Ultomiris® (ravulizumab-cwvz)
(Intravenous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 12 months thereafter.

II. Dosing Limits

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

- 300 units on Day 0 followed by 360 units on Day 14 and every 8 weeks thereafter

III. Initial Approval Criteria

Site of care specialty infusion program requirements are met (refer to Moda Site of Care Policy).

Target Agent(s) will be approved when ALL of the following are met:

- ONE of the following:
  - The patient has a diagnosis of Paroxysmal Nocturnal Hemoglobinuria (PNH) AND BOTH of the following:
    - The diagnosis was confirmed by flow cytometry with at least 2 independent flow cytometry reagents on at least 2 cell lineages (e.g., RBCs and WBCs) demonstrating that the patient's peripheral blood cells are deficient in glycosylphosphatidylinositol (GPI)-linked proteins (lab tests required); **AND**
    - The patient will NOT be using the requested agent in combination with Empaveli (pegcetacoplan), Fabhalta (iptacopan), or Piasky (crovalimab-akkz); **OR**
  - The patient has a diagnosis of atypical Hemolytic Uremic Syndrome (aHUS) AND BOTH of the following:
    - The diagnosis has been confirmed by ONE of the following: (medical records required)
      - Genetic mutation (e.g., *CFH, CD46, CFI, C3, CFB, THBD, CFHR1, CFHR3, CFHR5*); **OR**
      - Antibodies to complement factors; **OR**
      - A differential diagnosis of complement-mediated HUS has been demonstrated (i.e., screening for Shiga toxin-producing E. coli [STEC] for STEC-HUS, pneumococcal

culture of blood/sputum/cerebrospinal or pleural fluid for pneumococcal-associated HUS, ADAMTS13 less than 10% activity for thrombotic thrombocytopenic purpura [TTP], screening for defective cobalamin metabolism); **AND**

- The patient is negative for Shiga toxin-producing *E. coli* (STEC); **OR**

– The patient has a diagnosis of generalized Myasthenia Gravis (gMG) AND ALL of the following:

- The patient had an inadequate response, or has a contraindication or intolerance, to efgartigimod alfa-fcab (Vyvgart) or efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) or rozanolixizumab-noli (Rystiggo); **AND**
- The patient has a positive serological test for anti-AChR antibodies (medical records required); **AND**
- The patient has a Myasthenia Gravis Foundation of America (MGFA) clinical classification class of II-IVb; **AND**
- The patient has a MG-Activities of Daily Living total score of greater than or equal to 6; **AND**
- ONE of the following:
  - The patient'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**
- ONE of the following:
  - The patient 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 patient 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 patient 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 patient required chronic intravenous immunoglobulin (IVIG); **OR**
  - The patient required chronic plasmapheresis/plasma exchange; **AND**
- The patient will NOT be using the requested agent in combination with Rystiggo (rozanolixizumab-noli), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), Zilbrysq (zilucoplan), or Imaavy (nipocalimab-aahu); **OR**

- The patient has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) AND ALL of the following:
  - The patient 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 patient 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**
  - The patient will NOT be using the requested agent in combination with Enspryng (satralizumab-mwge), Rituximab, or Uplizna (inebilizumab-cdon); **OR**
- The patient has another FDA labeled indication for the requested agent and route of administration; **AND**

- If the patient has an FDA labeled indication, then ONE of the following:
  - The patient's age is within FDA labeling for the requested indication for the requested agent; **OR**
  - There is support for using the requested agent for the patient's age for the requested indication; **AND**
- The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, hematologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis; **AND**
- The patient will NOT be using the requested agent in combination with Soliris (eculizumab), Bkemv (eculizumab-aeeb), or Epysqli (eculizumab-aagh); **AND**
- The patient 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

IV. Renewal Criteria

Target Agent(s) will be approved when ALL of the following are met:

- The patient was previously approved for the requested agent through the plan's Medical Drug Review process (Note: patients not previously approved for the requested agent will require initial evaluation review); **AND**

- ONE of the following:
  - The patient has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) AND BOTH of the following:
    - The patient has had improvements or stabilization with the requested agent (e.g., decreased requirement for RBC transfusions, stabilization/improvement of hemoglobin, reduction of lactate dehydrogenase (LDH), stabilization/improvement of symptoms (medical records required); **AND**
    - The patient will NOT be using the requested agent in combination with Empaveli (pegcetacoplan), Fabhalta (iptacopan), or Piasky (crovalimab-akkz); **OR**
  - The patient has a diagnosis of Atypical Hemolytic Uremic Syndrome (aHUS) AND the patient has had improvements or stabilization with the requested agent (e.g., improved platelet count, reduction of lactate dehydrogenase (LDH), stabilization/improvement of renal function) (medical records required); **OR**
  - The patient has a diagnosis of generalized myasthenia gravis (gMG) AND BOTH of the following:
    - The patient has had clinical benefit with the requested agent; **AND**
    - The patient will NOT be using the requested agent in combination with Rystiggo (rozanolixizumab-noli), Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), Zilbrysq (zilucoplan), or Imaavy (nipocalimab-aahu); **OR**
  - The patient has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) AND BOTH of the following:
    - The patient has had stabilization or improvement with the requested agent (e.g., decreased relapses, improvement or stabilization of vision or paralysis) (medical records required); **AND**
    - The patient will NOT be using the requested agent in combination with Enspryng (satralizumab-mwge), Rituximab, or Uplizna (inebilizumab-cdon); **OR**
  - The patient has a diagnosis other than PNH, aHUS, gMG, or NMOSD AND the patient has had improvement or stabilization with the requested agent (e.g., improvement or stabilization of symptoms) (medical records required); **AND**
- The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, hematologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis; **AND**
- The patient will NOT be using the requested agent in combination with Soliris (eculizumab), Bkemv (eculizumab-aeeb), or Epysqli (eculizumab-aagh); **AND**
- The patient 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

V. Dosage/Administration

<table>
<tr><th>Indication</th><th>Dose*</th></tr>
<tr><td>All Indications</td><td>
<u>Dosing for patients not currently on Ultomiris or Eculizumab treatment:</u>
Administer the intravenous doses based on the patient's body weight. Starting 2 weeks after the loading dose, begin maintenance doses once every 4 weeks or every 8 weeks (depending on body weight)
<table>
<tr><th>Indications</th><th>Body Weight Range</th><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th><th>Dosing Interval</th></tr>
<tr><td rowspan="4">PNH, aHUS</td><td>5 kg to <10 kg</td><td>600</td><td>300</td><td rowspan="2">Every 4 weeks</td></tr>
<tr><td>10 kg to <20 kg</td><td>600</td><td>600</td></tr>
<tr><td>20 kg to <30 kg</td><td>900</td><td>2,100</td><td rowspan="2">Every 8 weeks</td></tr>
<tr><td>30 kg to <40 kg</td><td>1,200</td><td>2,700</td></tr>
<tr><td rowspan="3">PNH, aHUS, gMG, or NMOSD</td><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>
<u>Switch Therapy from Eculizumab:</u>
• At the time of the next scheduled eculizumab dose, provide the weight-based ravulizumab loading dose instead (using the dosing table above)
• 2 weeks after the ravulizumab loading dose was given, begin the first weight-based ravulizumab maintenance dose (using the dosing table above)
</td></tr>
<tr><td colspan="2">* For supplemental dose therapy after plasma exchange (PE), plasmapheresis (PP), and intravenous immunoglobulin (IVIg), please refer to the ravulizumab package insert for appropriate dosing.</td></tr>
</table>

VI. 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 300 mg/30 mL single-dose vial for injection: 25682-0022-xx**
- Ultomiris 1,100 mg/11 mL single-dose vial for injection: 25682-0028-xx

***Note: This NDC has been discontinued as of 06/11/2021.*

VII. References

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14. Shah N, Bhatt H. Paroxysmal nocturnal hemoglobinuria. StatPearls - NCBI Bookshelf. Published July 31, 2023. https://www.ncbi.nlm.nih.gov/books/NBK562292/.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D59.32	Hereditary hemolytic-uremic syndrome
D59.39	Other hemolytic-uremic syndrome
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
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 (applicable to existing NCD/LCA/LCD): N/A

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,	Noridian Healthcare Solutions, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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