POLICY Document for UPLIZNA (inebilizumab-cdon)

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*	• **Ultomiris** (ravulizumab-cwvz) • **Vyvgart** (efgartigimod alfa) • **Vyvgart** Hytrulo (efgartigimod alfa and hyaluronidase)
Targeted	• **Empaveli** (pegcetacoplan) • **Enspryng** (atralizumab-mwge) • **Piasky** (crovalimab)

	• **Rystiggo** (rozanolixizumab) • **Soliris** (eculizumab) • **Uplizna** (inebilizumab-cdon)

*: 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 Uplizna

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of Uplizna 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 Uplizna 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 Uplizna 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 Uplizna does not meet the criteria for outpatient hospital infusion, coverage for Uplizna 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):

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
Uplizna

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
Uplizna	inebilizumab-cdon

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 Indications[1]

Uplizna is indicated for the treatment of:

Neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.
Immunoglobulin G4-related disease (IgG4-RD) in adult patients.

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:

- Neuromyelitis optica spectrum disorder (NMOSD)
  - For initial requests: Immunoassay used to confirm anti-aquaporin-4 (AQP4) antibody is present.
  - For continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- Immunoglobulin G4-related disease (IgG4-RD)
  - For initial requests, chart notes or medical records documenting:
    - Member has a clinical diagnosis of IgG4-RD.
    - Member is experiencing an IgG4-RD flare requiring glucocorticoid treatment (within the past 4 weeks).
    - IgG4-RD is affecting at least 1 organ/site.
  - For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

Coverage Criteria

Neuromyelitis Optica Spectrum Disorder (NMOSD)[1,2]

Authorization of 12 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 magnetic resonance imaging (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.

Immunoglobulin G4-related Disease (IgG4-RD)[1,3-5]

Authorization of 12 months may be granted for treatment of immunoglobulin G4-related disease (IgG4-RD) when all of the following criteria are met:

- Member has a clinical diagnosis of IgG4-RD confirmed by either of the following (please see Appendix A for evaluations and characteristic organs to confirm diagnosis):
  - Clinical or radiologic involvement of a characteristic organ.
  - Pathologic evidence from a characteristic organ.
- Alternative causes of member's clinical signs and symptoms have been evaluated and ruled out (please see Appendix B for common mimickers of IgG4-RD).
- Member is experiencing an IgG4-RD flare that requires initiation or continuation of glucocorticoid treatment (within the past 4 weeks).
- Member has a history of IgG4-RD affecting at least 1 organ/site at any time in the course of IgG4-RD.

Continuation of Therapy

Neuromyelitis Optica Spectrum Disorder (NMOSD)

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.

Immunoglobulin G4-related Disease (IgG4-RD)

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 IgG4-RD flares).

Appendices

Appendix A: Adapted from the 2020 Revised Comprehensive Diagnostic Criteria for IgG4-RD and the 2019 ACR/EULAR Classification Criteria for IgG4-RD[4,5]

- Clinical or radiological features:
  - One or more organs show diffuse or localized swelling or a mass or nodule characteristic of IgG4-RD. In single organ involvement, lymph node swelling is omitted.
  - Note: Nearly any organ can be affected, but characteristic organs involved include:
    - Pancreas
    - Salivary gland
    - Bile ducts
    - Orbits
    - Kidney
    - Lung
    - Aorta
    - Retroperitoneum
    - Pachymeninges
    - Thyroid gland (Riedel's thyroiditis)
- Pathological diagnosis (positivity for two of the following three criteria):
  - Dense lymphocyte and plasma cell infiltration with fibrosis.
  - Ratio of IgG4-positive plasma cells /IgG-positive cells greater than 40% and the number of IgG4-positive plasma cells greater than 10 per high powered field.
  - Typical tissue fibrosis, particularly storiform fibrosis, or obliterative phlebitis.

Appendix B: Common Mimickers of IgG4-RD[4,5]

Malignancy
Vasculitis
Sjogren's syndrome
Primary granulomatous inflammation (including sarcoidosis)
Infection
Multicentric Castleman's disease
Erdheim-Chester disease
Crohn's disease or ulcerative colitis (if only pancreatobiliary disease is present)
Hashimoto thyroiditis (if only the thyroid is affected)

REFERENCES:

SECTION 1

1. Empaveli [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc; February 2024.
2. Enspryng [package insert]. San Francisco, CA: Genentech, Inc.; March 2022.
3. Piasky [package insert]. South San Francisco, CA: Genetech Inc; June 2024.
4. Rystiggo [package insert]. Smyrna, GA: UCB, Inc; June 2023.
5. Soliris [package insert]. Boston, MA: Alexion Pharmaceuticals Inc; September 2024.
6. Ultomiris [package insert]. Boston, MA: Alexion Pharmaceuticals Inc; September 2024.
7. Uplinza [package insert]. Deerfield, IL: Horizon Therapeutics; July 2021.
8. Vyvgart [package insert]. Boston, MA: argenx US, Inc; August 2024
9. Vyvgart Hytrulo [package insert]. Boston, MA: argenx US, Inc; August 2024

SECTION 2

1. Uplizna [package insert]. Gaithersburg, MD: Viela Bio, Inc.; July 2021.

SECTION 3

1. Uplizna [package insert]. Deerfield, IL: Horizon Therapeutics USA, Inc.; April 2025.
2. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85:177-189.
3. Stone JH, Khosroshahi A, Zhang W, et al. Inebilizumab for Treatment of IgG4-Related Disease. N Engl J Med. 2025 Mar 27;392(12):1168-1177.
4. Wallace, Z.S., Naden, R.P., Chari, S., Choi, H., et al. The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. Arthritis Rheumatol, 72: 7-19.
5. Umehara H, Okazaki K, Kawa S, et al. The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. *Mod Rheumatol*. 2021;31(3):529-533.