CareSource Rx Innovations

PHARMACY POLICY STATEMENT
Indiana Medicaid

DRUG NAME	Ultomiris (ravulizumab-cwvz)
BENEFIT TYPE	Medical, Pharmacy
STATUS	Prior Authorization Required

Ultomiris was originally approved by the FDA in 2018 for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). It is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a (the proinflammatory anaphylatoxin) and C5b (the initiating subunit of the membrane attack complex [MAC or C5b-9]) thus preventing MAC formation.
Ultomiris was engineered from an earlier product, Soliris, to have a longer half-life allowing for extended dosing intervals (every 2 weeks vs. every 8 weeks). Ultomiris and Soliris are virtually identical aside from Ultomiris having the longer half-life.
Ultomiris is also approved for the treatment of atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).
Ultomiris is also approved for the treatment of generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

Ultomiris (ravulizumab-cwvz) will be considered for coverage when the following criteria are met:

Atypical Hemolytic Uremic Syndrome (aHUS)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a hematologist or nephrologist; AND
2. Member has a diagnosis of aHUS supported by ALL of the following:
   a) Thrombocytopenia (platelet count < 150 x 10^9/L)
   b) Evidence of microangiopathic hemolytic anemia (MAHA) e.g., hemoglobin < 10 g/dL, elevated lactate dehydrogenase (LDH), low haptoglobin, presence of fragmented red blood cells or schistocytes on blood smear
   c) Evidence of renal impairment (e.g., raised SCr or low eGFR); AND
3. Shiga toxin-producing E. coli related HUS (STEC-HUS) has been ruled out; AND
4. ADAMTS13 activity level is > 10% (to rule out TTP); AND
5. Member has received meningococcal vaccine.
6. **Dosage allowed/Quantity limit:**
   IV infusion: loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.
   Subcutaneous (adults only): 490 mg once weekly (8 cartons per 28 days)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes must demonstrate hematologic normalization as evidenced by increased platelet count or LDH maintained below upper limit of normal; AND
2. Improved or preserved kidney function.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a hematologist; AND
2. Member has a documented diagnosis of PNH as confirmed by flow cytometry; AND
3. Member has a lactate dehydrogenase (LDH) level >1.5x upper limit of normal (ULN); AND
4. Member has at least one PNH-related sign/symptom e.g., fatigue, hemoglobin <10 g/dL, thrombosis, pRBC transfusion, shortness of breath; AND
5. Member has received meningococcal vaccine.
6. **Dosage allowed/Quantity limit:**
   IV infusion: loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.
   Subcutaneous (adults only): 490 mg once weekly (8 cartons per 28 days).

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Clinical evidence of positive response to therapy such as increased hemoglobin level, decreased need for transfusions, normalized LDH levels, improved fatigue.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Generalized Myasthenia Gravis (gMG)

For **initial** authorization:
1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a neurologist; AND
3. Member has a documented diagnosis of MGFA class II-IV myasthenia gravis (see appendix 2); AND
4. Lab result in chart notes shows the member is seropositive for AChR antibodies; AND
5. Member has tried and failed at least 1 conventional therapy:
   a) Pyridostigmine
   b) Corticosteroid for at least 3 months
   c) Non-steroid immunosuppressant (e.g., azathioprine) for at least 6 months; AND
6. Member has tried and failed IV Vyvgart; AND
7. Member has received meningococcal vaccine.
8. **Dosage allowed/Quantity limit:** Administered by IV infusion; loading dose followed by maintenance doses starting 2 weeks later, based on body weight, per prescribing information. See appendix 1.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes must document clinically meaningful improvement in symptom severity and daily functioning compared to pre-treatment baseline (e.g., improved MG-ADL or QMG scores).

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Ultomiris (ravulizumab-cwvz) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/07/2019	New policy for Ultomiris created.
10/26/2019	New diagnosis of aHUS added.
06/03/2021	aHUS: Updated references. Added specialist requirement. Revised diagnostic parameters. Summarized excluded causes. Removed list of restrictions from clinical trials. Revised renewal criteria. PNH: Updated references. Removed nephrology as specialist. Removed transfusion and organ damage requirements. Updated dosing information. Reduced initial approval duration from 12 months to 6 months. Revised renewal criteria.
05/19/2022	Diagnosis of myasthenia gravis added.
08/12/2022	Added dosing for new subQ product (adults with PNH or aHUS only); added pharmacy benefit.
07/19/2023	gMG: Added reference. Split list of conventional drug trials. Added trial of Vyvgart IV. aHUS: Updated and added references. Corrected ADAMTS13 level cutoff. Changed "evidence of hemolysis" to evidence of MAHA. PNH: Added reference. Added that they must be symptomatic.

APPENDIX 1:

Table 1: ULTOMIRIS Weight-Based Dosing Regimen – PNH, aHUS, and gMG*

Indications	Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg) and Dosing Interval	
PNH and aHUS	5 to less than 10	600	300	Every 4 weeks
	10 to less than 20	600	600	
	20 to less than 30	900	2,100	Every 8 weeks
	30 to less than 40	1,200	2,700	
PNH, aHUS, and gMG	40 to less than 60	2,400	3,000	
	60 to less than 100	2,700	3,300	
	100 or greater	3,000	3,600	

APPENDIX 2:

MG Foundation of America (MGFA) Clinical Classification	
Class I	any ocular weakness; all other muscle strength is normal
Class II	mild weakness affecting other than ocular muscles; may also have ocular weakness at any level

Class III	moderate weakness affecting other than ocular muscles; may also have ocular weakness at any level
Class IV	severe weakness affecting other than ocular muscles; may also have ocular weakness at any level
Class V	defined by intubation, with or without mechanical ventilation

References:

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