

SPECIALTY GUIDELINE MANAGEMENT

ULTOMIRIS (ravulizumab)

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 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.

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 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, use of two immunosuppressive therapies
- 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) 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

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%

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. Meets both of the following:
 - a. Member has had an inadequate response to at least two immunosuppressive therapies listed below:
 - i. azathioprine
 - ii. cyclosporine
 - iii. mycophenolate mofetil
 - iv. tacrolimus
 - v. methotrexate
 - vi. cyclophosphamide
 - vii. rituximab
 - b. Member has inadequate response to chronic IVIG

IV. 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).

V. DOSAGE AND ADMINISTRATION

Reference number(s)
2835-A

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.; July 2022.
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.
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.