

POLICY Document for ULTOMIRIS (ravulizumab-cwvz)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product

- Policy information specific to preferred medications

Section 2: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

CAREFIRST: EXCEPTIONS CRITERIA COMPLEMENT INHIBITORS

PREFERRED PRODUCTS: ULTOMIRIS, VYVGART, VYVGART HYTRULO

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the Complement inhibitor products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Complement Inhibitor Products

	Product(s)
Preferred*	<ul style="list-style-type: none"> Ultomiris (ravulizumab-cwvz) Vyvgart (efgartigimod alfa) Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)
Targeted	<ul style="list-style-type: none"> Empaveli (pegcetacoplan) Enspryng (atralizumab-mwge) Piasky (crovalimab)

	<ul style="list-style-type: none"> • Rystiggo (rozanolixizumab) • Soliris (eculizumab) • Uplizna (inebilizumab-cdon)
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*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review.

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred product.

For Myasthenia Gravis, coverage for the targeted product is provided when member has a documented inadequate response, contraindication, or intolerable adverse event to all the preferred products.

For all other indications, coverage for the targeted product is provided when member has a documented inadequate response, contraindication, or intolerable adverse event to Ultomiris.

Section 2: Site of Care

Site of Care Criteria Administration of Intravenous Ultomiris

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Ultomiris in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Ultomiris in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

- A. The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
- B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
- C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
- D. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
- E. Alternative infusion sites (pharmacy, physician office, ambulatory care, etc.) are greater than 30 miles from the member's home.
- F. The member is less than 14 years of age.

For situations where administration of Ultomiris does not meet the criteria for outpatient hospital infusion, coverage for Ultomiris is provided when administered in alternative sites such as; physician office, home infusion or ambulatory care.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

CareFirst Specialty Exceptions Complement Inhibitors C26772-A 10-2024.docx

Ultomiris Site Of Care P2024.docx

Ultomiris SGM 2835-A P2024a_R.docx

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- A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
- B. Medical records supporting the member is medically unstable
- C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
- D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
- E. Records supporting alternative infusion sites are greater than 30 miles from the member's home
- F. Medical records supporting the member is new to therapy

Section 3: Clinical Criteria

Specialty Guideline Management

Ultomiris

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Ultomiris	ravulizumab-cwvz

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications¹

- Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH).
- Ultomiris is indicated for the treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).
- Ultomiris is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

- Ultomiris is indicated for the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive.

Limitations of Use

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

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- For initial requests:
 - Paroxysmal nocturnal hemoglobinuria: Flow cytometry used to show results of glycosylphosphatidylinositol-anchored proteins (GPI-APs) deficiency
 - Atypical hemolytic uremic syndrome: ADAMTS 13 level
 - Generalized myasthenia gravis:
 - Positive anti-acetylcholine receptor (AChR) antibody test
 - Myasthenia Gravis Foundation of America (MGFA) clinical classification
 - MG activities of daily living score
 - Previous medications tried, including response to therapy. If therapy is not advisable, documentation of clinical reasons to avoid therapy.
 - Neuromyelitis optica spectrum disorder: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present
- For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

Coverage Criteria

Paroxysmal nocturnal hemoglobinuria^{1-4,7,10}

Authorization of 6 months may be granted for treatment of paroxysmal nocturnal hemoglobinuria (PNH) when all of the following criteria are met:

- The diagnosis of PNH was confirmed by detecting a deficiency of glycosylphosphatidylinositol-anchored proteins (GPI-APs) (e.g., at least 5% PNH cells, at least 51% of GPI-AP deficient polymorphonuclear cells)
- Flow cytometry is used to demonstrate GPI-APs deficiency

Member has and exhibits clinical manifestations of disease (e.g., LDH > 1.5 ULN, thrombosis, renal dysfunction, pulmonary hypertension, dysphagia)

The requested medication will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Piasky, Soliris) for the treatment of PNH (concomitant use with Voydeya is allowed).

Atypical hemolytic uremic syndrome^{1,6}

Authorization of 6 months may be granted for treatment of atypical hemolytic uremic syndrome (aHUS) not caused by Shiga toxin when all of the following criteria are met:

- Absence of Shiga toxin
- ADAMTS 13 activity level above 5%
- The requested medication will not be used in combination with another complement inhibitor (e.g., Soliris) for the treatment of aHUS.

Generalized myasthenia gravis^{1,8,9,11}

Authorization of 6 months may be granted for treatment of generalized myasthenia gravis (gMG) when all of the following criteria are met:

- Anti-acetylcholine receptor (AChR) antibody positive
- Myasthenia Gravis Foundation of America (MGFA) clinical classification II to IV
- MG activities of daily living (MG-ADL) total score of greater than or equal to 5
- Meets one of the following:
 - Member has had an inadequate response or intolerable adverse event to at least two immunosuppressive therapies over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, tacrolimus)
 - Member has had an inadequate response or intolerable adverse event to at least one immunosuppressive therapy and intravenous immunoglobulin (IVIG) over the course of at least 12 months
 - Member has a documented clinical reason to avoid therapy with immunosuppressive agents and IVIG
- The requested medication will not be used in combination with another complement inhibitor (e.g., Soliris, Zilbrysq) or neonatal Fc receptor blocker (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

Neuromyelitis optica spectrum disorder^{1,12}

Authorization of 6 months may be granted for treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

- Anti-aquaporin-4 (AQP4) antibody positive
- Member exhibits one of the following core clinical characteristics of NMOSD:
 - Optic neuritis
 - Acute myelitis

- Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
- Acute brainstem syndrome
- Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
- Symptomatic cerebral syndrome with NMOSD-typical brain lesions
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Continuation of Therapy

Paroxysmal nocturnal hemoglobinuria

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., improvement in hemoglobin levels, normalization of lactate dehydrogenase [LDH] levels).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Piasky, Soliris) for the treatment of PNH (concomitant use with Voydeya is allowed).

Atypical hemolytic uremic syndrome

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen
- The member demonstrates a positive response to therapy (e.g., normalization of lactate dehydrogenase (LDH) levels, platelet counts).
- The requested medication will not be used in combination with another complement inhibitor (e.g., Soliris) for the treatment of aHUS.

Generalized myasthenia gravis

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., improvement in MG-ADL score, MG Manual Muscle Test (MMT), MG Composite).

- The requested medication will not be used in combination with another complement inhibitor (e.g., Soliris, Zilbrysq) or neonatal Fc receptor blocker (e.g., Vyvgart, Vyvgart Hytrulo, Rystiggo).

Neuromyelitis optica spectrum disorder

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when all of the following criteria are met:

- There is no evidence of unacceptable toxicity or disease progression while on the current regimen.
- The member demonstrates a positive response to therapy (e.g., reduction in number of relapses).
- The member will not receive the requested medication concomitantly with other biologics for the treatment of NMOSD.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

REFERENCES:

SECTION 1

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3. Piasky [package insert]. South San Francisco, CA: Genetech Inc; June 2024.
4. Rystiggo [package insert]. Smyrna, GA: UCB, Inc; June 2023.
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8. Vyvgart [package insert]. Boston, MA: argenx US, Inc; August 2024
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SECTION 2

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2024.

SECTION 3

1. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals, Inc.; March 2024.
2. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. Hematology. 2011; 21-29.

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