Ultomiris® (Ravulizumab-cwvz)

Ultomiris is a monoclonal antibody that binds with high affinity to complement protein C5, which inhibits its cleavage to C5a and C5b and prevents the generation of the terminal complement complex C5b9. As a result, Ultomiris inhibits terminal complement-mediated intravascular hemolysis in patients with paroxysmal nocturnal hemoglobinuria (PNH) and complement-mediated thrombotic microangiopathy (TMA) in patients with atypical hemolytic uremic syndrome (aHUS). It is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Ultomiris has a Boxed Warning for life-threatening meningococcal infections. Patients should be immunized with the meningococcal vaccines at least 2 weeks prior to administering the first dose of Ultomiris, unless the risks of delaying therapy outweigh the risks of developing meningococcal infection. In this case, patients should be provided with 2 weeks of antibacterial drug prophylaxis. Vaccination does not eliminate the risk of infection but reduces the chance. Patients should be immunized accordingly with meningococcal vaccination following most current ACIP guidelines. Ultimoris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Prescribers must be enrolled in the REMS program to prescribe Ultimoris.

Length of Authorization

Initial coverage will be provided for 6 months for aHUS and 12 months for PNH and it may be renewed.

Dosing Limits

Max Units (per dose and over time) [Medical Benefit]:

Medical Guideline Disclaimer

Property of EmblemHealth. All rights reserved. The treating physician or primary care provider must submit to EmblemHealth the clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request for prior authorization. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary. If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication. EmblemHealth Services Company LLC, (“EmblemHealth”) has adopted the herein policy in providing management, administrative and other services to HIP Health Plan of New York, HIP Insurance Company of New York, Group Health Incorporated, GHI HMO Select, ConnectiCare, Inc., ConnectiCare Insurance Company, Inc. ConnectiCare Benefits, Inc., and ConnectiCare of Massachusetts, Inc. related to health benefit plans offered by these entities. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.
Paroxysmal Nocturnal Hemoglobinuria
- Loading dose: 3000 mg on first day
- Maintenance dose: 3600 mg 2 weeks after and then every 8 weeks

Atypical Hemolytic Uremic Syndrome
- Loading dose:
  - Patients ≥5 to <20 kg: 600 mg
  - Patients ≥20 to <100 kg: 3000 mg
- Maintenance dose:
  - Patients ≥5 to <20 kg: 600 mg 2 weeks after and then every 4 weeks
  - Patients ≥20 to <100 kg: 3600 mg 2 weeks after and then every 8 weeks

I. INITIAL APPROVAL CRITERIA

Ultomiris may be considered medically necessary if the below condition is met AND use is consistent with the medical necessity criteria that follows:

1. Paroxysmal Nocturnal Hemoglobinuria (PNH)
   a. Patient is ≥ 18 years of age; AND 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
   b. At least 10% PNH type III red cells; AND
   c. Patient has an LDH level of 1.5 times the upper limit of the normal range; AND
   d. Patient has greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP) deficient polymorphonuclear cells (PMNs); AND
   e. Patient is transfusion dependent as defined by one of the following:
      i. Hemoglobin < 7 g/dL; OR
      ii. Hemoglobin < 9 g/dL AND patient is experiencing symptoms of anemia; AND
   f. Patient has symptoms of thromboembolic complications (abdominal pain, shortness of breath, chest pain, end organ damage; AND
   g. Patient will or has received a meningococcal vaccine at least two weeks before start Ultomiris treatment; AND
   h. Ultomiris is being prescribed by or in consultation with a hematologist, oncologist or immunology specialist.

2. Atypical Hemolytic Uremic Syndrome (aHUS)
   a. Patient is at least one month of age or older and weighs ≥5 kg; AND
   b. Documentation supporting the diagnosis of aHUS by ruling out both of the following:
      i. Shiga toxin E. coli-related hemolytic uremic syndrome (STEC-HUS)
      ii. Thrombotic thrombocytopenia purpura (TTP) (e.g., rule out ADAMTS13 deficiency); AND
c. Laboratory results, signs, and/or symptoms attributed to aHUS (e.g., thrombocytopenia, microangiopathic hemolysis, thrombotic microangiopathy, acute renal failure, etc.); AND  
d. Patient will or has received a meningococcal vaccine at least two weeks before start Ultomiris treatment; AND  
e. Prescribed by a hematologist or nephrologist.

Limitations/Exclusions

Ultomiris is not considered medically necessary for when any of the following selection criteria is met:

1) Patient is asymptomatic or has mild symptoms. Active surveillance is clinically appropriate, without the need for therapy in this subset of patients.

2) Patient has unresolved Neisseria meningitidis

Patient is currently not vaccinated against N. meningitidis, unless the risks of delaying treatment outweigh the risks of developing a meningococcal infection.

II. RENEWAL CRITERIA

- Patient has experienced an improvement in fatigue and quality of life; AND
- Patient has demonstrated a positive clinical response from baseline (e.g., stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis) from Ultomiris, according to the prescribing physician; AND

Dosage/Administration

For both PNH and aHUS, dosing schedule is allowed to occasionally vary within 7 days of the scheduled infusion day (except for the first maintenance dose of ULTOMIRIS); but the subsequent doses should be administered according to the original schedule.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Body Weight Range (kg)</th>
<th>Loading Dose (mg)</th>
<th>Maintenance Dosing (mg) and Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal Nocturnal Hemoglobinuria (PNH)</td>
<td>≥40 to &lt; 60</td>
<td>–</td>
<td>2,400 – 3,000</td>
</tr>
<tr>
<td>Maintenance doses are given 2 weeks after the loading dose and once every 8-week interval.</td>
<td>– ≥ 60 to &lt; 100</td>
<td>2,700</td>
<td>– 3,300</td>
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<tr>
<td></td>
<td>– ≥ 100</td>
<td>3,000</td>
<td>– 3,6000</td>
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<tr>
<td></td>
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<td></td>
<td>Every 8 weeks</td>
</tr>
</tbody>
</table>

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Atypical Hemolytic Uremic Syndrome (aHUS)</td>
<td>– ≥5 to &lt; 10</td>
<td>600</td>
<td>– 300</td>
</tr>
<tr>
<td></td>
<td>– ≥10 to &lt; 20</td>
<td>600</td>
<td>– 600</td>
</tr>
<tr>
<td></td>
<td>– ≥20 to &lt; 30</td>
<td>900</td>
<td>– 2,100</td>
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<td></td>
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<td></td>
<td>Every 4 weeks</td>
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<td>Every 8 weeks</td>
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</table>
Maintenance doses are given 2 weeks after the loading dose and once every 4- or 8-week interval.

### Applicable Procedure Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J1303</td>
<td>Effective 10/1/19, Injection, ravulizumab-cwvz, 10 mg</td>
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<tr>
<td>C9052</td>
<td>Injection, ravulizumab-cwvz, 10 mg</td>
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### Applicable NDCs

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>25682-0022-xx</td>
<td>Ravulizumab-cwvz (Ultomiris) 300 mg/30 mL Intravenous Solution</td>
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### Applicable Diagnosis Codes

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
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<tbody>
<tr>
<td>D59.5</td>
<td>Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]</td>
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### Revision History

<table>
<thead>
<tr>
<th>Date</th>
<th>Revision Details</th>
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</table>
| 10/28/2019 | - Ultomiris definition was expanded to include PI updates for PNH, TMA, aHUS. Added in Boxed warning, and REMS program.  
- Length of Authorization – updated Initial coverage will be provided for 6 months for aHUS and 12 months for PNH and it may be renewed.  
- Updated dosing per PI for PNH, aHUS  
  8/15/2019  Removed code J3590, added new code J1303, effective 10/1/19.  
  7/1/2019   Removed unclassified code C9399. Added new Code C9052  
  4/1/2019   New Policy                                                                                                                              |

### References