BlueCross BlueShield Federal Employee Program

ULTOMIRIS (ravulizumab-cwvz)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Ultomiris (ravulizumab-cwvz) is a terminal complement inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and generalized myasthenia gravis (gMG). Ultomiris 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). The precise mechanism by which Ultomiris exerts its therapeutic effect in gMG is presumed to involve reduction of terminal complement complex C5b-9 deposition at the neuromuscular junction (1).

Regulatory Status

FDA-approved indications: Ultomiris is a complement inhibitor indicated for: (1)

1. the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).
2. 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).
    a. Limitations of Use: Ultomiris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).
3. the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.
4. the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

The International Consensus Guidance for Management of Myasthenia Gravis recommends the use of chronic IVIG and immunosuppressants (2).

Ultomiris includes a boxed warning citing the risk 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 Ultomiris dose, unless the risks of delaying therapy outweigh the risks of developing a meningococcal infection (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).

In addition, Ultomiris has warnings regarding infusion-related reactions and using caution when administering Ultomiris to patients with any other systemic infections. Ultomiris blocks terminal complement activation; therefore, patients may have increased susceptibility to infections, specifically encapsulated bacteria (1).

Ultomiris is contraindicated in patients with unresolved Neisseria meningitidis infection, and in patients who are not currently vaccinated against Neisseria meningitidis, unless risk of delaying Ultomiris treatment outweighs the risks of developing a meningococcal infection (1).

The safety and effectiveness of Ultomiris for PNH or aHUS in pediatric patients less than one month of age have not been established. The safety and effectiveness of Ultomiris for gMG or NMOSD in pediatric patients less than 18 years of age have not been established (1).

Summary

Ultomiris (ravulizumab-cwvz) is a terminal complement inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and generalized myasthenia gravis (gMG), and neuromyelitis optica spectrum disorder (NMOSD). Ultomiris includes a boxed warning citing the risk of life-threatening and fatal meningococcal infections/sepsis. Ultomiris is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). The safety and effectiveness of Ultomiris for PNH or aHUS in pediatric patients less than one month of age have not been established. The safety and effectiveness of Ultomiris for gMG and NMOSD in pediatric patients less than 18 years of age have not been established (1).

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

References

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; September 2024.
2. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology*. 2016; 87(4):419. Epub 2016 Jun 29.