MEDICAL MUTUAL®

Drug Policy

Policy:	**201905**	**Initial Effective Date: 02/22/2019**
Code(s):	**HCPCS J1303**	**Annual Review Date: 05/21/2024**
SUBJECT:	**Ultomiris™ (ravulizumab-cwvz)**	**Last Revised Date: 05/21/2024**

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

POLICY STATEMENT

This policy involves the use of Ultomiris. Prior authorization is recommended for pharmacy and medical benefit coverage of Ultomiris. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Ultomiris as well as the monitoring required for AEs and long-term efficacy, initial approval requires Ultomiris be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations under the medical benefit.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ultomiris is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Paroxysmal Nocturnal Hemoglobinuria (PNH).

Initial therapy: Approve Ultomiris for 6 months if the patient meets the following criteria (A, B, C, D, E, F, G, H, AND I):

A) Patient is ≥ 1 month of age; AND

B) PNH diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on at least two cell lineages; AND

C) Patient has an LDH level of 1.5 times the upper limit of the normal range; AND

D) Patient has greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP)- deficient polymorphonuclear cells (PMNs); AND

E) Patient is transfusion dependent as defined by one of the following:

1. Hemoglobin ≤ 7 g/dL; OR
2. Patient is experiencing symptoms of anemia; AND

F) Patient has symptoms of thromboembolic complications (abdominal pain, shortness of breath, chest pain, end organ damage; AND

G) Patient will or has received a meningococcal vaccine at least two weeks before start Ultomiris treatment; AND

H) Ultomiris is being prescribed by or in consultation with a hematologist, oncologist or immunology specialist; AND

I) Patient is not currently taking another compliment inhibitor (pegcetacoplan, eculizumab, iptacopan); AND

J) Site of care medical necessity is met*

Patient currently receiving Ultomiris: Approve Ultomiris for 1 year if the patient meets the following criteria (i, ii, and iii):

i. Patient has experienced an improvement in fatigue and quality of life; AND
ii. Patient has demonstrated a positive clinical response from baseline (e.g., stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis) from Ultomiris, according to the prescribing physician; AND
iii. Patient is not currently taking another compliment inhibitor (pegcetacoplan, eculizumab, iptacopan); AND
iv. Site of care medical necessity is met.

Dosing *(Medical Benefit Only)*. Approve the following dosing regimen:

- One-time weight-based loading dose (≥ 5 kg to < 20 kg: 600 mg; ≥ 20 kg to < 30 kg: 900 mg; ≥ 30 kg to < 40 kg: 1200 mg; ≥ 40 kg to < 60 kg: 2,400 mg; ≥ 60 kg to < 100 kg: 2,700 mg; ≥ 100 kg: 3,000).
- Followed by weight-based maintenance dosing of
  - (≥ 5 kg to < 10 kg: 300 mg; ≥ 10 kg to < 20 kg: 600 mg) Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 4-week interval.
  - (≥ 20 kg to < 30 kg: 2,100 mg; ≥ 30 kg to < 40 kg: 2,700 mg; ≥ 40 kg to < 60 kg: 3,000 mg; ≥ 60 kg to < 100 kg: 3,300 mg; ≥ 100 kg: 3,600) Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 8-week interval.

Duration of Therapy: Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).

The safety and effectiveness of Ultomiris for the treatment of PNH in pediatric patients have not been established.[1] PNH is a clinical diagnosis that should be confirmed with peripheral blood flow cytometry to detect the absence or severe deficiency of GPI-anchored proteins on at least two lineages.[2]

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 12 months*

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2. Atypical Hemolytic Uremic Syndrome (aHUS)

Initial therapy: Approve Ultomiris for 6 months if the patient meets the following criteria (A, B, C, D, E, F, G, AND H):

A. Patient is ≥ 1 month of age; AND
B. Patient does not have Shiga toxin *E. coli* related hemolytic uremic syndrome; AND
C. Patient has an LDH level of 2 times the upper limit of the normal range; AND
D. Patient is transfusion dependent as defined by one of the following (i or ii):
    i. Hemoglobin ≤ 7 g/dL; OR
    ii. The patient is transfusion dependent; AND
E. Patient has symptoms of thromboembolic complications (abdominal pain, shortness of breath, chest pain, end organ damage); AND
F. Ultomiris is being prescribed by or in consultation with a nephrologist; AND
G. Patient will or has received a meningococcal vaccine at least two weeks before start Ultomiris treatment; AND
H. Site of care necessity is met*

Patient currently receiving Ultomiris: Approve Ultomiris for 1 year if the patient meets the following criteria (i, ii, and iii):

i. Patient has experienced an improvement in fatigue and quality of life; AND
ii. Patient has demonstrated a positive clinical response from baseline (e.g., stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis) from Ultomiris, according to the prescribing physician; AND
iii. Site of care medical necessity is met.

Dosing *(Medical Benefit Only)*. Approve the dose meets the following weight-based regimen:

- One-time weight-based loading dose (≥ 5 kg to < 20 kg: 600 mg; ≥ 20 kg to < 30 kg: 900 mg; ≥ 30 kg to < 40 kg: 1200 mg; ≥ 40 kg to < 60 kg: 2,400 mg; ≥ 60 kg to < 100 kg: 2,700 mg; ≥ 100 kg: 3,000).
- Followed by weight-based maintenance dosing of
    - (≥ 5 kg to < 10 kg: 300 mg; ≥ 10 kg to < 20 kg: 600 mg) Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 4-week interval.
    - (≥ 20 kg to < 30 kg: 2,100 mg; ≥ 30 kg to < 40 kg: 2,700 mg; ≥ 40 kg to < 60 kg: 3,000 mg; ≥ 60 kg to < 100 kg: 3,300 mg; ≥ 100 kg: 3,600) Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 8-week interval.

Duration of Therapy: Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 12 months*

3. Generalized Myasthenia Gravis. Approve if the patient meets ONE of the following criteria (A or B):

A) Initial therapy. Approve for 6 months if the patient meets the following criteria (i, ii, iii, iv, v, vi, vii AND viii):

i. Patient had an inadequate response, contraindication, or intolerance to a trial of efgartimod alfa-fcab (Vyvgart®), efgartimod alfa-fcab and hyaluronidase-qvfc (Vyvgart Hytrulo®), or rozanolixizumab-noli (Rystiggo®); AND

ii. Patient is ≥ 18 years of age; AND

iii. Patient has confirmed anti-acetylcholine receptor antibody positive generalized myasthenia gravis; AND

iv. Patient meets both of the following (a and b):
- i. Myasthenia Gravis Foundation of America classification of II to IV; AND
- ii. Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 6; AND

v. Patient meets one of the following (a or b):
- i. Patient received or is currently receiving pyridostigmine; OR
- ii. Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND

vi. Patient meets one of the following (a or b):
- i. Patient received or is currently receiving two different immunosuppressant therapies for ≥ 1 year; OR
- ii. Patient had inadequate efficacy, a contraindication, or significant intolerance to two different immunosuppressant therapies; AND

  Note: Examples of immunosuppressant therapies tried include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, and cyclophosphamide.

vii. Patient has evidence of unresolved symptoms of generalized myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility); AND

viii. The medication is being prescribed by or in consultation with a neurologist.

B) Patient is Currently Receiving Ultomiris. Approve for 1 year if the patient meets the following (i, ii, AND iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient is continuing to derive benefit from Ultomiris, according to the prescriber; AND

Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.

iii. The medication is being prescribed by or in consultation with a neurologist.

Dosing *(Medical Benefit Only)*. Approve the dose meets the following weight-based regimen:

- One-time weight-based loading dose (≥ 40 kg to < 60 kg: 2,400 mg; ≥ 60 kg to < 100 kg: 2,700 mg; ≥ 100 kg: 3,000).
- Followed by weight-based maintenance dosing of ≥ 40 kg to < 60 kg: 3,000 mg; ≥ 60 kg to < 100 kg: 3,300 mg; ≥ 100 kg: 3,600. Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 8-week interval.

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 12 months*

2. Neuromyelitis Optica Spectrum Disorder (NMOSD)

Initial therapy: Approve Ultomiris for 6 months if the patient meets the following criteria (A, B, C, D, E, F, G, H, I, AND J):

A. Patient is ≥ 18 years of age; AND
B. Patient has confirmed diagnosis of Neuromyelitis Optica Spectrum Disorder; AND
C. Patient meets the following (a, b, and c):
   i. The patient is seropositive for aquaporin-4 IgG antibodies; AND
   ii. Patient has at least one core clinical characteristic (Acute optic neuritis, acute myelitis, acute area postrema syndrome (APS), acute brainstem syndrome over than APS, symptomatic narcolepsy or acute diencephalic clincal syndrome with NMOSD-typical diencephalic lesion, Acute cerebral syndrome with NMOSD-typical brain lesion); AND
   iii. Alternative Diagnoses have been excluded; AND
D. Patient has a history of at least 1 relapse in the last 12 months; AND
E. Patient has an expanded Disability Status Score (EDSS) of ≤ 7.0; AND
F. Patients on concurrent immunosuppressive therapy (corticosteroids, azathioprine, methotrexate, tacrolimus, etc.) are on stable dosing regimen; AND
G. Patient has not received therapy with rituximab or mitoxantrone in the last 3 months; AND
H. Patient has not received intravenous immune globulin (IVIG) in the last 3 weeks; AND
I. Patient will or has received a meningococcal vaccine at least two weeks before start Ultomiris treatment; AND
J. Site of care necessity is met*

Patient currently receiving Ultomiris: Approve Ultomiris for 1 year if the patient meets the following criteria ():
A. Patient has demonstrated a positive clinical response from baseline (e.g., improvement or stabilization of neurologic symptoms, reduction in hospitalizations, or reduction/discontinuation in plasma exchange treatments) from Ultomiris, according to the prescriber; AND
B. Site of care medical necessity is met.

Dosing *(Medical Benefit Only)*. Approve the dose meets the following weight-based regimen:

- One-time weight-based loading dose (≥ 40 kg to < 60 kg: 2,400 mg; ≥ 60 kg to < 100 kg: 2,700 mg; ≥ 100 kg: 3,000).
- Followed by weight-based maintenance dosing of ≥ 40 kg to < 60 kg: 3,000 mg; ≥ 60 kg to < 100 kg: 3,300 mg; ≥ 100 kg: 3,600. Starting 2 weeks after the loading dose administration, begin maintenance doses at a once every 8-week interval.

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 12 months*

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Ultomiris has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

2. Ultomiris is not recommended for patients that are asymptomatic or those with mild symptoms. Active surveillance is clinically appropriate, without the need for therapy in this subset of patients.

3. Concomitant Use with Another Complement Inhibitor, a Rituximab Product, or a Neonatal Fc Receptor Blocker. There is no evidence to support concomitant use of Ultomiris intravenous with another complement inhibitor, a rituximab product, or a neonatal Fc receptor blocker.
Note: Examples of complement inhibitors are Empaveli (pegcetacoplan subcutaneous injection), Fabhalta (iptacopan capsule), Soliris (eculizumab intravenous infusion), and Zilbrysq (zilucoplan subcutaneous injection).
Note: Examples of neonatal Fc receptor blockers are Rystiggo (rozanolixizumab-noli subcutaneous infusion), Vyvgart (efgartigimod alfa-fcab intravenous infusion], and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection).

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or

performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Ultomiris™ injection [prescribing information]. New Haven, CT: Alexion Pharmaceuticals, Inc.; March 2024.
2. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. *Blood*. 2014;124(18):2804–2811.
3. Soliris® injection [prescribing information]. New Haven, CT: Alexion Pharmaceuticals, Inc.; February 2018.
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 November 21, 2019.
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.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J1303

†When ravulizumab-cwvz (J1303) is determined to be Ultomiris

Edits and Denials:

Prior approval: Prior approval is required for Ultomiris **(HCPCS Codes J1303)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes J1303** will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J1303	Injection, ravulizumab-cwvz, 10 mg