

Ultomiris™ (ravulizumab-cwvz)



When requesting Ultomiris (ravulizumab-cwvz), the individual requiring treatment must be diagnosed with an FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved Indications

Ultomiris is indicated for:

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH).
- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.
- The treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

Coverage Guidelines

Paroxysmal nocturnal hemoglobinuria (PNH)

The individual must meet all of the following criteria for initial authorization of Ultomiris intravenous:

- The diagnosis of PNH has been confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on at least 2 cell lineages;
- Ultomiris is prescribed by or in consultation with a hematologist.

For initial authorization of Ultomiris subcutaneous injection, the individual must meet all of the above criteria **and** the following:

- Is 18 years of age or older;
- Has received or will receive Ultomiris intravenous loading dose prior to initiation of Ultomiris subcutaneous.

For re-authorization (intravenous), the individual must meet all of the following criteria:

- An individual is continuing to receive benefit from Ultomiris (e.g., stabilization of hemoglobin levels, decreased transfusion requirement or transfusion independence, reduction in hemolysis);
- Ultomiris is prescribed by or in consultation with a hematologist.

For re-authorization (subcutaneous), the individual must meet all of the above criteria and be 18 years of age or older.

- Note: An individual who has received < 6 months of therapy, or who is restarting therapy with Ultomiris, is reviewed under initial authorization criteria.

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Atypical Hemolytic Uremic Syndrome (aHUS)

The individual must meet all of the following criteria for authorization of Ultomiris intravenous:

- The individual does not have Shiga toxin *Escherichia coli* related hemolytic uremic syndrome;
- Ultomiris is prescribed by or in consultation with a nephrologist.

For authorization of Ultomiris subcutaneous injection, the individual must meet all of the above criteria **and** the following:

- Is 18 years of age or older;
- Has received or will receive Ultomiris intravenous loading dose prior to initiation of Ultomiris subcutaneous.

Approval duration: 12 months

Generalized Myasthenia Gravis (gMG)

The individual must meet all of the following criteria for initial authorization of Ultomiris intravenous:

- Has a confirmed diagnosis of anti-acetylcholine receptor (AChR) antibody positive generalized myasthenia gravis;
- Is 18 years of age or older;
- Meets both of the following:
 - Myasthenia Gravis Foundation of America classification of II to IV;
 - Myasthenia Gravis Activities of Daily Living (MG-ADL) score of 5 or higher;
- Meets one of the following:
 - Is currently receiving pyridostigmine; OR
 - Has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine;
- Meets one of the following:
 - Has received or is currently receiving two different immunosuppressive therapies for at least 1 year; OR
 - Has had inadequate efficacy, a contraindication, or significant intolerance to two different immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, cyclophosphamide);
- Has evidence of unresolved symptoms of generalized myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability (e.g., double vision, impairment of mobility);
- Ultomiris intravenous is prescribed by or in consultation with a neurologist.

Ultomiris™ (ravulizumab-cwvz)

For re-authorization, the individual must meet all of the following criteria:

- Is 18 years of age or older;
- The individual is continuing to receive benefits from Ultomiris therapy (e.g., reductions in exacerbations of myasthenia gravis; improvement in speech, swallowing, mobility, or respiratory functions).
- Ultomiris is prescribed by or in consultation with a neurologist.

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Dosing Recommendations

Paroxysmal nocturnal hemoglobinuria (PNH) and Atypical hemolytic uremic syndrome (aHUS) (intravenous administration)

Administer loading dose once by intravenous infusion, followed 2 weeks later by maintenance dose. Administer maintenance dose once every 8 weeks or every 4 weeks depending on body weight.

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg)	Maintenance Dosing Interval
Greater than or equal to 5 to less than 10	600	300	Every 4 weeks
Greater than or equal to 10 to less than 20	600	600	Every 4 weeks
Greater than or equal to 20 to less than 30	900	2,100	Every 8 weeks
Greater than or equal to 30 to less than 40	1,200	2,700	Every 8 weeks
Greater than or equal to 40 to less than 60	2,400	3,000	Every 8 weeks
Greater than or equal to 60 to less than 100	2,700	3,300	Every 8 weeks
Greater than or equal to 100	3,000	3,600	Every 8 weeks

Paroxysmal nocturnal hemoglobinuria (PNH) and Atypical hemolytic uremic syndrome (aHUS) (subcutaneous administration)

The recommended subcutaneous maintenance dose is 490 mg administered once weekly in adult patients greater than or equal to 40 kg body weight.

Ultomiris™ (ravulizumab-cwvz)

Generalized myasthenia gravis (gMG) (intravenous administration only)

Administer loading dose once by intravenous infusion, followed 2 weeks later by maintenance dose. Administer maintenance dose once every 8 weeks.

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg)	Maintenance Dosing Interval
Greater than or equal to 40 to less than 60	2,400	3,000	Every 8 weeks
Greater than or equal to 60 to less than 100	2,700	3,300	Every 8 weeks
Greater than or equal to 100	3,000	3,600	Every 8 weeks

References

1. Ultomiris® intravenous infusion and subcutaneous injection [prescribing information]. New Haven, CT: Alexion; July 2022.
2. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804–2811.
3. Soliris® intravenous infusion [prescribing information]. New Haven, CT: Alexion; April 2021.
4. Campistol JM, Arias M, Ariceta G, et al. An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. A consensus document. *Nefrologia*. 2015;35:421–447.
5. Genetics Home Reference. Atypical hemolytic-uremic syndrome. National Institutes of Health (NIH). Available at: <https://ghr.nlm.nih.gov/condition/atypical-hemolytic-uremic-syndrome#sourcesforpage>. Accessed on July 29, 2022.
6. National Institute of Neurological Disorders and Stroke (NINDS). Myasthenia Gravis Fact Sheet. National Institutes of Health (NIH) Publication No. 17-768. Publication last updated: November 15, 2021. Available at: <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Myasthenia-Gravis-Fact-Sheet>. Accessed on April 28, 2022.
7. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016;87:419–425.
8. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021 Jan 19;96(3):114-122.