Ultomiris (ravulizumab-cwvz) will be considered for coverage when the following criteria are met:

**Atypical Hemolytic Uremic Syndrome (aHUS)**

For **initial** authorization:

1. Medication is prescribed by or in consultation with a hematologist or nephrologist; AND
2. Member has a diagnosis of aHUS supported by ALL of the following:
   a) Thrombocytopenia (platelet count < 150 x 10⁹/L),
   b) Evidence of hemolysis i.e. elevated lactate dehydrogenase (LDH), low haptoglobin count, or presence of fragmented red blood cells or schistocytes on blood smear,
   c) Evidence of renal impairment (e.g. raised SCr or low eGFR); AND
3. Shiga toxin-producing E. coli related HUS (STEC-HUS) has been ruled out; AND
4. ADAMTS13 activity level is > 5% (to rule out TTP); AND
5. Member has received meningococcal vaccine.

6. **Dosage allowed/Quantity limit:**
   - IV infusion: loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.
   - Subcutaneous (adults only): 490 mg once weekly (8 cartons per 28 days)

**If all the above requirements are met, the medication will be approved for 6 months.**

For **reauthorization**:

1. Chart notes must demonstrate hematologic normalization as evidenced by increased platelet count or LDH maintained below upper limit of normal; AND
2. Improved or preserved kidney function.

**If all the above requirements are met, the medication will be approved for an additional 12 months.**

**Paroxysmal Nocturnal Hemoglobinuria (PNH)**
For initial authorization:
1. Medication is prescribed by or in consultation with a hematologist; AND
2. Member has a diagnosis of PNH as confirmed by flow cytometry; AND
3. Member has a lactate dehydrogenase (LDH) level >1.5x upper limit of normal (ULN); AND
4. Member has received meningococcal vaccine.
5. **Dosage allowed/Quantity limit:**
   - IV infusion: loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.
   - Subcutaneous (adults only): 490 mg once weekly (8 cartons per 28 days).

*If all the above requirements are met, the medication will be approved for 6 months.*

For reauthorization:
1. Clinical evidence of positive response to therapy such as increased hemoglobin level, decreased need for transfusions, normalized LDH levels, improved fatigue.

*If all the above requirements are met, the medication will be approved for an additional 12 months.*

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**Generalized Myasthenia Gravis (gMG)**

For initial authorization:
1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a neurologist; AND
3. Member has a documented diagnosis of MGFA class II-IV myasthenia gravis (see appendix 2); AND
4. Lab result in chart notes shows the member is seropositive for AChR antibodies; AND
5. Member has tried and failed at least 1 conventional therapy for at least 3 months (e.g., pyridostigmine, corticosteroid, azathioprine, mycophenolate mofetil); AND
6. Member has received meningococcal vaccine.
7. **Dosage allowed/Quantity limit:** Administered by IV infusion; loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.

*If all the above requirements are met, the medication will be approved for 6 months.*

For reauthorization:
1. Chart notes must document clinically meaningful improvement in symptom severity and daily functioning compared to pre-treatment baseline (e.g., improved MG-ADL or QMG scores).

*If all the above requirements are met, the medication will be approved for an additional 12 months.*

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CareSource considers Ultomiris (ravulizumab-cwvz) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

<table>
<thead>
<tr>
<th>DATE</th>
<th>ACTION/DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/07/2019</td>
<td>New policy for Ultomiris created.</td>
</tr>
<tr>
<td>10/26/2019</td>
<td>New diagnosis of aHUS added.</td>
</tr>
<tr>
<td>06/03/2021</td>
<td>aHUS: Updated references. Added specialist requirement. Revised diagnostic parameters. Summarized excluded causes. Removed list of restrictions from clinical trials. Revised renewal criteria.</td>
</tr>
</tbody>
</table>
PNH: Updated references. Removed nephrology as specialist. Removed transfusion and organ damage requirements. Updated dosing information. Reduced initial approval duration from 12 months to 6 months. Revised renewal criteria.

05/19/2022 Diagnosis of myasthenia gravis added.

08/12/2022 Added dosing for new subQ product (adults with PNH or aHUS only); added pharmacy benefit.

APPENDIX 1:

Table 1: ULTOMIRIS Weight-Based Dosing Regimen – PNH, aHUS, and gMG*

<table>
<thead>
<tr>
<th>Indications</th>
<th>Body Weight Range (kg)</th>
<th>Loading Dose (mg)</th>
<th>Maintenance Dose (mg) and Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNH and aHUS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 to less than 10</td>
<td>600</td>
<td>300</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td>10 to less than 20</td>
<td>600</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>20 to less than 30</td>
<td>900</td>
<td>2,100</td>
<td></td>
</tr>
<tr>
<td>30 to less than 40</td>
<td>1,200</td>
<td>2,700</td>
<td></td>
</tr>
<tr>
<td>40 to less than 60</td>
<td>2,400</td>
<td>3,000</td>
<td></td>
</tr>
<tr>
<td>60 to less than 100</td>
<td>2,700</td>
<td>3,300</td>
<td></td>
</tr>
<tr>
<td>100 or greater</td>
<td>3,000</td>
<td>3,600</td>
<td></td>
</tr>
<tr>
<td>PNH, aHUS, and gMG</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

APPENDIX 2:

MG Foundation of America (MGFA) Clinical Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>any ocular weakness; all other muscle strength is normal</td>
</tr>
<tr>
<td>II</td>
<td>mild weakness affecting other than ocular muscles; may also have ocular weakness at any level</td>
</tr>
<tr>
<td>III</td>
<td>moderate weakness affecting other than ocular muscles; may also have ocular weakness at any level</td>
</tr>
<tr>
<td>IV</td>
<td>severe weakness affecting other than ocular muscles; may also have ocular weakness at any level</td>
</tr>
<tr>
<td>V</td>
<td>defined by intubation, with or without mechanical ventilation</td>
</tr>
</tbody>
</table>

References:


Effective date: 01/01/2023
Revised date: 08/12/2022