Clinical Policy: Ravulizumab-cwvz (Ultomiris)

Reference Number: LA.PHAR.415
Effective Date: 05.07.22
Last Review Date: ~~06.23~~04.29.24 Coding Implications
Line of Business: Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description
Ravulizumab-cwvz (Ultomiris®) is a complement inhibitor.

FDA Approved Indication(s)
Ultomiris is indicated for the treatment of:

- Adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH)
- Adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)
- Adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive
- Adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive

Limitation(s) of use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Ultomiris is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 1 month;
4. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or ≥ 5% PNH cells;
5. Member meets one of the following (a or b):
   a. History of ≥ 1 red blood cell transfusion in the past 24 months and (i or ii):
      i. Documentation of hemoglobin < 7 g/dL in members without anemia symptoms;

ii. Documentation of hemoglobin < 9 g/dL in members with anemia symptoms;
b. History of thrombosis;
6. Ultomiris is not prescribed concurrently with Empaveli™ or Soliris®;
7. Dose does not exceed the following (a, b, c, and d):
a. IV loading dose on Day 1:
i. Weight ≥ 5 to < 10 kg: 600 mg;
ii. Weight ≥ 10 to < 20 kg: 600 mg;
iii. Weight ≥ 20 to < 30 kg: 900 mg;
iv. Weight ≥ 30 to < 40 kg: 1,200 mg;
v. Weight ≥ 40 to < 60 kg: 2,400 mg;
vi. Weight ≥ 60 to < 100 kg: 2,700 mg;
vii. Weight ≥ 100 kg: 3,000 mg;
b. If member is switching therapy from Soliris, administration of the IV loading dose should occur at the time of the next scheduled Soliris dose;
c. Maintenance dose (i or ii):
i. IV maintenance dose on Day 15 after IV Ultomiris loading dose (or starting 1 week after the last SC Ultomiris maintenance dose if switching from SC Ultomiris) and at the specified frequency thereafter:
1) Weight ≥ 5 to < 10 kg: 300 mg every 4 weeks;
2) Weight ≥ 10 to < 20 kg: 600 mg every 4 weeks;
3) Weight ≥ 20 to < 30 kg: 2,100 mg every 8 weeks;
4) Weight ≥ 30 to < 40 kg: 2,700 mg every 8 weeks;
5) Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
6) Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
7) Weight ≥ 100 kg: 3,600 mg every 8 weeks;
ii. SC maintenance dose on Day 15 after IV Ultomiris loading dose (or starting 8 weeks after the last IV Ultomiris maintenance dose if switching from IV Ultomiris) and at the specified frequency thereafter:
1) Age ≥ 18 years and weight ≥ 40 kg: 490 mg every week;
d. If member has received plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg), a supplemental dose of Ultomiris may be administered within 4 hours following each PE/PP intervention or IVIg cycle (*see section V*).

Approval duration: 6 months

B. Atypical Hemolytic Uremic Syndrome (must meet all)**:**
1. Diagnosis of aHUS (i.e., complement-mediated HUS);
2. Prescribed by or in consultation with a hematologist or nephrologist;
3. Age ≥ 1 month;
4. Member has signs of TMA as evidenced by all of the following (a, b, and c):
a. Platelet count ≤ 150 x 10^9/L;
b. Hemolysis such as an elevation in serum lactate dehydrogenase (LDH);
c. Serum creatinine above the upper limits of normal or member requires dialysis;
5. Documentation that member does not have either of the following:
a. A disintegrin and metalloproteinase with thombospondin type 1 motif, member 13 (ADAMTS13) deficiency;

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b. STEC-HUS;
6. Ultomiris is not prescribed concurrently with Soliris;
7. Dose does not exceed the following (a, b, c, and d):
   a. IV loading dose on Day 1:
      i. Weight ≥ 5 to < 10 kg: 600 mg;
      ii. Weight ≥ 10 to < 20 kg: 600 mg;
      iii. Weight ≥ 20 to < 30 kg: 900 mg;
      iv. Weight ≥ 30 to < 40 kg: 1,200 mg;
      v. Weight ≥ 40 to < 60 kg: 2,400 mg;
      vi. Weight ≥ 60 to < 100 kg: 2,700 mg;
      vii. Weight ≥ 100 kg: 3,000 mg;
   b. If member is switching therapy from Soliris, administration of the IV loading dose should occur at the time of the next scheduled Soliris dose;
   c. Maintenance dose (i or ii):
      i. IV maintenance dose on Day 15 after IV Ultomiris loading dose ~~s~~(or starting 1 week after the last SC Ultomiris maintenance dose if switching from SC Ultomiris) and at the specified frequency thereafter:
         1) Weight ≥ 5 to < 10 kg: 300 mg every 4 weeks;
         2) Weight ≥ 10 to < 20 kg: 600 mg every 4 weeks;
         3) Weight ≥ 20 to < 30 kg: 2,100 mg every 8 weeks;
         4) Weight ≥ 30 to < 40 kg: 2,700 mg every 8 weeks;
         5) Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
         6) Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
         7) Weight ≥ 100 kg: 3,600 mg every 8 weeks;
      ii. SC maintenance dose on Day 15 after IV Ultomiris loading dose (or starting 8 weeks after the last IV Ultomiris maintenance dose if switching from IV Ultomiris) and at the specified frequency thereafter:
         1) Age ≥ 18 years and weight ≥ 40 kg: 490 mg every week;
   d. If member has received PE, PP, or IVIg, a supplemental dose of Ultomiris may be administered within 4 hours following each PE/PP intervention or IVIg cycle (*see section V*).

Approval duration: 6 months

C. Generalized Myasthenia Gravis (must meet all):
1. Diagnosis of gMG;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥ 6 at baseline;
5. Myasthenia Gravis Foundation of America (MGFA) clinical classification of Class II to IV;
6. Member has positive serological test for anti-~~AChR~~aChR antibodies;
7. Failure of a corticosteroid (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
8. Failure of a cholinesterase inhibitor (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;

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9. Failure of at least one immunosuppressive therapy (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
10. Ultomiris is not prescribed concurrently with Soliris or Vyvgart®;
11. Dose does not exceed the following (a, b, c, and d):
    a. IV loading dose on Day 1:
        i. Weight ≥ 40 to < 60 kg: 2,400 mg;
        ii. Weight ≥ 60 to < 100 kg: 2,700 mg;
        iii. Weight ≥ 100 kg: 3,000 mg;
    b. If member is switching therapy from Soliris, administration of the IV loading dose should occur at the time of the next scheduled Soliris dose;
    c. IV maintenance dose on Day 15 after IV Ultomiris loading dose and at the specified frequency thereafter:
        i. Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
        ii. Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
        iii. Weight ≥ 100 kg: 3,600 mg every 8 weeks;
    d. If member has received PE, PP, or IVIg, a supplemental dose of Ultomiris may be administered within 4 hours following each PE/PP intervention or IVIg cycle (*see section V*).

Approval duration: 6 months

D. Neuromyelitis Optica Spectrum Disorder (must meet all)**:**
1. Diagnosis of NMOSD;
2. Prescribed by or in in consultation with a neurologist;
3. Age ≥ 18 years;
4. Member has positive serologic test for anti-AQP4 antibodies;
5. Member has experienced at least one relapse within the previous 12 months;
6. Baseline expanded disability status scale (EDSS) score of ≤ 7;
7. Failure of rituximab (*Ruxience™ and Truxima® are preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for rituximab*
8. Ultomiris is not prescribed concurrently with rituximab, Enspryng™, Soliris, or Uplizna®;
9. Dose does not exceed the following (a, b, c, and d):
    a. IV loading dose on Day 1:
        i. Weight ≥ 40 to < 60 kg: 2,400 mg;
        ii. Weight ≥ 60 to < 100 kg: 2,700 mg;
        iii. Weight ≥ 100 kg: 3,000 mg;
    b. If member is switching therapy from Soliris, administration of the IV loading dose should occur at the time of the next scheduled Soliris dose;
    c. IV maintenance dose on Day 15 after IV Ultomiris loading dose and at the specified frequency thereafter:
        i. Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
        ii. Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
        iii. Weight ≥ 100 kg: 3,600 mg every 8 weeks;

d. If member has received PE, PP, or IVIg, a supplemental dose of Ultomiris may be administered within 4 hours following each PE/PP intervention or IVIg cycle (*see section V*).

Approval duration: 6 months

~~D.~~E. **Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters (a, b, c, or ~~e~~d):
   a. PNH:
      i. Improved measures of intravascular hemolysis (e.g., normalization of LDH);
      ii. Reduced need for red blood cell transfusions;
      iii. Increased or stabilization of hemoglobin levels;
      iv. Less fatigue;
      v. Improved health-related quality of life;
      vi. Fewer thrombotic events;
   b. aHUS:
      i. Improved measures of intravascular hemolysis (e.g., normalization of LDH);
      ii. Increased or stabilized platelet counts;
      iii. Improved or stabilized serum creatinine or estimated glomerular filtration rate (eGFR);
      iv. Reduced need for dialysis;
   c. gMG:
      i. Improved MG-ADL total score as evidenced by a 2-point reduction from baseline;
   d. NMOSD:
      i. Frequency of relapse;
      ii. EDSS;
      iii. Visual acuity;
3. Ultomiris is not prescribed concurrently with (a, b, c, or ~~e~~d):
   a. PNH: Empaveli or Soliris;
   b. aHUS: Soliris;
   c. gMG: Soliris or Vyvgart;
   d. NMOSD: rituximab, Enspryng, Soliris, or Uplizna;
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. PNH/aHUS (i or ii):

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i. IV (at least 1 week must have elapsed since last dose of SC Ultomiris if switching):
   1) Weight ≥ 5 to < 10 kg: 300 mg every 4 weeks;
   2) Weight ≥ 10 to < 20 kg: 600 mg every 4 weeks;
   3) Weight ≥ 20 to < 30 kg: 2,100 mg every 8 weeks;
   4) Weight ≥ 30 to < 40 kg: 2,700 mg every 8 weeks;
   5) Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
   6) Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
   7) Weight ≥ 100 kg: 3,600 mg every 8 weeks;

ii. SC (at least 8 weeks must have elapsed since last maintenance dose of IV Ultomiris if switching):
   1) Age ≥ 18 years and weight ≥ 40 kg: 490 mg every week;

b. gMG/NMOSD:
   i. Weight ≥ 40 to < 60 kg: 3,000 mg every 8 weeks;
   ii. Weight ≥ 60 to < 100 kg: 3,300 mg every 8 weeks;
   iii. Weight ≥ 100 kg: 3,600 mg every 8 weeks;

c. All indications: If member has received PE, PP, or IVIg, a supplemental dose of Ultomiris may be administered within 4 hours following each PE/PP intervention or IVIg cycle (*see section V*).

~~5.~~ **Approval duration: 6 months**

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policyLA.PMN.53

B. Amyotrophic lateral sclerosis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

~~AChR~~aChR: acetylcholine receptor
ADAMTS13: a disintegrin and metalloproteinase with thombospondin type 1 motif, member 13
aHUS: atypical hemolytic uremic syndrome
AQP-4: aquaporin-4
EDSS: Expanded Disability Status Scale
FDA: Food and Drug Administration
gMG: generalized myasthenia gravis
GPI: glycosyl phosphatidylinositol
IVIg: intravenous immunoglobulin
LDH: lactate dehydrogenase
MG-ADL: Myasthenia Gravis Activities of Daily Living
MGFA: Myasthenia Gravis Foundation of America
NMOSD: neuromyelitis optica spectrum disorder
PE: plasma exchange
PNH: paroxysmal nocturnal hemoglobinuria

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PP: plasmapheresis
STEC-HUS: Shiga toxin E. coli related hemolytic uremic syndrome
TMA: thrombotic microangiopathy

Appendix B: Therapeutic Alternatives
~~Not applicable~~
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids		
betamethasone	Oral: 0.6 to 7.2 mg PO per day	7.2 mg/day
dexamethasone	Oral: 0.75 to 9 mg/day PO	9 mg/day
methylprednisolone	Oral: 12 to 20 mg PO per day; increase as needed by 4 mg every 2-3 days until there is marked clinical improvement or to a maximum of 40 mg/day	40 mg/day
prednisone	Oral: 15 mg/day to 20 mg/day; increase by 5 mg every 2-3 days as needed. Maximum: 60 mg/day	60 mg/day
Cholinesterase Inhibitors		
pyridostigmine (Mestinon®, Regonol®)	Oral immediate-release: 600 mg daily in divided doses (range, 60-1500 mg daily in divided doses) Oral sustained release: 180-540 mg QD or BID IV or IM: 2 mg every 2-3 hours	See regimen
neostigmine (Bloxiverz®)	Oral: 15 mg TID. The daily dosage should be gradually increased at intervals of 1 or more days. The usual maintenance dosage is 15-375 mg/day (average 150 mg) IM or SC: 0.5 mg based on response to therapy	See regimen
Immunosuppressants		
azathioprine (Imuran®)	Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day	3 mg/kg/day
mycophenolate mofetil (Cellcept®)*	Oral: Dosage not established. 1 gram BID has been used with adjunctive corticosteroids or other non-steroidal immunosuppressive medications	2 g/day
cyclosporine (Sandimmune®)*	Oral: initial dose of cyclosporine (non-modified), 5 mg/kg/day in 2 divided doses	5 mg/kg/day
Rituxan® (rituximab), Riabni™ (rituximab-arrx), Ruxience™ (rituximab-pvvr),	IV: 375 mg/m^2 once a week for 4 weeks; an additional 375 mg/m^2 dose may be given every 1 to 3 months afterwards **NMOSD**	See regimen

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Truxima® (rituximab-abbs)*†	IV: 375 mg/m^2 per week for 4 weeks as induction, followed by 375 mg/m^2 biweekly every 6 to 12 months	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*
†Prior authorization is required for rituximab products

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients with unresolved ~~*Neisseria Meningitidis* infection; patients who are not currently vaccinated against Neisseria meningitidis, unless the risks of delaying Ultomiris treatment outweigh the risks of developing a meningococcal~~serious *Neisseria meningitidis* infection
- Boxed warning(s): serious meningococcal infections

Appendix D: General Information

- Ultomiris is only available through a REMS (Risk Evaluation and Mitigation Strategy) program due to the risk of life-threatening and fatal meningococcal infection. ~~Patients should be vaccinated with a~~ Vaccination for meningococcal ~~vaccine~~bacteria (for serogroups A, C, W, Y, and B) should be completed or updated at least 2 weeks prior to ~~receiving~~ the first dose of Ultomiris~~ and revaccinated according to current medical guidelines for vaccine use.~~, unless the risks of delaying therapy with Ultomiris outweigh the risk of developing a serious infection. Patients should be monitored for early signs ~~of~~and symptoms of serious meningococcal infections, evaluated immediately if infection is suspected, and treated with antibiotics if necessary.
- Examples of symptoms of anemia include but are not limited to: dizziness or lightheadedness, fatigue, pale or yellowish skin, shortness of breath, chest pain, cold hands and feet, and headache.
- Ultomiris is a humanized monoclonal antibody to complement component C5 that was engineered from Soliris. It is virtually identical to Soliris but has a longer half-life that allows for less frequent dosing intervals.
- In August 2021, Alexion announced it is discontinuing the global CHAMPION-ALS phase 3 clinical study of Ultomiris in adults with amyotrophic lateral sclerosis due to an interim data review showing a lack of efficacy.
- The MGFA classification has some subjectivity in it when it comes to distinguishing mild (Class II) from moderate (Class III) and moderate (Class III) from severe (Class IV). Furthermore, it is insensitive to change from one visit to the next.
- gMG: a 2-point reduction in MG-ADL total score is considered a clinically meaningful improvement. The scale can be accessed here: https://myasthenia.org/Portals/0/ADL.pdf
- NMOSD:
  - AQP-4: AQP-4-IgG-seroposotive status is confirmed with the use of commercially available cell-binding kit assay (Euroimmun).
  - Stabilization or reduction in EDSS total score is an example of positive response. EDSS ranges from 0 (no disability) to 10 (death).

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen*</th><th>Maximum Dose</th></tr>
<tr><td>PNH,
aHUS</td><td>IV dosing:
Day 1: Loading dose IV
Day 15 and thereafter: Maintenance dose IV. If currently receiving SC Ultomiris, administer IV Ultomiris maintenance dose starting 1 week after last SC Ultomiris maintenance dose

<table><tr><th>Body Weight Range (kg)</th><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th></tr><tr><td>≥ 5 to < 10</td><td>600</td><td>300 every 4 weeks</td></tr><tr><td>≥ 10 to < 20</td><td>600</td><td>600 every 4 weeks</td></tr><tr><td>≥ 20 to < 30</td><td>900</td><td>2,100 every 8 weeks</td></tr><tr><td>≥ 30 to < 40</td><td>1,200</td><td>2,700 every 8 weeks</td></tr><tr><td>≥ 40 to < 60</td><td>2,400</td><td>3,000 every 8 weeks</td></tr><tr><td>≥ 60 to < 100</td><td>2,700</td><td>3,300 every 8 weeks</td></tr><tr><td>≥ 100</td><td>3,000</td><td>3,600 every 8 weeks</td></tr></table>
SC dosing (maintenance only for age ≥ 18 years and weight ≥ 40 kg): 490 mg SC per week, starting 2 weeks after IV Ultomiris loading dose or 8 weeks after last IV Ultomiris maintenance dose</td><td>IV: 3,600 mg/ 8 weeks

SC: 490 mg/week</td></tr>
<tr><td>gMG,
NMOSD</td><td><table><tr><th>Body Weight Range (kg)</th><th>Loading Dose (mg)</th><th>Maintenance Dose (mg)</th></tr><tr><td>≥ 40 to < 60</td><td>2,400</td><td>3,000 every 8 weeks</td></tr><tr><td>≥ 60 to < 100</td><td>2,700</td><td>3,300 every 8 weeks</td></tr><tr><td>≥ 100</td><td>3,000</td><td>3,600 every 8 weeks</td></tr></table>Day 1: Loading dose IV
Day 15 and thereafter: Maintenance dose IV</td><td>3,600 mg/ 8 weeks</td></tr>
<tr><td>Supple-mental doses</td><td>A supplemental dose of Ultomiris is required within 4 hours of PE, PP, or IVIg as they have been shown to reduce Ultomiris serum levels:<table><tr><th rowspan="2">Body Weight Range (kg)</th><th rowspan="2">Most Recent Ultomiris Dose (mg)</th><th colspan="2">Supplemental Dose (mg)</th></tr><tr><th>After PE/PP</th><th>After IVIg</th></tr><tr><td rowspan="2">≥ 40 to < 60</td><td>2,400</td><td>1,200</td><td rowspan="4">600</td></tr><tr><td>3,000</td><td>1,500</td></tr><tr><td rowspan="2">≥ 60 to < 100</td><td>2,700</td><td>1,500</td></tr><tr><td>3,300</td><td>1,800</td></tr><tr><td rowspan="2">≥ 100</td><td>3,000</td><td>1,500</td></tr><tr><td>3,600</td><td>1,800</td></tr></table></td><td>See regimen</td></tr>
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**For patients switching from Soliris to Ultomiris, administer the loading dose of Ultomiris IV at the time of the next scheduled Soliris dose, and then administer maintenance doses at the specified frequency, starting 2 weeks after loading dose administration.*

VI. Product Availability

- Single-dose vials for IV injection: 300 mg/30 mL, 300 mg/3 mL, 1,100 mg/11 mL
- Single-dose prefilled cartridge for use with supplied single-use on-body injector for SC injection: 245 mg/3.5 mL

VII. References

1. Ultomiris Prescribing Information. Boston, MA: Alexion Pharmaceuticals, Inc.; ~~June 2021~~March 2024. Available at: www.ultomiris.com. Accessed ~~November 3, 2022~~March 28, 2024.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005; 106(12):3699-3709. doi:10.1182/blood-2005-04-1717.
3. Loirat C, Fakhouri F, Ariceta G, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. Pediatr Nephrol. 2016; 31: 15-39.
4. AstraZeneca. Update on CHAMPION-ALS Phase III trial of Ultomiris in amyotrophic lateral sclerosis. Press release published August 20, 2021. Available at: https://www.astrazeneca.com/media-centre/press-releases/2021/update-on-ultomiris-phase-iii-als-trial.html. Accessed ~~September 15, 2021~~May 8, 2023.
5. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021; 96: 114-122.
6. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidelines for the management of myasthenia gravis. Neurology. 2016; 87: 419-425.
7. ClinicalTrials.gov. NCT03920293. Safety and efficacy study of ravulizumab in adults with generalized myasthenia gravis. Available at www.clinicaltrials.gov. Accessed ~~November 3, 2022~~May 8, 2023.
8. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. European Journal of Neurology. 2010; 17: 1019–1032.
9. ClinicalTrials.gov. NCT04201262. An efficacy and safety study of ravulizumab in adult participants with NMOSD. Available at www.clinicaltrials.gov. Accessed March 28, 2024.

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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1303	Injection, ravulizumab-cwvz, 10 mg

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted corporate to local policy	03.21	
Updated age and dosing requirements for PNH per FDA pediatric expansion (from age at least 18 years to age at least 1 month). For PNH, added requirement for no concurrent use with Empaveli; added amyotrophic lateral sclerosis to section III as an indication not covered due to lack of efficacy; references reviewed and updated.	02.22	05.07.22
Criteria added for new FDA indication: gMG Added new SC injection dosage form and updated dosing requirements in criteria and section V (including allowance for supplemental doses if member has received PE, PP, or IVIg); for gMG, added requirement for no concurrent use with Vyvgart. For gMG modified from two to one immunosuppressive therapy required; clarified MG-ADL total score should be assessed on continuation of therapy requests; template changes applied to other diagnoses/indications and continued therapy section. References reviewed and updated. Added blurb this policy is for medical benefit only.	06.27.23	10.24.23
Annual review; criteria added for new FDA indication: NMOSD; updated contraindications per revised FDA labeling.	04.29.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the

requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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