MEDICAL COVERAGE POLICY	
SERVICE:	**Ravulizumab (Ultomiris®)**
Policy Number:	**319**
Effective Date:	**01/01/2026**
Last Review:	**12/08/2025**
Next Review:	**12/08/2026**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Ravulizumab (Ultomiris®)

PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider ravulizumab medically necessary when documentation is submitted showing ALL of the following criteria are met:

Universal Criteria Applied To All Requests

1. Member received meningococcal vaccine in one of the following manners:
    a. At least 2 weeks prior to first dose; **OR**
    b. As soon as possible and on prophylactic antibiotics

    AND
2. Ravulizumab will be dosed and administered according to FDA approved labeling; **AND**
3. Member does not have an active bacterial, viral, or fungal infection within 14 days of starting drug; **AND**
4. Provider attests all Risk Evaluation and Mitigation Strategy (REMS) program requirements are met

Indication Specific Criteria

Paroxysmal Nocturnal Hemoglobinuria (PNH) specific criteria:

1. Member meets all universal criteria; **AND**
2. Member is 1 month or older; **AND**
3. Member has a diagnosis of PNH; **AND**
4. Ravulizumab is prescribed by or in consultation with a hematologist; **AND**

5. Confirmed diagnosis by high sensitivity flow cytometry of red blood cells and white blood cells with granulocyte or monocyte clone size of at least 5%; **AND**
6. Ravulizumab will not be used in combination with another complement inhibitor (i.e. Empaveli, Fabhalta, PiaSky, Soliris) for the indication of PNH (concomitant use with Voydeya is allowed) ; **AND**
7. Initial authorization requires additional clinical documentation submitted:
    a. One of the following:
        i. If complement inhibitor naïve, LDH level ≥ 1.5 x the upper limit of normal; **OR**
        ii. If complement inhibitor experienced, LDH level < 1.5 x the upper limit of normal

    AND
    b. More than 1 signs or symptoms of PNH (ex. fatigue, hemoglobinuria, abdominal pain, dyspnea, anemia, or history of major adverse vascular events (thrombosis), dysphagia, erectile dysfunction, or history of packed red blood cell transfusion because of PNH

    AND
8. Authorization renewal requires additional clinical documentation submitted showing:
    a. Improvement, stabilization, or a reduction in normal decline as evidenced by:
        i. LDH level ≤ 1.5x the upper limit of normal; **AND**
        ii. Reduced or no signs and symptoms of PNH

    AND
    b. Manageable or no side effects

Atypical Hemolytic Uremic Syndrome (aHUS) specific criteria:

1. Member meets all universal criteria; **AND**
2. Member is 1 month or older; **AND**
3. Ravulizumab is prescribed by or in consultation with a hematologist or nephrologist; **AND**
4. Member has a diagnosis of aHUS; **AND**
5. Ravulizumab will not be used in combination with another complement inhibitor (ex.Soliris) for the indication of aHUS; **AND**
6. Initial authorization requires additional clinical documentation submitted:
    a. Absence of Shiga toxin; **AND**
    b. ADAMTS13 activity above 5%; **AND**
    c. Member has signs or symptoms of aHUS (ex. acute renal failure, thrombocytopenia, microangiopathic hemolysis, hemolytic anemia)

    AND
7. Authorization of renewal requires additional clinical documentation submitted showing:
    a. Improvement, stabilization, or a reduction in normal decline as evidenced by reduced or no signs and symptoms of aHUS; **AND**
    b. Manageable or no side effects

Generalized Myasthenia Gravis (gMG) specific criteria:

1. Member meets all universal criteria; **AND**
2. Member is 18 years or older; **AND**
3. Member has a diagnosis of gMG; **AND**
4. Ravulizumab is prescribed by or in consultation with a neurologist; **AND**
5. Ravulizumab will not be used in combination with another complement inhibitor (ex. Soliris, Zilbrysq) or neonatal Fc receptor blocker (ex. Vyvgart, Vyvgart Hytrulo, Rystiggo); **AND**
6. Initial authorization requires additional clinical documentation submitted:
    a. Anti-acetylcholine receptor antibody positive; **AND**
    b. Member has Myasthenia Gravis Foundation of America clinical classification of II-IV; **AND**
    c. Myasthenia Gravis Activities of Daily Living total score of at least 6 or higher; **AND**
    d. Member had a trial and inadequate response or intolerance to both of the following:
        i. An acetylcholinesterase inhibitor; **AND**
        ii. One or more immunosuppressive agents including but not limited to systemic corticosteroids or non-steroidal immunosuppressants

    AND
7. Authorization of renewal requires additional clinical documentation submitted showing:
    a. Improvement, stabilization, or a reduction in normal decline as evidenced by myasthenia Gravis Activities of Daily Living total score less than 6; **AND**
    b. Manageable or no side effects

Neuromyelitis Optica Spectrum Disorder (NMOSD) specific criteria:

1. Member meets all universal criteria; **AND**
2. Member is 18 years or older; **AND**
3. Member has a diagnosis of NMOSD; **AND**
4. Ravulizumab is prescribed by or in consultation with a neurologist; **AND**
5. Ravulizumab will not be used in combination with any other biologics (ex. Soliris, Uplizna, Enspryng, rituximab, tocilizumab) for the indication of NMOSD; **AND**
6. Initial authorization requires additional clinical documentation submitted:
    a. Member is anti-aquaporin-4 (AQP4) antibody positive; **AND**
    b. Member has history of 1 or more relapses within 1 year; **AND**
    c. Member has at least one or more signs and symptoms of NMOSD (i.e. optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, or symptomatic cerebral syndrome with NMOSD-typical brain lesions)

    AND
7. Authorization of renewal requires additional clinical documentation submitted showing:
    a. Improvement, stabilization, or a reduction in normal decline as evidenced by:
        i. Reduced or no relapses; **OR**

ii. Reduced or no signs or symptoms of NMOSD

AND

b. Manageable or no side effects

Authorization duration – the shortest of clinically appropriate duration, requested duration, or 6 months

BSWHP considers ravulizumab for the treatment of all other indications to be experimental and investigational because the effectiveness of this strategy has not been established.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:

Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare autoimmune disease where the hemopoietic cell membranes lack complement inhibitors, which protect the cell from being attacked by the complement cascade. The complement cascade will detect these cells and signal the immune system to attack, which results in complement-mediated hemolysis. This causes many patients to present with hemolytic anemia, fatigue, hemoglobinuria, dyspnea, chest pain, abdominal pain, and patients have an increased risk for thrombosis. Mortality before the discovery of terminal complement C5 inhibitors was 35% with the best supportive care at 5 years of PNH. Currently with treatment, individual survival rates of PNH have increased by at least 75%.

Ravulizumab (Ultomiris) is a terminal complement inhibitor indicated for the treatment of PNH in pediatric and adult patients. It is a complement inhibitor that binds to complement protein C5 with high specificity and affinity, where it inhibits cleavage into C5a and C5b. This inhibition of cleavage prevents membrane attack complex (MAC) formation, which inhibits terminal complement mediated intravascular hemolysis. In clinical studies, ravulizumab treatment resulted in both avoidance of red blood cell transfusion and normalization of lactate dehydrogenase (LDH) coprimary endpoints showing noninferiority to treatment with eculizumab.

Atypical hemolytic uremic syndrome (aHUS) is a type of thrombotic microangiopathy that is typically caused by deficiency of complement regulatory proteins which results in dysregulation of the alternative complement pathway. The lack of regulatory proteins leads to an unchecked generation of C3 and C5 convertases that are responsible for the formation of MAC. MAC causes cell lysis at the vascular endothelium and platelet sites, which causes a constant prothrombic state leading to vascular bed damage that is often worsened by inflammation. Infections can induce aHUS with initial clinical characteristics being nonspecific like fatigue and pallor, whereas progression can turn into hemolytic anemia, thrombocytopenia, and acute kidney injury (AKI) with symptoms of oliguria, uremia, and volume overload. There is risk of chronic kidney disease and end stage renal disease in aHUS and left untreated can result in patients failing to regain kidney function. 50% of untreated patients progress to require dialysis with a 25% mortality rate.

Ravulizumab (Ultomiris) is a terminal complement inhibitor indicated for the treatment of aHUS in pediatric and adult patients. It is a complement inhibitor that binds to complement protein C5 with high specificity and affinity, where it inhibits cleavage into C5a and C5b. This inhibition of cleavage prevents MAC formation, which inhibits terminal complement mediated thrombotic microangiopathy. In clinical studies, ravulizumab treatment resulted in clinical improvement in the kidney and hematologic parameters and is safe and effective when switching from eculizumab to ravulizumab.

Generalized Myasthenia Gravis (gMG) is a rare autoimmune disease caused by a dysfunction of the neuromuscular junction. Patients with gMG commonly present with diplopia, facial bulbar muscle weakness, ptosis, and limb weakness. Acetylcholine receptor antibody positive (AChR-Ab+) disease is the most common serological subgroup, and the only type of gMG that has an FDA indication for treatment with ravulizumab. Mortality rate of gMG is 0.06 to 0.89 deaths per million persons year.

Ravulizumab (Ultomiris) is a terminal complement inhibitor indicated for the treatment of AChR-Ab+ gMG in adult patients. It is a complement inhibitor that has an unknown mechanism of action but presumed to involve inhibition of aquaporin-4 antibody (AQP4) induced terminal complement C5b-9 deposition. In clinical studies, ravulizumab treatment resulted in clinical efficacy and long-term safety in adults with AChR-Ab+ gMG compared to placebo.

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare inflammatory autoimmune disease that affects the spinal cord and optic nerve primarily. Normally, AQP4 is coexpressed with excitatory amino acid transporter 2, which allows glutamate uptake by astrocytes. In NMOSD AQP4 antibody positive, AQP4 activity is lost, and glutamate accumulates in excess in the extracellular space leading to neuroinflammation and dysregulation of sensory neurons. Ultimately, this results in demyelination and axonal damage which typically causes transverse myelitis and optic neuritis. Another characteristic of NMOSD are relapses (attacks) that can be recurrent and unpredictable, which can lead to irreversible neurologic disability.

Ravulizumab (Ultomiris) is a terminal complement inhibitor indicated for the treatment of NMOSD in adult patients. It is a complement inhibitor that has an unknown mechanism of action but presumed to involve inhibition of aquaporin-4 antibody (AQP4) induced terminal complement C5b-9 deposition. In clinical studies, ravulizumab treatment resulted in significant reduce of relapse risk in adult patients with AQP4+ NMOSD compared to placebo group.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	
HCPCS Codes:	J1303 - Injection, ravulizumab-cwvz, 10 mg

ICD10 codes:	
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	12/08/2025	New Policy

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. *HIGHLIGHTS of PRESCRIBING INFORMATION*. Accessed September 28, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761108s037lbl.pdf
2. Ravulizumab (Ultomiris): CADTH Reimbursement Reviews and Recommendations: Therapeutic area: Paroxysmal nocturnal hemoglobinuria [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2022 Apr. Table 3, Key Characteristics of Ravulizumab and Eculizumab. Available from: https://www.ncbi.nlm.nih.gov/books/NBK599307/table/tr8269861151140700_ch01_t03/
3. Gulbis B, Eleftheriou A, Angastiniotis M, et al. Epidemiology of rare anaemias in Europe. *Adv Exp Med Biol*. 2010;686:375-396. doi:10.1007/978-90-481-9485-8_22
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12. Tanaka K, Adams B, Aris AM, et al. The long-acting C5 inhibitor, ravulizumab, is efficacious and safe in pediatric patients

with atypical hemolytic uremic syndrome previously treated with eculizumab. Pediatr Nephrol. 2021;36(4):889-898. doi:10.1007/s00467-020-04774-2

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***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.