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Policy Number: 044.001

Title: Coverage Determination Policy for Uplizna (Inebilizumab-cdon)

Regions:	☒ **Texas**	☐ **Florida**	☐ **Indiana**	☐ **New Jersey**	☒ **New Mexico**

Impacted Areas:

☒ Network Management/Provider Services	☒ Utilization Management
☐ Member services	☐ Case management
☐ Quality Management	☐ Disease management
☐ Credentialing	☒ Claims
☐ IT	☐ Human resources
☐ Administration	☐ Finance
☐ Compliance/delegation	☒ Pharmacy
	☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

Note: Patients should be screened for Hepatitis B virus, quantitative serum immunoglobulins, and tuberculosis screening prior starting Uplizna. Uplizna is Contraindicated if patient has an Active Hepatitis B infection & Active or untreated latent tuberculosis

Uplizna (inebilizumab-cdon) is proven and medically necessary for the treatment of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** when **ALL** the following criteria are met:

1. Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of **NMOSD** by a neurologist confirming **ALL** of the following:
   - **A.** Past medical history of ONE of the following:
     - i. Optic neuritis
     - ii. Acute myelitis
     - iii. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
     - iv. Acute brainstem syndrome
     - v. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
     - vi. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
   - **B.** Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies
   - **C.** Diagnosis of multiple sclerosis or other diagnoses have been ruled out
2. **ONE** of the following:
   - **A.** History of failure of rituximab therapy
   - **B.** BOTH of the following:
     - i. History of intolerance or contraindication to rituximab
     - ii. Physician attests that, in their clinical opinion, the same intolerance or severe adverse event would not be expected to occur with Uplizna
3. **ONE** of the following:
   - **A.** History of one or more relapses that required rescue therapy during the previous 12 months prior to initiating Uplizna
   - **B.** History of two or more relapses that required rescue therapy during the previous 24 months, prior to initiating Uplizna
4. Uplizna is initiated according to the U.S. FDA labeled dosing for NMOSD
5. Patient is NOT receiving Uplizna in combination with ANY of the following:
   - **A.** Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]
   - **B.** Complement inhibitors [e.g., Soliris (eculizumab)]
   - **C.** Anti-IL6 therapy [e.g., Actemra (tocilizumab)]
   - **D.** Anti-CD20 therapy [e.g., rituximab]

Renewal/Continuation of Therapy Requests

Uplizna (inebilizumab-cdon) is proven and medically necessary for the continuation of treatment of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** when **ALL** the following criteria are met:

A. Documentation of positive clinical response

B. Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by at least BOTH of the following

i. Reduction in the number and/or severity of relapses or signs and symptoms of NMOSD

ii. Maintenance, reduction, or discontinuation of dose(s) of any baseline immunosuppressive therapy (IST) prior to starting Uplizna. *Note: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat NMOSD or exacerbation of symptoms while on Uplizna therapy will be considered as treatment failure*

C. Uplizna is dosed according to the U.S. FDA labeled dosing for NMOSD

D. Patient is NOT receiving Uplizna in combination with ANY of the following:

iii. Disease modifying therapies for the treatment of multiple sclerosis [e.g., Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Ocrevus (ocrelizumab), etc.]

iv. Anti-IL6 therapy [e.g., Actemra (tocilizumab)]

v. Complement inhibitors [e.g., Soliris (eculizumab)]

vi. Anti-CD20 therapy [e.g., rituximab]

FDA Approved Dose and Indication

Indication	Dosing
Treatment of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** in adult patients who are anti-aquaporin-4 (AQP4) antibody positive	**Initial dose:** 300 mg intravenous infusion followed two weeks later by a second 300 mg intravenous infusion **Subsequent doses:** (starting 6 months from the first infusion): single 300 mg intravenous infusion every 6 months

General Background

Uplizna (inebilizumab-cdon) is a CD19-directed humanized afucosylated IgG1 monoclonal antibody. The exact mechanism of action by which inebilizumab exerts its therapeutic effects in neuromyelitis optica spectrum disorder (NMOSD) is not known, but is presumed to involve binding to CD19, a cell surface antigen on pre-B and mature B lymphocytes. After cell surface binding to B lymphocytes, inebilizumab results in antibody-dependent cellular cytolysis.

Clinical Evidence

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Inebilizumab-cdon is indicated for the treatment of NMOSD. Cree et al., evaluated the efficacy and safety of inebilizumab, in 230 patients with NMOSD over 44 months in a multicenter, double-blind, randomized placebo-controlled phase 2/3 study. 174 participants received inebilizumab and 56 participants received placebo. Eligible patients were adults (≥18 years old), an expanded disability status score (EDSS) of 8 or less, who required at least one rescue therapy treatment during the year prior to screening, or at least 2 attacks requiring rescue therapy in the 2 years before screening. Patients who were AQP4-IgG-seropositive and AQP4-IgG-seronegative were eligible; however, patients who were seronegative also needed to meet the criteria described by Wingerchuk and colleagues. The mean EDSS score was 4.0. The number of relapses in the two years prior to randomization was 2 or more in 83% of the patients. Participants were randomly allocated (3:1) to receive 300 mg intravenous inebilizumab or placebo on days 1 and 15, with a total dose of inebilizumab in the randomized controlled period of 600 mg. No further doses occured after day 15 within the study period. All participants received oral corticosteroids to minimize the risk of an attack immediately following the first inebilizumab treatment. Primary endpoint was the time in days to the onset of an NMOSD attack, on or before day 197. Secondary endpoints included worsening of EDSS score from baseline, change from baseline in low-contrast visual acuity binocular score; cumulative total number of active MRI lesions, and number of NMOSD-related inpatient hospitalizations, longer than an overnight stay. The randomized controlled period was stopped prior to completion of enrollment, as there was a clear demonstration of efficacy: 12% of participants receiving inebilizumab had an attack, versus 39% of participants receiving placebo (RR 73%; HR 0.272 [95% CI 0.150-0.496]; $p<0.0001$). In the anti-AQP4 antibody positive population, there was a 77.3% relative reduction (HR 0.227, $p<0.0001$), whereas, patients who were anti-AQP4 antibody negative had no evidence of benefit. Adverse events occurred in 72% of participants receiving inebilizumab and 73% of participants receiving placebo. Service adverse events occurred in 5% of participants reciving inebilizumab and 9% of participants reciving placebo. The authors concluded that compared to placebo, inebilizumab reduced the risk of an NMOSD attack.

HCPCS Code

HCPCS Code	Description
J1823	Uplizna (Inebilizumab-cdon)

Drug	Dosage Form, Strength, and Route of Administration
Uplizna	100 mg/10 mL (10 mg/mL) solution in a single-dose vial, administered intravenously (IV)

Acronyms

NMOSD = Neuromyelitis Optica Spectrum Disorder

NCD = National Coverage Determination

LCD = Local Coverage Determination

IST = Immunosuppressive therapy

AQP4-IgG = Anti-aquaporin-4 immunoglobulin G

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