

Corporate Medical Policy

Inebilizumab-cdon (Uplizna™)

File Name:	inebilizumab_uplizna
Origination:	9/2020
Last CAP Review:	1/2021
Next CAP Review:	5/2021
Last Review:	2/2021

Description of Procedure or Service

Inebilizumab-cdon (Uplizna) 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.

NMOSD is a relapsing, inflammatory disease of the central nervous system (CNS) that is characterized by severe, immune-mediated demyelination and axonal damage typically affecting the optic nerves and spinal cord. NMOSD presents as recurrent attacks of optic neuritis and myelitis, and such attacks are often associated with poor recovery. Approximately 50% of patients with NMOSD have permanent visual impairment and paralysis caused by NMOSD attacks. The aquaporin-4 (AQP4) autoantibody is a specific biomarker for NMOSD that has been shown to correlate with clinical disease activity and is associated with complement-mediated damage to the CNS. Due to the characteristic progressive deterioration of NMOSD, long-term immunosuppressive therapy (e.g. azathioprine, rituximab, mycophenolate mofetil, mitoxantrone, oral glucocorticoids) is indicated as relapse prevention directly following diagnosis; however, 25-60% of patients continue to have recurrent attacks while receiving these treatments.

Inebilizumab-cdon (Uplizna) was approved by the U.S. Food and Drug Administration (FDA) in June 2020 for the treatment of adult patients with NMOSD who are anti-aquaporin-4 (AQP4) antibody positive. The exact mechanism by which inebilizumab exerts its therapeutic effects in NMOSD is unknown. However, it is thought to work by binding to the CD19 surface antigen present on B-cells, which results in antibody-dependent cellular cytotoxicity.

Related Medical Policies:

Eculizumab (Soliris®)

Related Pharmacy Policies:

Enspryng™

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

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Policy

BCBSNC will provide coverage for inebilizumab-cdon (Uplizna™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Inebilizumab-cdon (Uplizna) is covered

Initial Therapy

Inebilizumab-cdon (Uplizna) may be considered medically necessary for the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) in adults when the following criteria are met:

1. The patient has a diagnosis of NMOSD (see Policy Guidelines); **AND**
- ~~2.~~ The patient is anti-aquaporin-4 (AQP4) antibody seropositive; **AND**
3. The patient will not receive inebilizumab concurrently with other biologics used to treat NMOSD (e.g., eculizumab, satralizumab); **AND**
4. The patient has tried and had an inadequate response to satralizumab (Enspryng); **OR**
5. The patient has a clinical contraindication or intolerance to satralizumab (Enspryng).

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with inebilizumab-cdon (Uplizna) beyond 6 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) when the following criteria are met:

6. The patient has been receiving inebilizumab treatment and continues to meet initial criteria; **AND**
7. The patient has had clinical benefit (i.e., reduction of relapses or disease stabilization) while on inebilizumab treatment.

When Inebilizumab-cdon (Uplizna) is not covered

Inebilizumab-cdon (Uplizna) is considered **investigational** and therefore not covered when the above criteria are not met, and for all other indications not listed above.

Policy Guidelines

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Diagnostic Criteria

The diagnosis of NMOSD is based on the presence of core clinical characteristics, AQP4 antibody status, and magnetic imaging (MRI) neuroimaging features. There are six core clinical characteristics recognized, as described below:

- 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

The diagnosis of NMOSD in patients with AQP4-immunoglobulin G (IgG) antibodies present requires at least one core clinical characteristic present, a positive AQP4-IgG test using the best available detection method, and exclusion of alternative diagnoses.

Inebilizumab-cdon (Uplizna™) is indicated for the treatment of adult patients with neuromyelitis optica spectrum disorder who are anti-aquaporin-4 antibody positive.

Dosing and Administration

The recommended dosing regimen for inebilizumab-cdon (Uplizna™) for adult patients (18 years of age and older) consists of:

- Initial dose: 300 mg intravenous (IV) infusion followed by a second 300 mg IV infusion given 2 weeks later.
- Subsequent doses (starting 6 months from the first infusion): single 300 mg IV infusion given every 6 months.

Uplizna should be administered under close supervision of an experienced healthcare professional with access to appropriate medical support to manage potential severe reactions such as serious infusion reactions. The patient should be monitored closely for infusion reactions during and for at least one hour after the infusion is completed.

Use of Uplizna is contraindicated in patients with a history of life-threatening infusion reactions to Uplizna, active hepatitis B infection, and/or activated or untreated latent tuberculosis. Prior to administering the infusion, patients should be pre-medicated with a corticosteroid, an antihistamine, and an anti-pyretic to reduce the risk of infusion reactions. Hepatitis B virus, quantitative serum immunoglobulins, and tuberculosis screening are required before patients receive the first dose of Uplizna. Prior to each infusion, patients should be assessed to determine if an active infection is present.

Vaccination with live-attenuated or live vaccines is not recommended during Uplizna treatment and after discontinuation until B-cell repletion. All immunizations should be administered according to immunization guidelines at least 4 weeks prior to initiating Uplizna for live or live-attenuated vaccines.

Clinical Trial Evidence

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The efficacy of inebilizumab for the treatment of NMOSD was evaluated in a randomized (3:1), double-blind, placebo-controlled trial (N-MOMentum; NCT02200770) assessing 230 adult patients with NMOSD (with 92% seropositive for anti-AQP4 antibodies). Patients included in the trial were at least 18 years of age with a history of at least one relapse during the previous 12 months requiring rescue therapy or at least two relapses during the previous 24 months requiring rescue therapy. Eligible patients also had to have an Expanded Disability Status Scale (EDSS) score of 8 or less (consistent with the presence of at least limited ambulation with aid). Patients enrolled in the trial were randomized 3:1 to receive either intravenous inebilizumab 300 mg (n=174) or placebo (n=56), administered on days 1 and 15. The primary efficacy endpoint was the time to onset of the first adjudicated relapse on or before Day 197, which occurred in 12% (n=21/174) of patients in the inebilizumab group and 39% (n=22/56) of patients in the placebo group (hazard ratio, 0.27; 95% CI, 0.15 to 0.50; p<0.0001). The time to the first adjudicated relapse was significantly longer in inebilizumab-treated patients compared to placebo-treated patients. In adults with AQP4-IgG-seropositive NMOSD, attacks during 6.5 months of randomized treatment were significantly reduced with inebilizumab compared with placebo. However, there was no significant change in low-contrast visual acuity binocular score from baseline. The clinical trial was ended early after an interim analysis at 6.5 months determined inebilizumab efficacy, as defined by fewer attacks among patients assigned to inebilizumab compared with those receiving placebo.

Certain limitations of the clinical trial include short duration of follow-up and early discontinuation, which can result in overestimation of treatment effect. Further evaluation is needed to establish long-term efficacy and safety of inebilizumab compared to other complement inhibitor treatment for NMOSD.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J1823

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Viela Bio, Inc. Uplizna (inebilizumab-cdon) injection, for intravenous use. Highlights of prescribing information. June 2020. Available at: https://www.uplizna.com/Uplizna_Prescribing_Information.pdf. Last accessed August 2020.

U.S. Food and Drug Administration. FDA approves new therapy for rare disease affecting optic nerve, spinal cord: Second FDA approved therapy for neuromyelitis optica spectrum disorder offers patients additional treatment option. June 11, 2020. Available at: <https://www.fda.gov/news->

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[events/press-announcements/fda-approves-new-therapy-rare-disease-affecting-optic-nerve-spinal-cord](#).
Last accessed August 2020.

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. Epub 2019 Sep 5.

Medical Director review 9/2020

Blue Cross NC Pharmacy and Therapeutics Committee 1/2021

Medical Director review 2/2021

Policy Implementation/Update Information

- 9/22/20 New policy developed. Uplizna may be considered medically necessary for the treatment of adults with NMOSD when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, and J3590 to Billing/Coding section. References added. Medical Director review 9/2020. (krc)
- 12/31/20 Added HCPCS code J1823 to Billing/Coding section effective 1/1/2021 and deleted codes C9399, J3490, and J3590 termed 12/31/2020. (krc)
- 2/9/21 Removed the following criteria from “When Covered” section: “patient has a history of at least one relapse requiring rescue therapy during the previous 12 months OR at least two relapses requiring rescue therapy during the previous 24 months.” Blue Cross NC Pharmacy and Therapeutics Committee 1/5/2021. Medical Director review 2/2021. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.