RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	ravulizumab-cwvz
Policy Number:	RxA.289
Drug(s) Applied:	Ultomiris®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of Business

Background

Ravulizuamb-cwvz (Ultomiris®) is a complement inhibitor. It is indicated for:

- the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH);
- the treatment of adults and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

Limitations of Use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Dosing Information

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Ravulizumab-cwvz (Ultomiris®)</td><td>PNH</td><td>
<table>
<tr><th rowspan="2">Body Weight Range (kg)</th><th colspan="2">Weight-Based Dosing Regimen</th><th rowspan="2">Maintenance Interval</th></tr>
<tr><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th></tr>
<tr><td>≥ 40 to < 60</td><td>2400</td><td>3000</td><td rowspan="3">Every 8 weeks</td></tr>
<tr><td>≥ 60 to < 100</td><td>2700</td><td>3300</td></tr>
<tr><td>≥ 100</td><td>3000</td><td>3600</td></tr>
</table>

For patients switching from eculizumab to Ultomiris, administer the loading dose of Ultomiris IV 2 weeks after the last eculizumab infusion, and then administer maintenance doses IV once every 8 weeks, starting 2 weeks after loading dose administration.
</td><td>3,600 mg/ 8 weeks</td></tr>
</table>

Dosing Information

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Ravulizumab-cwvz (Ultomiris®)</td><td>aHUS</td><td>
<table>
<tr><th rowspan="2">Body Weight Range (kg)</th><th colspan="2">Weight-Based Dosing Regimen</th><th rowspan="2">Maintenance Interval</th></tr>
<tr><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th></tr>
<tr><td>≥ 5 to 10</td><td>600</td><td>300</td><td rowspan="2">Every 4 weeks</td></tr>
<tr><td>≥ 10 to < 20</td><td>600</td><td>600</td></tr>
<tr><td>≥ 20 to < 30</td><td>900</td><td>2100</td><td rowspan="5">Every 8 weeks</td></tr>
<tr><td>≥ 30 to < 40</td><td>1200</td><td>2700</td></tr>
<tr><td>≥ 40 to < 60</td><td>2400</td><td>3000</td></tr>
<tr><td>≥ 60 to < 100</td><td>2700</td><td>3300</td></tr>
<tr><td>≥ 100</td><td>3000</td><td>3600</td></tr>
</table>
For patients switching from eculizumab to Ultomiris, administer the loading dose of Ultomiris IV 2 weeks after the last eculizumab infusion, and then administer maintenance doses IV once every 8 weeks, starting 2 weeks after loading dose administration.
</td><td>3,600 mg/ 8 weeks</td></tr>
</table>

Dosage Forms

- Single-dose vial: 300 mg/30 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Flow cytometry shows detectable GPI-deficient hematopoietic clones or ≥ 5% PNH cells;
5. Member meets one of the following (a or b):

a. History of ≥ 1 red blood cell transfusion in the past 24 months and (i or ii):
   i. Documentation of hemoglobin < 7 g/dL in members without anemia symptoms;
   ii. Documentation of hemoglobin < 9 g/dL in members with anemia symptoms;
b. History of thrombosis;

6. Dose does not exceed (a, b, and c):
   a. Loading dose on Day 1 (i, ii, or iii):
      i. Weight ≥ 4 to < 60 kg: 2,400 mg;
      ii. Weight ≥ 60 to < 100 kg: 2,700 mg;
      iii. Weight ≥ 100 kg: 3,000 mg;
   b. If member is switching therapy from Soliris®, administration of the loading dose should occur 2 weeks after the last Soliris infusion;
   c. Maintenance dose on Day 15 and every 8 weeks thereafter (i, ii, or iii):
      i. Weight ≥ 40 to < 60 kg: 3,000 mg;
      ii. Weight ≥ 60 to < 100 kg: 3,300 mg;
      iii. Weight ≥ 100 kg: 3,600 mg.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

B. Atypical Hemolytic Uremic Syndrome (must meet all):
1. Diagnosis of aHUS;
2. Prescribed by or in consultation with a nephrologist or hematologist;
3. Age ≥ 1 month;
4. Documentation that patient does not have Shiga toxin E.coli infection
5. Documentation that patient does not have ADAMTS13 deficiency
6. Meets all of the following (a, b, and c):
   a. If member is switching therapy from Soliris®, administration of the loading dose should occur 2 weeks after the last Soliris infusion;
   b. Loading dose (Day 1) does not exceed the weight based loading dose in the Dosing Information table;
   c. Maintenance dose (Day 15 and every 4 or 8 weeks thereafter) does not exceed the weight based maintenance dose in the Dosing Information table;

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters:
   a. Improved measures of intravascular hemolysis (e.g., normalization of lactate dehydrogenase [LDH]);
   b. Reduced need for red blood cell transfusions;

c. Increased or stabilization of hemoglobin levels;
d. Less fatigue;
e. Improved health-related quality of life;
f. Fewer thrombotic events.

3. If request is for a dose increase, new dose does not exceed one of the following every 8 weeks (a, b, or c):

a. Weight ≥ 40 to < 60 kg: 3,000 mg;
b. Weight ≥ 60 to < 100 kg: 3,300 mg;
c. Weight ≥ 100 kg: 3,600mg.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

B. Atypical Hemolytic Uremic Syndrome (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by one of the following parameters (a, b, c, d, or e):

a. Increase in Platelet count;
b. decrease in serum creatinine;
c. decrease in serum LDH;
d. Reduced need for red blood cell transfusions;
e. Reduced need for dialysis

3. If request is for a dose increase, new dose does not exceed the weight based maintenance dose in the Dosing Information table;

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GPI: glycosyl phosphatidylinositol
PNH: paroxysmal nocturnal hemoglobinuria
aHUS: atypical hemolyticuremic syndrome
TMA: thrombotic microangiopathy
STEC-HUS: Shiga toxin E. coli related hemolytic uremic syndrome
ADAMTS13: a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

  - Unresolved *Neisseria Meningitidis* infection
- Boxed Warning(s):
  - Serious meningococcal infections

APPENDIX D: General Information

- Ultomiris is only available through a REMS (Risk Evaluation and Mitigation Strategy) program due to the risk of life-threatening and fatal meningococcal infection. Patients should be vaccinated with a meningococcal vaccine at least 2 weeks prior to receiving the first dose of Ultomiris and revaccinated according to current medical guidelines for vaccine use. Patients should be monitored for early signs of meningococcal infections, evaluated immediately if infection is suspected, and treated with antibiotics if necessary.
- Examples of symptoms of anemia include but are not limited to: dizziness or lightheadedness, fatigue, pale or yellowish skin, shortness of breath, chest pain, cold hands and feet, and headache.

References

1. Ultomiris Prescribing Information. Boston, MA: Alexion Pharmaceuticals, Inc.; October 2019. Available at: www.ultomiris.com. Accessed July 3, 2020.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005; 106(12):3699-3709. doi:10.1182/blood-2005-04-1717.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. Background was updated: Limitations of Use and new Indication (aHUS) were added. 4. Dosing Information: aHUS dosing information was added. 5. PNH approval duration updated to specify Medicaid, HIM and Commercial approval durations. 6. Criteria for aHUS was added. 7. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." in PNH and Continued Therapy criteria was added for aHUS. 8. APPENDIX A was updated to included TMA, aHUS, STEC-HUS. 9. APPENDIX C Boxed Warnings was updated.	07/03/2020	09/14/2020

10. References were updated.		