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, 05/21/2025		

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

Scope: Medicaid, Commercial, Medicare

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 and for the treatment of of Immunoglobulin G4-related disease (IgG4-RD) in adult patients. 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. The approval of Uplizna for IgG4-RD was based on a Phase 3 multicenter, double-blind, randomized, placebo-controlled MITIGATE trial, which evaluated the safety and efficacy of Uplizna compared with placebo in adults with active IgG4-RD. The primary efficacy endpoint was the time to First Treated and Adjudication Committee (AC)-determined IgG4-RD flare within the 52-week RCP. The time to the First Treated and AC determined IgG4-RD flare was significantly longer in the Uplinza group, compared with the placebo group. Uplizna reduced the risk of treated and AC-determined IgG4-RD flare by 87%, compared with placebo (hazard ratio: 0.13; $p < 0.0001$). Common adverse events include urinary tract infections, headache, and arthralgia.

Initial Criteria:

Medicare 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 has had baseline serum immunoglobulin 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
- 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
- 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 used in combination with other immunomodulatory biologic therapies or other therapies which can result in prolonged additive immunosuppression (*excluding corticosteroids used as premedication, rescue therapy, or flare treatment*); **AND**

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)
- Patient has experienced failure, contraindication, or intolerance to Enspryng (satralizumab)*

* This requirement **ONLY** applies to **Medicaid** Members

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

Immunoglobulin G4-Related Disease (IgG4-RD) † [1,7-10]

- Patient has a confirmed diagnosis of IgG4-RD (e.g., physical exam findings, imaging results, laboratory tests, pathological findings in involved organ/sites, etc.); AND
- Other conditions that mimic IgG4-RD have been ruled out (e.g., malignancy, infection, other autoimmune disorders, etc.); AND
- Patient is experiencing (or recently experienced) an IgG4-RD flare that required corticosteroid treatment; AND
    - Patient has disease that is refractory to corticosteroids; OR
    - Patient has a contraindication or intolerance to corticosteroid treatment; AND
- Patient is at high risk of recurrent disease flares based on a history of disease in ≥2 organs/sites; AND
- At least one of the following organs are affected:
    - Pancreas, bile ducts/biliary tree, orbits, lungs, kidneys, lacrimal glands, major salivary glands, retroperitoneum, aorta, pachymeninges, and/or thyroid gland

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

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- 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
    - Reduction/discontinuation in plasma exchange treatments

Immunoglobulin G4-Related Disease (IgG4-RD)

- Disease response as indicated by one or more of the following:
  - Reduction in corticosteroid requirement for IgG4-RD flare treatment from baseline
  - Reduction in IgG4-RD flares from baseline
  - Stabilization/improvement in symptoms, physical exam findings, imaging results, laboratory tests, and/or pathological findings in IgG4-RD involved organ/sites compared to baseline

Coverage durations:

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

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare 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 Medicare 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)**
All Indications	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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G36.0	**Neuromyelitis optica [Devic]**
D89.84	**IgG4-related disease**

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:

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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.
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10. Nambiar S, Oliver TI. IgG4-Related Disease. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499825/