Medical Policy:

Uplizna (inebilizumab-cdon) intravenous injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.317	February 7, 2025	January 1, 2021

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Uplizna (inebilizumab-cdon) is a CD19-directed cytolytic antibody indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

Length of Authorization

Initial authorization will be for no more than 6 months and reauthorization will be for no more than 12 months.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

A. 300 billable units on day 1 and 15, then 300 billable units every 6 months (beginning 6 months after the first dose)

Guideline

I. INITIAL APPROVAL CRITERIA

Coverage is provided in the following condition:

1. **<u>Neuromyelitis Optica Spectrum Disorder (NMOSD)</u>**
   A. Patient is 18 years of age and older; **AND**
   B. Prescribed by, or in consultation with, a neurologist; **AND**
   C. Patient does not have an active infection, including clinically important localized infections; **AND**
   D. Patient has been evaluated and screened for the presence of latent TB infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; **AND**
   E. Patient has been evaluated and screened for the presence hepatitis B virus (HBV) prior to initiating treatment; **AND**
   F. Patient does not have an underlying immunodeficiency disorder (i.e., acquired/congenital primary immunodeficiency, HIV, etc.); **AND**
   G. Patient has had baseline serum immunoglobulin measured prior to the start of therapy; **AND**
   H. Patient has not received intravenous immunoglobulin (IVIG) within 1 month prior to the start of therapy**; AND**
   I. Live or live-attenuated vaccinations will not be administered within the 4-weeks prior to the start of therapy and will not be administered concurrently while on therapy; **AND**
   J. Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMP-IgG antibodies; **AND**
   K. Alternative diagnoses have been excluded [e.g., myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD), multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.]; **AND**
   L. Patient has at least one core clinical characteristic § (Note: some core clinical characteristics require both clinical and typical MRI findings); **AND**
   M. Patient has not failed a previous course of Uplizna therapy; **AND**
   N. **<u>One</u>** of the following:
      i. History of at least one relapse during the previous 12 months prior to initiating Uplizna ; **OR**
      ii. History of at least two relapses during the previous 24 months, at least one relapse occurring within the past 12 months prior to initiating Uplizna; **AND**
   O. Patient is not receiving Uplizna in combination with <u>any</u> of the following:
      i. Immunosuppressive therapy (IST), such as oral or intravenous corticosteroids, with the exception of premedication for treatment;
      ii. Other immunosuppressant procedures (e.g., total lymphoid irradiation, bone marrow transplant, T-cell vaccination therapy, etc.); **AND**
      iii. Soliris, or Ultomiris
      iv. Complement-inhibitors (i.e., eculizumab, ravulizumab)
      v. Anti-CD20-directed antibody (i.e., rituximab)
      vi. IL-6 inhibitor (i.e., satralizumab, tocilizimab, sarilumab, etc.) therapies

§ Core Clinical Characteristics of NMOSD
• Acute optic neuritis • Acute myelitis • Area postrema syndrome (APS): episode of otherwise unexplained hiccups and/or nausea and • vomiting (lasting for at least 48 hours or with MRI evidence of a dorsal brainstem lesion) • Acute brainstem syndrome other than APS • Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic lesion on MRI ¥ • Acute cerebral syndrome with NMOSD-typical brain lesion on MRI ψ
¥ Diencephalic syndrome: Periependymal lesion (3rd ventricle) OR hypothalamic/thalamic lesion ψ Cerebral syndrome: Extensive periependymal lesion (lateral ventricle; often with Gd) OR long (> 1⁄2 length), diffuse, heterogeneous or edematous corpus callosum lesion OR long corticospinal tract lesion (unilateral or bilateral, contiguously involving internal capsule and cerebral peduncle) OR large, confluent (unilateral or bilateral) subcortical or deep white matter lesion

II. RENEWAL CRITERIA

Coverage can be renewed based upon the following criteria:

A. Patient continues to meet the criteria identified above; **AND**

B. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: tuberculosis (TB) infections, hepatitis B reactivation, infusion reactions, serious infections, Progressive Multifocal Leukoencephalopathy (PML), hypogammaglobulinemia, etc.; **AND**

C. Disease response indicated by ONE or more of the following:
   i. symptoms as evidenced by a decrease in acute relapses, improvement in stability, or improvement in EDSS
   ii. Reduced hospitalizations
   iii. Reduction/discontinuation in plasma exchange treatments

Limitations/Exclusions

1. Uplizna (inebilizumab-cdon) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

Code	Description
J1823	Injection, inebilizumab-cdon; 1 billable unit = 1 mg

Applicable NDCs

Code	Description
75987-0150-xx	Uplizna 100 mg/10 mL single-dose vials for injection

ICD-10 Diagnoses

Code	Description
G36.0	Neuromyelitis optica (Devic)

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	2/7/2025	Annual Review: Initial Criteria: Neuromyelitis Optica Spectrum Disorder (NMOSD) Added "or in consultation with" to the following statement: Prescribed by, or in consultation with, a neurologist; AND. Added: "and will receive ongoing monitoring for the presence of TB during treatment; " to the following statement: Patient has been evaluated and screened for the presence of latent TB infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; AND. Added: "Patient does not have an underlying immunodeficiency disorder (i.e., acquired/congenital primary immunodeficiency, HIV, etc.); AND Patient has had baseline serum immunoglobulin measured prior to the start of therapy; AND Patient has not received intravenous immunoglobulin (IVIG) within 1 month prior to the start of therapy; AND. Reworded the following statement: "Must not be administered concurrently with live vaccines;" to " Live or live-attenuated vaccinations will not be administered within the 4-weeks prior to the start of therapy and will not be administered concurrently while on therapy; AND" Removed: "Submission of medical records (e.g. chart notes,

		laboratory values, etc.) to support the diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist confirming all of the following:Past medical history of ONE of the following: 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; AND" Reworded the following statement: "Diagnosis of multiple sclerosis or other diagnoses have been ruled out;" to "Alternative diagnoses have been excluded [e.g., myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD), multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.]; AND" Added:"Patient has at least one core clinical characteristic § (Note: some core clinical characteristics require both clinical and typical MRI findings);" Also added chart Added: "Other immunosuppressant procedures (e.g., total lymphoid irradiation, bone marrow transplant, T-cell vaccination therapy, etc.); AND" also added: "or Ultomiris " Renewal Criteria: Removed: "Patient is receiving ongoing monitoring for presence of TB or other active infections; AND" (duplicative captured in initial criteria) Reworded the following: "Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD" to " Neurologic symptoms as evidenced by a decrease in acute relapses, improvement in stability, or improvement in EDSS Reduced hospitalizations Reduction/discontinuation in plasma exchange treatments" Removed: "Patient is not receiving Uplizna in combination with any of the following: Immunosuppressive therapy (IST), such as oral or intravenous corticosteroids, with the exception of premedication for treatment; Soliris Complement-inhibitors (i.e., eculizumab, ravulizumab) Anti-CD20-directed antibody (i.e., rituximab), IL-6 inhibitor (i.e., satralizumab, tocilizimab, sarilumab, etc.) therapies" since it is duplicative.
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: updated NDC, no criteria changes
EmblemHealth & ConnectiCare	10/02/2023	Initial Criteria: Removed "History of failure of, contraindication, or intolerance to rituximab therapy; AND"
EmblemHealth & ConnectiCare	4/25/2023	Annual Revision: Corrected formatting, Removed from Initial Criteria 1.Neuromyelitis Optica Spectrum Disorder (NMOSD) •Patient is not receiving Uplizna in combination with any of the following: D. Disease modifying therapies for the treatment of multiple sclerosis (e.g. Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.) Added: •Patient is not receiving Uplizna in combination with any of the following: oComplement-inhibitors (i.e., eculizumab, ravulizumab) oAnti-CD20-directed antibody (i.e., rituximab) oIL-6 inhibitor (i.e., satralizumab, tocilizimab, sarilumab, etc.) therapies
EmblemHealth & ConnectiCare	1/17/2023	Transfer to New Template
EmblemHealth & ConnectiCare	1/1/2021	New Policy, Updated J-Code: J1823

References

1. Uplizna (Inebilizumab-cdon) [Prescribing Information] Gaithersburg, MD: Vela BIo; June 2020. Accessed Aug 5, 2020.