Policy Title:	Uplizna (inebilizumab-cdon) (Intravenous)		
		Department:	PHA
Effective Date:	12/01/2020		
Review Date:	11/2/2020, 7/15/2021, 7/7/2022, 4/27/2023, 12/14/2023, 01/04/2024		

Purpose: To support safe, effective, and appropriate use of Uplizna (inebilizumab-cdon).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:
Uplizna (inebilizumab-cdon) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:
Coverage of Uplizna will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:
Uplinza (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. The N-MOmentum trial demonstrated that Uplinza reduced the risk of NMOSD relapse by 77% compared to placebo over a 197-week period. Additionally, Uplinza showed efficacy in reducing the risk of disability worsening by 50% compared to placebo. Common adverse events include urinary tract infections, headache, and arthralgia.

Initial Criteria:

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

- Patient is 18 years or older; AND
- Prescribed by, or in consultation with, a neurologist; AND
- Patient has been evaluated and screened for the presence of hepatitis B virus (HBV) prior to initiating treatment and confirmed negative for active HBV; AND
- Patient serum immunoglobulin baseline measured prior to the start of therapy; AND
- Patient does not have an underlying immunodeficiency disorder (i.e., acquired/congenital primary immunodeficiency, HIV, etc.); AND
- Patient has not received any vaccinations in the 4-weeks prior to the start of therapy; AND

- Patient has been evaluated and screened for the presence of latent TB infection prior to initiating treatment and will receive ongoing monitoring for presence of TB during treatment; AND
- Patient does not have an active infection, including clinically important localized infections; AND
- Will not be administered concurrently with live or live-attenuated vaccines; AND
- Patient is not concomitantly receiving therapy with other immunosuppressant type drugs [i.e., alemtuzumab, natalizumab, cyclosporine, methotrexate, mitoxantrone, cyclophosphamide, tocilizumab, maintenance corticosteroids (not including pre-medications or rescue therapy), etc.] or other immunosuppressant procedures (i.e., total lymphoid irradiation, bone marrow transplant, etc.); AND
- Will not be used in combination with a complement-inhibitor (i.e., eculizumab, ravulizumab) or anti-CD20-directed antibody (i.e., rituximab) or IL-6 inhibitor (e.g., satralizumab) therapies; AND
- Patient has experienced a failure, contraindication, or intolerance to Enspryng (satralizumab)*
  * This requirement **ONLY** applies to **Medicaid** Members

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- 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 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
  - Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies; AND
  - Diagnosis of multiple sclerosis or other diagnoses have been ruled out; AND

- Patient has a history of one or more relapses that required rescue therapy within the year prior to screening, or 2 or more relapses that required rescue therapy in 2 years prior to screening; AND
- Patient has an Expanded Disability Status Score (EDSS) of ≤ 7.5 (i.e., inability to take more than a few steps; restricted to wheelchair and may need aid in transferring; can wheel self but cannot carry on in standard wheelchair for a full day and may require a motorized wheelchair)

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

Continuation of Therapy Criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: serious or life-threatening infusion related reactions, serious infections including PML, hypogammaglobulinemia necessitation IVIG or leading to recurrent infections, etc.; AND
- Disease response as indicated by stabilization/improvement in any of the following: neurologic symptoms as evidenced by a decrease in acute relapses, stability or improvement in EDSS, reduced hospitalizations, and/or reduction in plasma exchange treatments

Coverage durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 12 months

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Uplizna was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Uplizna according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 1 mg)
Neuromyelitis Optica Spectrum Disorder (NMOSD)	Uplizna is administered as an intravenous infusion, as follows: • Initial dose: 300 mg IV infusion followed 2 weeks later by a second 300 mg IV infusion. • Subsequent doses (starting 6 months from the first infusion): single 300 mg IV infusion every 6 months.	300 units on days 1, 15 and then 300 units every 6 months thereafter

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J1823	injection, inebilizumab-cdon, 1mg

References:
1. Uplizna [package insert]. Gaithersburg, MD; Viela Bio, Inc; July 2021. Accessed November 2022.
2. Cree BAC, Bennett JL, Kim HJ, et al; N-MOmentum study investigators. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomised placebo-controlled phase 2/3 trial. Lancet. 2019 Oct 12;394(10206):1352-1363. doi: 10.1016/S0140-6736(19)31817-3. Epub 2019 Sep 5.
3. Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 2014; 261:1.

4. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.