APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematopoietic stem cell disorder of the X chromosome. It is estimated that there are as many as 1 to 10 cases per million, however, it is thought that many cases go undiagnosed. The average age of onset is the thirties and males and females are equally affected. The most commonly experienced symptoms with PNH are those associated with hemolytic anemia including fatigue, jaundice, and discolored, red, pink or black urine. Some patients present with a thrombosis in an unusual location such as an abdominal or cerebral vein. Patients may also have symptoms related to increased smooth muscle tone such as dysphagia, abdominal pain, or erectile dysfunction. The patient may eventually develop renal insufficiency or pulmonary hypertension due to hemoglobinemia.

It is recommended that any patients with Coombs negative hemolytic anemia, aplastic anemia, refractory anemia, or unexplained thrombosis with cytopenias or hemolysis be screened for PNH. Autoimmune disorders should be ruled out as well any other causes of hemolysis. Tests for PNH include a complete blood count, a reticulocyte count, and review of a peripheral blood smear for red blood cell abnormalities. The patient will have haptoglobin, lactase dehydrogenase as well as direct and indirect bilirubin and Coombs testing. The patient will also need to have a urine test of hemoglobin and hemosiderin. If the patient’s results are consistent with DAT-negative intravascular, the doctor will do a flow cytometry test to confirm a diagnosis of PNH. Flow cytometry incubates peripheral blood cells with fluorescently-labeled monoclonal antibodies that bind to glycosylphosphatidylinositol (GPI) anchored proteins, which are reduced or absent on blood cells in PNH.

Ultomiris™ is a complement inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria approved by the FDA in 2018. The drug is administered as an intravenous infusion. Dosing is per a weight-based dosage regimen as follows:

<table>
<thead>
<tr>
<th>Body Weight Range (kg)</th>
<th>Loading Dose (mg)</th>
<th>Maintenance Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater or equal to 40 to less than 60</td>
<td>2,400</td>
<td>3,000</td>
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<tr>
<td>greater than or equal to 60 to less than 100</td>
<td>2,700</td>
<td>3,300</td>
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</tbody>
</table>

Ultomiris™

Policy Number: HS-282

Original Effective Date: 2/7/2019

Revised Date(s): 4/4/2019

WellCare of Kentucky

Ultomiris™

Policy Number: HS-282

Original Effective Date: 2/7/2019

Revised Date(s): 4/4/2019
ULTOMIRIS™ is contraindicated in patients with unresolved Neisseria Meningitidis infection and caution should be used when administering the drug to patients with any other systemic infection. The most frequently adverse drug reactions were upper respiratory infection and headache.²

POSITION STATEMENT

Applicable To:
☑ Medicaid – Kentucky

Exclusions

Initial authorization of Ultomiris™ is considered medically necessary and a covered benefit when all of the following criteria are met:

1. Member has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); AND,
2. Vaccinated against meningococcal infections within 3 years prior to, or at the time of, initiating therapy
   a. If Ultomiris™ is initiated less than 2 weeks after vaccination, patients must receive prophylactic antibiotics until 2 weeks after vaccination; AND,
3. Member has documented flow cytometry results demonstrating at least 5% PNH cells; AND,
4. Documentation includes submission of baseline complete blood count (CBC) (must include hemoglobin); AND,
5. Submission of baseline serum LDH; AND,
6. Documentation includes
   A. History of RBC transfusion; OR,
   B. History of thrombotic event; AND,
7. Therapy has been prescribed by a hematologist, oncologist, or immunology specialist; AND,
8. For patients previously treated with Soliris, must be treated with Soliris for at least 6 months; AND,
9. Initial authorization period is 6 months.

Continued authorization of Ultomiris™ is considered medically necessary and a covered benefit when all of the following criteria are met:

1. Member has a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); AND,
2. Member has demonstrated adequate treatment response documented by one or more of the following:
   A. Improvement/normalization in hemoglobin levels from pre-treatment baseline; OR,
   B. Decrease in serum LDH level from pre-treatment baseline; OR,
   C. Decrease in need for RBC transfusion from pre-treatment baseline; AND,
3. Reauthorization period is 12 months.

CODING

Covered HCPCS Codes
C9399 Unclassified drugs or biologicals
J3490 Unclassified drugs
J3590 Unclassified biologics

Covered ICD-10 Code
D59.5 Paroxysmal nocturnal hemoglobinuria

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal/state laws.

REFERENCES

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>4/4/2019</td>
<td>Approved by MPC. Updated criteria with vaccine schedule.</td>
</tr>
<tr>
<td>2/7/2019</td>
<td>Approved by MPC. New.</td>
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