Policy Title:	Ultomiris (ravulizumab-cwvz)		
		Department:	PHA
Effective Date:	12/04/2019		
Review Date:	12/04/2019		
Revision Date:	12/04/2019		

Purpose: To support safe, effective and appropriate use of Ultomiris (ravulizumab-cwvz).

Scope: Medicaid, Exchange, Medicare-Medicaid Plan (MMP)

Policy Statement:

Ultomiris (ravulizumab-cwvz) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Ultomiris (ravulizumab-cwvz) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria:

- Patient does not have a systemic infection; AND
- Patients must be administered a meningococcal vaccine at least two weeks prior to initiation of therapy and revaccinated according to current medical guidelines for vaccine use; AND
- Will not be used in combination with other complement-inhibitor therapy (i.e., eculizumab); AND

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Patient is 18 years or older; AND
- Prescribed by a hematologist or oncologist; AND
- Diagnosis must be accompanied by detection of PNH clones of at least 5% by flow cytometry diagnostic testing; AND
    - Demonstrate the presence of at least 2 different glycosylphosphatidylinositol (GPI) protein deficiencies (e.g. CD55, CD59, etc.) within at least 2 different cell lines (granulocytes, monocytes, erythrocytes); AND
- Laboratory results, signs, and/or symptoms attributed to PNH (e.g., abdominal pain, anemia, dyspnea, extreme fatigue, smooth muscle dystonia, unexplained/unusual thrombosis, hemolysis/hemoglobinuria, kidney disease, pulmonary hypertension, etc.); AND
- Patient has one of the following indications for therapy:

- Presence of a thrombotic event
- Presence of organ damage secondary to chronic hemolysis
- Patient is pregnant and potential benefit outweighs potential fetal risk
- Patient is transfusion dependent
- Patient has high LDH activity (defined as ≥1.5 x ULN) with clinical symptoms; AND

- Documented baseline values for one or more of the following (necessary for renewal): serum lactate dehydrogenase (LDH), hemoglobin level, and packed RBC transfusion requirement; AND
- Ultomiris is dosed according to the US FDA labeled dosing for PNH

Atypical hemolytic uremic syndrome (aHUS)

- Prescribed by a hematologist or nephrologist;
- Laboratory results, signs, and/or symptoms attributed to aHUS (e.g., thrombocytopenia, microangiopathic hemolysis, thrombotic microangiopathy, acute renal failure, etc.); AND
- Patient has a confirmed diagnosis of aHUS as evidenced by all of the following:
  - Diagnosis of thrombocytopenic purpura (TTP) has been excluded (i.e. normal ADAMTS 13 activity) OR a trail of plasma exchange did not result in clinical improvement;
  - Absence of Shiga toxin- producing Escherichia Coli (E.coli) infection; AND
- Ultomiris is dosed according to US FDA labeled dosing for aHUS

Continuation of Therapy Criteria:

- Patients continues to meet initial criteria; AND
- Patient is tolerating medications; AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: serious meningococcal infections (septicemia and/or meningitis), infusion reactions, serious infections, thrombotic microangiopathy complications (TMA), etc.; AND
- Disease response indicated by one or more of the following:

PNH:

- Prescribed by a hematologist or oncologist; AND
- Decrease in serum LDH from pretreatment baseline; OR
- Stabilization/improvement in hemoglobin level from pretreatment baseline; OR
- Decrease in packed RBC transfusion requirement from pretreatment baseline

aHUS:

- Prescribed by a hematologist or nephrologist; AND
- Documentation demonstrating a positive clinical response from baseline (e.g., reduction of plasma exchanges, reduction of dialysis, increased platelet count, reduction of hemolysis)

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable.***

Dosage/Administration:

<table>
<tr><th>Indication</th><th>Dose</th><th>Maximum dose (1 billable unit = 10 mg)</th></tr>
<tr><td>PNH</td><td>Administer the loading dose based on weight. Two weeks later, begin maintenance doses at a once every 8-week interval:
<table>
<tr><th>Body weight range</th><th>Loading dose</th><th>Maintenance dose</th></tr>
<tr><td>≥40 kg - <60kg</td><td>2400 mg</td><td>3000mg</td></tr>
<tr><td>≥60 kg - <100kg</td><td>2700mg</td><td>3300mg</td></tr>
<tr><td>≥100 kg</td><td>3000mg</td><td>3600mg</td></tr>
</table></td><td>Loading doses:
3000mg (300 units) on day 0
Maintenance Dose:
3600mg (360 units) on day 14 and every 8 weeks thereafter</td></tr>
<tr><td>aHUS</td><td>Administer the loading dose based on weight. Two weeks later, begin maintenance doses at a once every 8-weeks or every 4 weeks:
<table>
<tr><th>Body weight range</th><th>Loading dose</th><th>Maintenance dose and dosing interval</th></tr>
<tr><td>≥5 - <10kg</td><td>600mg</td><td>300mg every 4 weeks</td></tr>
<tr><td>≥10kg - <20kg</td><td>600mg</td><td>600mg every 4 weeks</td></tr>
<tr><td>≥20 - <30kg</td><td>900mg</td><td>2100mg every 8 weeks</td></tr>
<tr><td>≥30 - <40kg</td><td>1200mg</td><td>2700mg every 8 weeks</td></tr>
<tr><td>≥40- <60kg</td><td>2400mg</td><td>3,000mg every 8 weeks</td></tr>
<tr><td>≥60 - <100kg</td><td>2700mg</td><td>3300mg every 8 weeks</td></tr>
<tr><td>≥100kg</td><td>3000mg</td><td>3,600mg every 8 weeks</td></tr>
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3000mg (300 units) on day 0
Maintenance Dose:
3600mg (360 units) on day 14 and every 8 weeks thereafter</td></tr>
</table>

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J1303	Injection, ravulizumab-cwvz, 10mg

References:

1. Ultomiris [package insert]. New Haven, CT: Alexion Pharmaceuticals, Inc.; October 2017.
2. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. Published online: April 11, 2015.
3. Parker CJ. Management of paroxysmal nocturnal hemoglobulinuria in the era of complement inhibitory therapy. *Hematology*. 2011; 21-29.
4. Sanders D, Wolfe G, Benatar M et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016; 87 (4):419-425.
5. Jaretzki A, Barohn RJ, Ernstoff RM et al. Myasthenia Gravis: Recommendations for Clinical Research Standards. *Ann Thorac Surg*. 2000;70: 327-34.
6. Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *NEJM*. 2006;335:1233-43.
7. Howard JF, Utsugisawa K, Benatar M. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (REGAIN); a phase 3, randomized, double-blind, placebo-controlled, multicenter study. *Lancet Neurol*. 2017 Oct 20. http://dx.doi.org/10.1016/S1474-4422(17)30369-1Ingenix HCPCS Level II, Expert 2011.