Ultomiris (ravulizumab-cwvz)

Background
Ultomiris (ravulizumab-cwvz) 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 terminal complement complex) and preventing the generation of the terminal complement complex C5b9. Ultomiris inhibits terminal complement-mediated intravascular hemolysis in patients with paroxysmal nocturnal hemoglobinuria (PNH) and complement-mediated thrombotic microangiopathy (TMA) in patients with atypical hemolytic uremic syndrome (aHUS) (1).

Regulatory Status
FDA- approved indication: Ultomiris is indicated for: (1)

- the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH)
- the treatment of adults and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)

Limitations of use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS) (1).
Ultomiris includes a boxed warning of life-threatening and fatal meningococcal infections/sepsis. Additionally, all patients must be vaccinated with a meningococcal vaccine at least 2 weeks prior to receiving their first dose (1).

Ultomiris blocks terminal complement activation; therefore, patients may have increased susceptibility to encapsulated bacteria infections, especially infections caused by *Neisseria meningitides* but also *Streptococcus pneumoniae*, *Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*.

Ultomiris is contraindicated in: (1)

- patients with unresolved *Neisseria meningitidis* infection
- patients who are not currently vaccinated against *Neisseria meningitidis*, unless risk of delaying Ultomiris treatment outweighs the risks of developing a meningococcal infection

The safety and effectiveness of Ultomiris for PNH in pediatric patients have not been established. The safety and effectiveness of Ultomiris for aHUS have been established in pediatric patients aged one month and older (1).

Ultomiris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Ultomiris REMS, prescribers must enroll in the program (1).

**Related policies**

*Soliris*

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Ultomiris may be considered **medically necessary** for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) or atypical hemolytic uremic syndrome (aHUS) and if the conditions indicated below are met.

Ultomiris is considered **investigational** for all other indications.

**Prior-Approval Requirements**

**Diagnosis**

The patient must have **ONE** of the following:
1. Paroxysmal nocturnal hemoglobinuria (PNH)
   a. 18 years of age or older
2. Atypical hemolytic uremic syndrome (aHUS)
   a. 1 month of age or older

AND ALL of the following:
   a. Documented baseline value for serum lactate dehydrogenase (LDH)
   b. Vaccination against Neisseria meningitides at least 2 weeks prior to initiation
      [unless Ultomiris (ravulizumab-cwvz) treatment cannot be delayed]
   c. Does NOT have Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
   d. Prescriber is enrolled in Ultomiris REMS program
   e. NO dual therapy with another terminal complement inhibitor such as Soliris
      (eculizumab)

Prior – Approval Renewal Requirements

Diagnosis

The patient must have ONE of the following:

1. Paroxysmal nocturnal hemoglobinuria (PNH)
   a. 18 years of age or older
2. Atypical hemolytic uremic syndrome (aHUS)
   a. 1 month of age or older

AND ALL of the following:
   a. Decrease in serum LDH from pretreatment baseline
   b. Does NOT have Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)
   c. Prescriber is enrolled in Ultomiris REMS program
   d. Absence of unacceptable toxicity from the drug
   e. NO dual therapy with another terminal complement inhibitor such as Soliris
      (eculizumab)
Pre – PA Allowance
None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits
Same as above

**Rationale**

**Summary**
Ultomiris (ravulizumab-cwvz) 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 terminal complement complex) and preventing the generation of the terminal complement complex C5b9. Ultomiris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Ultomiris while maintaining optimal therapeutic outcomes.

**References**

**Policy History**

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<td>January 2019</td>
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<td>Addition of indication: aHUS. Addition of requirement to not have STEC-HUS and vaccination requirement is only necessary if Ultomiris treatment can be delayed</td>
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**Keywords**
Section: Prescription Drugs  Effective Date: January 1, 2020
Subsection: Hematological Agents  Original Policy Date: January 11, 2019
Subject: Ultomiris  Page: 5 of 5

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.