Because of the specialized skills required for evaluation and diagnosis of patients treated with Ultomiris as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Ultomiris to be prescribed by or in consultation with a physician who specializes in the condition being treated. Initial approvals are provided for a duration of 6 months and extended approvals for patients currently receiving Ultomiris are provided for a duration of 12 months.

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for ravulizumab-cwvz (Ultomiris) include: history and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service.

BACKGROUND

Ravulizumab-cwvz is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a (the proinflammatory anaphylatoxin) and C5b (the initiating subunit of the terminal complement complex [C5b-9]) and preventing the generation of the terminal complement complex C5b9. ULTOMIRIS inhibits terminal complement-mediated intravascular hemolysis in patients with PNH and complement-mediated thrombotic microangiopathy (TMA) in patients with aHUS.¹

Ultomiris has a Boxed Warning regarding life-threatening and fatal meningococcal infections.¹ Meningococcal infections have occurred in patients receiving Ultomiris and may become rapidly life-threatening or fatal if not recognized and treated early. Ultomiris is contraindicated in patients with unresolved serious Neisseria meningitidis infection. Ultomiris has a Risk Evaluation and Mitigation Strategy (REMS) program to mitigate the occurrence and morbidity associated with meningococcal infections. The REMS program also educates healthcare professionals and patients regarding the increased risk of meningococcal infections with Ultomiris, the early signs of invasive meningococcal infections, and the need for immediate medical evaluation of signs and symptoms consistent with possible meningococcal infections.

DEFINITIONS

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product.
INDICATIONS/Criteria

<table>
<thead>
<tr>
<th>Medicaid Members</th>
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<td>Step-utilization of Part D drugs not required.</td>
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FDA-Approved Indications

1. **Atypical hemolytic uremic syndrome (aHUS).**

   **Criteria.** *Ultomiris is approved for the duration noted if the patient meets ONE of the following (A OR B):*

   A) **Initial therapy:** Approval duration of Ultomiris is for 6 months if the patient meets the following criteria (i, ii, and iii)
      
      i. Patient is ≥ 1 month of age; AND
      
      ii. aHUS diagnosis confirmed with ruling out of Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS) and thrombotic thrombocytopenia purpura (TTP) (e.g., rule out ADAMTS13 deficiency); AND
      
      iii. Prescribed by or in consultation with a hematologist or nephrologist; OR

   B) **Patient is currently receiving Ultomiris:** Approval duration of Ultomiris is for 1 year if the patient is continuing to derive benefit (e.g., stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis) from Ultomiris, according to the prescribing physician.

   **Dosing.** Dosing must meet the following:

   - (20 to less than 30 kg) Loading, 900 mg IV infusion; maintenance, 2100 mg 2 weeks after loading dose then every 8 weeks
   - (30 to less than 40 kg) Loading, 1200 mg IV infusion; maintenance, 2700 mg 2 weeks after loading dose then every 8 weeks
   - (40 to less than 60 kg) Loading, 2400 mg IV infusion; maintenance, 3000 mg 2 weeks after loading dose then every 8 weeks
   - (60 to less than 100 kg) Loading, 2700 mg IV infusion; maintenance, 3300 mg 2 weeks after loading dose then every 8 weeks
   - (100 kg or greater) Loading, 3000 mg IV infusion; maintenance, 3600 mg 2 weeks after loading dose then every 8 weeks
   - Duration of therapy: At least 6 months; individualize treatment beyond 6 months
   - Switching from eculizumab, administer loading dose 2 weeks after last eculizumab infusion, then administer maintenance doses once every 8 weeks, starting 2 weeks after the loading dose
Duration of Therapy: Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).

2. Paroxysmal Nocturnal Hemoglobinuria (PNH).

Criteria. Ultomiris is approved for the duration noted if the patient meets ONE of the following (A OR B):

A) Initial therapy: Approval duration of Ultomiris is for 6 months if the patient meets the following criteria (i, ii, and iii):
   
i. Patient is ≥ 18 years of age; AND
   
ii. PNH diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins on at least two cell lineages; AND
   
iii. Ultomiris is being prescribed by or in consultation with a hematologist; OR

A) Patient is currently receiving Ultomiris: Approval duration of Ultomiris is for 1 year if the patient is continuing to derive benefit (e.g., stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis) from Ultomiris, according to the prescribing physician.

Dosing. Dosing must meet the following:

- (40 to less than 60 kg) Loading dose, 2400 mg IV infusion; begin maintenance dosing in 2 weeks
- (60 to less than 100 kg) Loading dose, 2700 mg IV infusion; begin maintenance dosing in 2 weeks
- (100 kg or greater) Loading dose, 3000 mg IV infusion; begin maintenance dosing in 2 weeks
- (40 to less than 60 kg) Maintenance dose, 3000 mg IV infusion every 8 weeks beginning 2 weeks after loading dose
- (60 to less than 100 kg) Maintenance dose, 3300 mg IV infusion every 8 weeks beginning 2 weeks after loading dose
- (100 kg or greater) Maintenance dose, Maintenance dose, 3600 mg IV infusion every 8 weeks beginning 2 weeks after loading dose
- Switching from eculizumab, administer loading dose 2 weeks after last eculizumab infusion, then administer maintenance doses once every 8 weeks, starting 2 weeks after the loading dose⁴

Duration of Therapy: Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).
SPECIAL CONSIDERATIONS
For patients switching from eculizumab to ULTOMIRIS, administer the loading dose of ULTOMIRIS 2 weeks after the last eculizumab infusion, and then administer maintenance doses once every 8 weeks or every 4 weeks (depending on body weight), starting 2 weeks after loading dose administration. Administration of PE/PI (plasmapheresis or plasma exchange, or fresh frozen plasma infusion) may reduce ULTOMIRIS serum levels. There is no experience with administration of supplemental doses of ULTOMIRIS.

LIMITATIONS/EXCLUSIONS
Please refer to a product line’s certificate of coverage for benefit limitations and exclusions for these services:

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<tr>
<th>PRODUCT LINE</th>
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Citations & References

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CFR
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Other Requirements
### NCQA Elements

### Revision History

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<tr>
<td>11/12/2019</td>
<td>New policy</td>
<td>Catherine Vu, PharmD</td>
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<tr>
<td>11/26/2019</td>
<td>Approval</td>
<td>UM Committee</td>
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