



Missouri Care

'Ohana Health Plan, a plan offered by WellCare Health Insurance of Arizona

Staywell of Florida

Children's Medical Services Health Plan (CMS Health Plan)

WellCare (Alabama, Arizona, Arkansas, California, Connecticut, Florida, Georgia, Illinois, Indiana, Louisiana, Maine, Michigan, Mississippi, Missouri, New Hampshire, New Jersey, New York, North Carolina, Ohio, South Carolina, Tennessee, Texas, Washington)

WellCare Heritage Health

WellCare Prescription Insurance

WellCare TexanPlus (Medicare – Dallas & Houston markets)

Ultomiris™

Policy Number: HS-282

Original Effective Date: 2/7/2019

Revised Date(s): 4/4/2019, 11/7/2019

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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.¹ 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

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Original Effective Date: 2/7/2019 - Revised: 4/4/2019, 11/7/2019

PRO_50510E Internal/State Approved 04102020

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dysphagia, abdominal pain, or erectile dysfunction. The patient may eventually develop renal insufficiency or pulmonary hypertension due to hemoglobinemia.¹

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 as 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.¹

Atypical hemolytic uremic syndrome (aHUS) is a rare genetic disease that occurs in approximately 1 in 500,000 people per year in the United States⁴. Although this disease is caused by gene mutations, the inheritance pattern is sporadic⁴. These mutated genes cause less immune responding proteins to be created, which compromises the complement system. Therefore, the immune system loses the ability to accurately identify healthy cells from foreign bodies. This leads the immune system to target the cells that line blood vessels in the kidney, which form clots that restrict blood flow. This disease state is characterized by the presence of hemolytic anemia, thrombocytopenia, and kidney failure.

In 2018 the FDA approved Ultomiris™, a complement inhibitor, for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria. The drug is administered as an intravenous infusion. Dosing is per a weight-based dosage regimen as follows:²

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg)
greater or equal to 40 to less than 60	2,400	3,000
greater than or equal to 60 to less than 100	2,700	3,300
greater than or equal to 100	3,000	3,600

Ultomiris™ was approved by the FDA in 2019 for the treatment of atypical hemolytic uremic syndrome (aHUS) in pediatric patients over one month of age and adult patients. Before beginning Ultomiris™, a baseline serum creatine, LDH, and platelet count are necessary for diagnosis and monitoring throughout therapy. The dosing for this medication is based on weight seen below.

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Dosing Interval
Greater than or equal to 5 to less than 10	600	300
Greater than or equal to 10 to less than 20	600	600
Greater than or equal to 20 to less than 30	900	2100
Greater than or equal to 30 to less than 40	1200	2700
Greater than or equal to 40 to less than 60	2400	3000
Greater than or equal to 60 to less than 100	2700	3300
Greater than or equal to 100	3000	3600

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 – All Markets (excluding KY)
- Medicare – All Markets (excluding KY)
- Children's Medical Services Health Plan (CHIP)

Exclusions

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.

Coverage

Initial Authorization

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) or atypical hemolytic uremic syndrome (aHUS); **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. One of the following applies to the member:
 - A. Member has PNH and has documented flow cytometry results demonstrating at least 5% PNH cells; **OR**,
 - B. Member has aHUS and has documented serum creatinine levels above the upper limits of normal **or** requires dialysis and platelet count is less than $150 \times 10^9/L$; **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

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) or atypical hemolytic uremic syndrome (aHUS); **AND**,
2. Member has demonstrated adequate treatment response documented by one or more of the following:
 - A. PNH Members:
 - i. Improvement/normalization in hemoglobin levels from pre-treatment baseline;
 - ii. Decrease in serum LDH level from pre-treatment baseline;

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- iii. Decrease in need for RBC transfusion from pre-treatment baseline;
- B. aHUS Members
 - i. Decrease in serum LDH level from pre-treatment baseline;
 - ii. Improvement of platelet count;
 - iii. Improvement of serum creatinine from baseline
- 3. Reauthorization period is 12 months.

CODING

Covered HCPCS Codes

J1303 Injection, ravulizumab-cwvz, 10 mg

Covered ICD-10 Code

D59.3 Hemolytic-uremic syndrome

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

1. Brodsky, R.A. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria. UpToDate Web site https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-paroxysmal-nocturnal-hemoglobinuria?source=see_link. Published November 13, 2017. Accessed January 10, 2019.
2. Ultomiris. [package insert]. Alexion Pharmaceuticals Inc. Boston, MA. December 2018.
3. Röth A, Rottinghaus ST, Hill A, et al. Ravulizumab (ALXN1210) in patients with paroxysmal nocturnal hemoglobinuria: results of 2 phase 1b/2 studies. Blood Adv. 2018;2(17):2176-2185.
4. Noris M, Remuzzi G. Hemolytic Uremic Syndrome. JASN April 2005; 16(4): 1035-1050.

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

Date	Action
11/7/2019	<ul style="list-style-type: none"> • Approved by MPC. Added indication for aHUS.
4/4/2019	<ul style="list-style-type: none"> • Approved by MPC. Updated criteria with vaccine schedule.
2/7/2019	<ul style="list-style-type: none"> • Approved by MPC. New.