Corporate Medical Policy: Inebilizumab-cdon (Uplizna®) **"Notification"** **POLICY EFFECTIVE JANUARY 1, 2026**

Restricted Product(s):

- inebilizumab-cdon (Uplizna®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults who are anti-aquaporin-4 (AQP4) antibody positive
- For the treatment of immunoglobulin G4-related disease (IgG4-RD) in adults

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient has a diagnosis of **neuromyelitis optica spectrum disorder (NMOSD) [medical record documentation required]**; **AND**
    a. The patient is 18 year of age or older; **AND**
    b. The patient is anti-aquaporin-4 (AQP4) antibody seropositive **[medical record documentation required]**; **AND**
    c. The diagnosis has been confirmed by the presence of at least ONE of the following core clinical characteristics **[medical record documentation required]**:
        i. Optic neuritis; **OR**
        ii. Acute myelitis; **OR**
        iii. Area postrema syndrome: Episode of otherwise unexplained hiccups or nausea and vomiting; **OR**
        iv. Acute brainstem syndrome; **OR**
        v. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions; **OR**
        vi. Symptomatic cerebral syndrome with NMOSD-typical brain lesions; **AND**
    d. The patient has had at least ONE attack or relapse in the last 12 months prior to treatment with an immunotherapy or complement inhibitor for NMOSD (e.g., an eculizumab product, inebilizumab, ravulizumab, a rituximab product, satralizumab, etc.) **[medical record documentation required]**; **AND**
    e. The patient does NOT have any other alternative diagnoses to explain or cause the current disease symptoms (e.g., multiple sclerosis, ischemic optic neuropathy, etc.) **[medical record documentation required]**; **AND**

f. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent used in the treatment of NMOSD (e.g., an eculizumab product, ravulizumab, a rituximab product, satralizumab, etc.) **[medical record documentation required]**; **AND**
g. ONE of the following:
    i. The patient has tried and had an inadequate response to satralizumab (Enspryng®) **[medical record documentation required]**; **OR**
    ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to satralizumab (Enspryng®) **[medical record documentation required]**; **OR**

2. The patient has a diagnosis of **immunoglobulin G4-related disease (IgG4-RD) [medical record documentation required]**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The diagnosis has been confirmed by the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Classification Criteria for IgG4-RD (i.e., fulfillment of entry criteria, lack of any exclusion criteria, and ≥ 20 classification criteria inclusion points) **[medical record documentation required]**; **AND**
    c. The patient has IgG4-RD affecting two or more organs/sites at any time in the course of disease (e.g., pancreas, major salivary glands, lacrimal glands, bile ducts/biliary tree, orbits, kidneys, lungs, aorta, retroperitoneum, pachymeninges, thyroid gland [Riedel's thyroiditis]) **[medical record documentation required]**; **AND**
    d. The patient does NOT have any other alternative diagnoses to explain or cause the current disease symptoms (e.g., malignancy, infection, other autoimmune disorders, etc.) **[medical record documentation required]**; **AND**
    e. The patient is experiencing or has recently experienced an IgG4-RD flare that requires initiation or continuation of glucocorticoid treatment, and/or the patient has recurrent disease **[medical record documentation required]**; **AND**
    f. ONE of the following:
        i. The patient has tried and had an inadequate response to glucocorticoids (e.g., ≥ 1 flare, new or worsening symptoms, no reduction in mass/organ size, no improvement in organ function, inadequate decreases in serum IgG4 concentrations from glucocorticoids alone) used in the treatment of IgG4-RD **[medical record documentation required]**; **OR**
        ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to glucocorticoids used in the treatment of IgG4-RD **[medical record documentation required]**; **AND**
    g. The patient will NOT be using the requested agent in combination with a rituximab product used in the treatment of IgG4-RD **[medical record documentation required]**; **AND**

3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist, immunologist, neurologist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
4. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**

5. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

   Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy **[medical record documentation required]**; **AND**
3. For patients with a diagnosis of **neuromyelitis optica spectrum disorder (NMOSD)**:
   a. The patient has had a positive clinical response while using the requested agent, as demonstrated by disease stabilization or improvement (e.g., reduced number of relapses, improvement or stabilization of vision or paralysis) **[medical record documentation required]**; **AND**
   b. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent used in the treatment of NMOSD (e.g., an eculizumab product, ravulizumab, a rituximab product, satralizumab, etc.) **[medical record documentation required]**; **OR**
4. For patients with a diagnosis of **immunoglobulin G4-related disease (IgG4-RD)**:
   a. The patient has had a positive clinical response while using the requested agent (i.e., reduction in number of IgG4-RD flares or no disease activity) **[medical record documentation required]**; **AND**
   b. The patient will NOT be using the requested agent in combination with a rituximab product used in the treatment of IgG4-RD **[medical record documentation required]**; **AND**
5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist, immunologist, neurologist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
6. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
7. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

   Duration of Approval: 365 days (1 year)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
inebilizumab-cdon (Uplizna®) intravenous (IV) infusion	NMOSD in patients ≥18 years old IgG4-RD in patients ≥18 years old	Initial: 300 mg IV followed by 300 mg IV 2 weeks later Subsequent doses (starting 6 months from the first infusion): 300 mg IV every 6 months	J1823	Initial: 900 Continuation: 600

***Maximum units allowed for duration of approval**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
    c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
    d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
    e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
    f. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
    g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Cree BAC, Bennett JL, Kim HJ, et al. 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):1352-63.
2. Stone JH, Khosroshahi A, Zhang W, et al. (MITIGATE Trial Investigators). Inebilizumab for Treatment of IgG4-Related Disease. *N Engl J Med*. 2025 Mar 27;392(12):1168-1177.
3. Wallace ZS, et al. The 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease. *Arthritis Rheumatol*. 2020;72(1):7–19.
4. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015;85(2):177-189.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

January 2026: Criteria change: For NMOSD indication, added requirement of at least one attack or relapse in the last 12 months prior to treatment with an immunotherapy/complement inhibitor for NMOSD, and no other alternative diagnoses to explain or cause the current disease symptoms; adjusted list of drugs not to be used in combination for clarity; adjusted continuation criteria verbiage for clarity. For IgG4-RD indication, added requirement of no other alternative diagnoses to explain or cause the current disease symptoms. For all indications, added requirement to be prescribed by or in consultation with a specialist. Other minor updates made throughout policy for clarity. **Policy notification given 11/1/2025 for effective date 1/1/2026**.
November 2025: Criteria change: Updated Site of Care medical necessity criteria to add additional bypass for patients with a history of severe adverse events or conditions that cause an increased risk for severe adverse event to align with the Place of Service for Medical Infusions policy for clarity of intent.
June 2025: Criteria change: Added new indication for IgG4-RD in adults with corresponding criteria. Updated initial duration of approval to 365 days (1 year) and adjusted maximum units accordingly. Other formatting adjustments made throughout policy for clarity with no change to intent.
October 2021: Criteria change: Added Site of Care medical necessity criteria. **Policy notification given 8/2/2021 for effective date 10/1/2021**.
June 2021: Criteria change: Added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.