Neighborhood Health Plan OF RHODE ISLAND™
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Ultomiris® (ravulizumab-cwvz)
Non-Hematology Policy
(Intravenous)

Effective date: 01/01/2020

Dates Reviewed: 09/18/2019, 12/20/2019, 1/22/2020, 12/2020, 5/27/2021, 3/3/2022, 8/4/2022, 4/27/2023, 12/14/2023, 01/10/2024, 05/08/2024, 04/09/2025, 10/28/2025

Scope: Medicaid, Commercial, Medicare

For Hematology indications, please refer to the Neighborhood/Evolent Ultomiris Hematology Policy.

I. Length of Authorization

Coverage will be provided for six (6) months and may be renewed every 6 months thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- gMG and NMOSD: 300 units on Day 0 followed by 360 units on Day 14 and every 8 weeks thereafter (1 billable unit = 10 mg)

III. Summary of Evidence

Ultomiris (ravulizumab-cwvz) is a complement inhibitor indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive and for adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody-positive. Ultomiris binds with high affinity to complement protein C5, blocking its cleavage into C5a and C5b and thereby preventing formation of the terminal complement complex (C5b-9). For gMG, the presumed mechanism is reduction of terminal complement complex deposition, and in NMOSD, the presumed mechanism involves inhibition of AQ-4 antibody-inducing terminal complement of C5b-9 deposition. In the treatment of gMG, the efficacy and safety of Ultomiris was evaluated in a randomized, double-blind, placebo-controlled trial (ALXN1210-MG-306) involving 175 adult patients. Results showed that ravulizumab significantly improved clinical outcomes, including muscle strength and daily function. Most patients experienced sustained improvements over time. The most frequently reported adverse events in Ultomiris-treated patients (≥10%) included diarrhea and upper respiratory tract infections. Serious

infections occurred in approximately 9% of patients, and there was one reported case of fatal COVID-19 pneumonia. In NMOSD, Ultomiris was assessed in adult patients in an open-label, multicenter study (ALXN1210-NMO-307). Ultomiris was associated with a reduction in disease relapses and demonstrated a safety profile consistent with its mechanism. The most common adverse reactions included COVID-19 infection, headache, back pain, urinary tract infection, and joint pain (arthralgia). Serious adverse events were reported in approximately 14% of patients and due to the increased risk of life-threatening meningococcal infections (black box warning), patients must receive meningococcal vaccination prior to initiation of therapy and be monitored for signs of infection. Ultomiris is only available through the Risk Evaluation and Mitigation Strategy (REMS) program.

IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Universal Criteria [1]

- Member is at least 18 years of age *(unless otherwise specified)*; **AND**
- Will not be used in combination with other immunomodulatory biologic therapies (e.g., Rituxan (rituximab), Soliris/Epysqli/Bkemv (eculizumab), Empaveli or Syfovre (pegcetacoplan), Enspryng (satralizumab), Uplizna (inebilizumab), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase), Rystiggo (rozanolixizumab), Imaavy (nipocalimab), etc.); **AND**
- The member does NOT have any FDA labeled contraindications to the requested agent; **AND**
- The requested quantity (dose) is within FDA labeled dosing for the requested indication

Generalized Myasthenia Gravis (gMG) † Φ [1, 2-8]

- Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of generalized myasthenia gravis (gMG); **AND**
- Prescribed by, or in consultation with a neurologist; **AND**
- Member has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IVb disease §; **AND**
- Member has a positive serologic test for anti-acetylcholine receptor (AChR) antibodies; **AND**
- Physician has assessed objective signs of neurological weakness and fatiguability on a baseline neurological examination (e.g., including, but not limited to, the Quantitative Myasthenia Gravis [QMG] score, etc.); **AND**
- The member's current medications have been assessed and any medications known to exacerbate myasthenia gravis (e.g., beta blockers, procainamide, quinidine, magnesium, anti-programmed death receptor-1 monoclonal antibodies, hydroxychloroquine, aminoglycosides) have been discontinued **OR** discontinuation of the offending agent is NOT clinically appropriate; **AND**
- The member meets one of the following:
    - The member has tried and had an inadequate response to at least ONE conventional agent used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide); **OR**
    - The member has an intolerance or hypersensitivity to ONE conventional agent used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide); **OR**

    - The member has an FDA labeled contraindication to ALL conventional agents used for the treatment of myasthenia gravis (i.e., corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide); **OR**
    - The member required chronic intravenous immunoglobulin (IVIG); **OR**
    - The member required chronic plasmapheresis/plasma exchange; AND
- Member must have an inadequate response, intolerance/hypersensitivity or FDA-labeled contraindication to efgartigimod (Vyvgart IV or Vyvgart Hytrulo SC) that is not expected to occur with the requested agent [medical documentation must be provided]

§Myasthenia Gravis Foundation of America (MGFA) Disease Clinical Classification [5]:

– **Class I**: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.

– **Class II**: Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.

- **IIa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
- **IIb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.

– **Class III**: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.

- **IIIa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
- **IIIb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.

– **Class IV**: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.

- **IVa**. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
- **IVb**. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.

– **Class V**: Defined as intubation, with or without mechanical ventilation, except when employed during routine
postoperative management. The use of a feeding tube without intubation places the member in class IVb.

Neuromyelitis Optica Spectrum Disorder (NMOSD) † Φ [1,9-12]

- Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the following:
    - Member is anti-aquaporin-4 (AQP4) antibody positive (lab test required); **AND**
    - The diagnosis was confirmed by at least ONE of the following:
        - Optic neuritis; **OR**
        - Acute myelitis; **OR**
        - Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting; **OR**
        - Acute brainstem syndrome; **OR**
        - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions; **OR**
        - Symptomatic cerebral syndrome with NMOSD-typical brain lesions; **AND**
    - The member has had at least ONE discrete clinical attack of CNS symptoms; **AND**
    - Alternative diagnoses (e.g., multiple sclerosis, ischemic optic neuropathy) have been ruled out; **AND**
- Prescribed by, or in consultation with, a neurologist; **AND**
- Member must have experienced failure, contraindication or intolerance to Enspryng (satralizumab)* AND Uplizna (inebilizumab)

* This requirement **ONLY** applies to **Medicaid** Members

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

- The member was previously approved for the requested agent through the plan's Medical Drug Review process (Note: members not previously approved for the requested agent will require initial evaluation review); **AND**
- Prescribed by, or in consultation with, a neurologist; **AND**
- The member will NOT be using the requested agent in combination with other immunomodulatory biologic therapies (e.g., Rituxan (rituximab), Soliris/Epysqli/Bkemv (eculizumab), Empaveli or Syfovre (pegcetacoplan), Enspryng (satralizumab), Uplizna (inebilizumab), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase), Rystiggo (rozanolixizumab), Imaavy (nipocalimab), etc.); **AND**
- The member does NOT have any FDA labeled contraindications to the requested agent; **AND**
- The requested quantity (dose) is within FDA labeled dosing for the requested indication; **AND**

Generalized Myasthenia Gravis (gMG) [1,2-8]

- Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by all of the following:
    - Improvement and/or maintenance of at least a 3-point improvement (i.e., reduction in score) from pre-treatment baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score sustained for at least 4 weeks **Δ**; **AND**
    - Improvement in muscle strength testing with fatigue maneuvers as evidenced on neurologic examination when compared to baseline

*[**Δ** May substitute an improvement of at least 4-point from baseline in the Quantitative Myasthenia Gravis (QMG) total score sustained for at least 4-weeks, if available]*

NMOSD [1,11]

- Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by at least both of the following:
    - Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD (e.g., reduced hospitalizations, improvement or stabilization of vision or paralysis)

VI. Dosage/Administration [1]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Generalized Myasthenia Gravis (gMG) and Neuromyelitis Optica Spectrum Disorder (NMOSD)</td><td>Administer the INTRAVENOUS doses based on the member's body weight. Starting 2 weeks after the loading dose, begin maintenance doses once every 8 weeks (depending on body weight).
<table>
<tr><th>Body Weight Range</th><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th><th>Dosing Interval</th></tr>
<tr><td>40 kg to <60 kg</td><td>2,400</td><td>3,000</td><td rowspan="3">Every 8 weeks</td></tr>
<tr><td>60 kg to <100 kg</td><td>2,700</td><td>3,300</td></tr>
<tr><td>100 kg or greater</td><td>3,000</td><td>3,600</td></tr>
</table></td></tr>
</table>

VII. Billing Code/Availability Information

HCPCS Code:

- J1303 − Injection, ravulizumab-cwvz, 10 mg; 1 billable unit = 10 mg

NDC(s):

- Ultomiris 300 mg/3 mL single-dose vial for injection: 25682-0025-xx
- Ultomiris 1,100 mg/11 mL single-dose vial for injection: 25682-0028-xx

VIII. References

1. Ultomiris [package insert]. Boston, MA; Alexion Pharmaceuticals, Inc; March 2024. Accessed July 2025.
2. Jayam-Trouth A, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: a review. Autoimmune Dis. 2012;2012:874680. doi:10.1155/2012/874680
3. Gronseth GS, Barohn R, Narayanaswami P. Practice advisory: Thymectomy for myasthenia gravis (practice parameter update): Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2020;94(16):705. Epub 2020 Mar 25.
4. Sussman J, Farrugia ME, Maddison P, et al. Myasthenia gravis: Association of British Neurologists' management guidelines. Pract Neurol 2015; 15: 199-206.
5. Institute for Clinical and Economic Review. Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value. Draft evidence report. July 22, 2021. https://icer.org/wp-content/uploads/2021/03/ICER_Myasthenia-Gravis_Draft-Evidence- Report_072221.pdf. Accessed December 22, 2021.
6. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.
7. Jarius, S., Aktas, O., Ayzenberg, I. et al. Update on the diagnosis and treatment of neuromyelits optica spectrum disorders (NMOSD) – revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part I: Diagnosis and differential diagnosis. J Neurol 270, 3341–3368 (2023). https://doi.org/10.1007/s00415-023-11634-0.
8. Pittock SJ, Barnett M, Bennett JL, et al. Ravulizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder. Ann Neurol. 2023 Jun;93(6):1053-1068. doi: 10.1002/ana.26626. Epub 2023 Apr 5. PMID: 36866852.
9. Kümpfel T, Giglhuber K, Aktas O, et al. Neuromyelitis Optica Study Group (NEMOS). Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) - revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. J Neurol. 2023 Sep 7. doi: 10.1007/s00415-023-11910-z. Epub ahead of print

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G36.0	Neuromyelitis optica [Devic]
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage- database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
6, K	A54548	National Government Services, Inc

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:
Ultomiris was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Ultomiris according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.