Ultomiris® (ravulizumab-cwvz)
(Intravenous)

I. Length of Authorization
Coverage will be provided for twelve months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:
   - Ultomiris 10 mg/mL** – 30 mL SDV: 10 vials on day zero followed by 13 vials starting on day 14 and every 8 weeks thereafter
   - Ultomiris 100 mg/mL – 3 mL SDV: 10 vials on day zero followed by 13 vials starting on day 14 and every 8 weeks thereafter
   - Ultomiris 100 mg/mL – 11 mL SDV: 3 vials on day zero followed by 3 vials starting on day 14 and every 8 weeks thereafter

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Loading Dose Units</th>
<th>Maintenance Dose Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNH/aHUS</td>
<td>300 units on Day 0</td>
<td>360 units on Day 14 and every 8 weeks thereafter</td>
</tr>
</tbody>
</table>

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 1 month of age; **AND**
- Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of therapy. *(If urgent Ultomiris therapy is indicated in an unvaccinated patient, administer meningococcal vaccine(s) as soon as possible and provide patients with two weeks of antibacterial drug prophylaxis.); **AND**
Universal Criteria 

- Prescriber is enrolled in the Ultomiris Risk Evaluation and Mitigation Strategy (REMS) program; 
  AND 
- Confirmation that the patient will revaccinated with the meningococcal vaccine according to current medical guidelines for vaccine use; 
  AND 
- Will not be used in combination with other complement-inhibitor therapy (i.e., eculizumab); 
  AND 

Paroxysmal Nocturnal Hemoglobinuria (PNH) † 

- Used as Soliris switch therapy (please refer to Section IV for the pertinent renewal criteria); OR 
  - Diagnosis must be accompanied by detection of PNH clones of at least 5% by flow cytometry diagnostic testing; 
    AND 
  - Demonstrate the presence of at least 2 different glycosylphosphatidylinositol (GPI) protein deficiencies (e.g., CD55, CD59, etc.) within at least 2 different cell lines (granulocytes, monocytes, erythrocytes); 
    AND 
  - Patient has one of the following indications for therapy: 
    ▪ Presence of a thrombotic event 
    ▪ Presence of organ damage secondary to chronic hemolysis 
    ▪ Patient is pregnant and potential benefit outweighs potential fetal risk 
    ▪ Patient is transfusion dependent 
    ▪ Patient has high LDH activity (defined as ≥1.5 x ULN) with clinical symptoms; 
      AND 
  - Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, and packed RBC transfusion requirement 

Atypical Hemolytic Uremic Syndrome (aHUS) † 

- Used as Soliris switch therapy (please refer to Section IV for the pertinent renewal criteria); OR 
  - Patient shows signs of thrombotic microangiopathy (TMA) (e.g., changes in mental status, seizures, angina, dyspnea, thrombosis, increasing blood pressure, decreased platelet count, increased serum creatinine, increased LDH, etc.); 
    AND 
  - Thrombotic Thrombocytopenic Purpura (TTP) has been ruled out by evaluating ADAMTS-13 level (ADAMTS-13 activity level > 10%); 
    AND 
  - Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) has been ruled out; 
    AND
Other causes have been ruled out such as coexisting diseases or conditions (e.g., bone marrow transplantation, solid organ transplantation, malignancy, autoimmune disorder, drug-induced, etc.) or known genetic defect in cobalamin C metabolism; **AND**

Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), serum creatinine/eGFR, platelet count, and dialysis requirement

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

### IV. Renewal Criteria

Coverage may be renewed based upon the following criteria:

- Used as switch therapy, for a diagnosis of PNH or aHUS, if a patient has shown a beneficial disease response and absence of unacceptable toxicity while on Soliris; **OR**
- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
  - Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious meningococcal infections (septicemia and/or meningitis), infusion-related reactions, other serious infections (i.e. *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria gonorrhoeae*), thrombotic microangiopathy (TMA) complications, etc.; **AND**
  - Disease response indicated by one or more of the following:
    - **PNH**<sup>1,4,8</sup>
      - Decrease in serum LDH from pretreatment baseline
      - Stabilization/improvement in hemoglobin level from pretreatment baseline
      - Decrease in packed RBC transfusion requirement from pretreatment baseline
    - **aHUS**<sup>1,5,7</sup>
      - Decrease in serum LDH from pretreatment baseline
      - Stabilization/improvement in serum creatinine/eGFR from pretreatment baseline
      - Increase in platelet count from pretreatment baseline
      - Patient no longer requires dialysis treatments
V. Dosage/Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal nocturnal hemoglobinuria (PNH) &amp; Atypical Hemolytic Uremic Syndrome (aHUS)</td>
<td>Complement-Inhibitor Therapy Naïve*&lt;br&gt;Administer the 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)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body Weight Range</th>
<th>Loading Dose (mg)</th>
<th>Maintenance Dose (mg)</th>
<th>Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5 kg - &lt;10 kg</td>
<td>600</td>
<td>300</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td>≥10 kg - &lt;20 kg</td>
<td>600</td>
<td>600</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td>≥20 kg - &lt;30 kg</td>
<td>900</td>
<td>2,100</td>
<td>Every 8 weeks</td>
</tr>
<tr>
<td>≥30 kg - &lt;40 kg</td>
<td>1,200</td>
<td>2,700</td>
<td>Every 8 weeks</td>
</tr>
<tr>
<td>≥40 kg - &lt;60 kg</td>
<td>2,400</td>
<td>3,000</td>
<td>Every 8 weeks</td>
</tr>
<tr>
<td>≥60 kg - &lt;100 kg</td>
<td>2,700</td>
<td>3,300</td>
<td>Every 8 weeks</td>
</tr>
<tr>
<td>≥100 kg</td>
<td>3,000</td>
<td>3,600</td>
<td>Every 8 weeks</td>
</tr>
</tbody>
</table>

*Note: for Soliris switch therapy please refer to the package insert for appropriate switch dosing.

VI. Billing Code/Availability Information

HCPCS Code:
- J1303 – Injection, ravulizumab-cwvz, 10 mg; 1 billable unit = 10 mg

NDC:
- Ultomiris 300 mg/3 mL single-use vials for injection: 25682-0025-xx
- Ultomiris 300 mg/30 mL single-use vials for injection: 25682-0022-xx**
- Ultomiris 1100 mg/11 mL single-use vials for injection: 25682-0028-xx

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

VII. References


Appendix 1 – Covered Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D59.3</td>
<td>Hemolytic-uremic syndrome</td>
</tr>
<tr>
<td>D59.5</td>
<td>Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]</td>
</tr>
</tbody>
</table>

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

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 Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

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