Soliris) for the treatment of PNH (concomitant use with Voydeya is allowed).

B. Atypical hemolytic uremic syndrome

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of 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.

C. Generalized myasthenia gravis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of 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).

D. Neuromyelitis optica spectrum disorder

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of 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.

V. DOSAGE AND ADMINISTRATION

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

VI. REFERENCES

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2024.

2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. *Hematology.* 2011; 21-29.
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.
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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.
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