09-J3000-73

Original Effective Date: 10/01/20

Reviewed: 04/10/24

Revised: 05/15/24

Subject: Inebilizumab (Uplizna) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, severe inflammatory, autoimmune disease of the central nervous system. Clinical core characteristics may include attacks involving optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy, or symptomatic cerebral syndrome. At least one clinical attack is required to establish diagnosis which may be confirmed by the presence of an antibody against the astrocyte water channel aquaporin-4 (AQP4) and exclusion of other diagnoses. When AQP4 is negative or not detected, the diagnosis is more complex and requires more 2 or more clinical characteristics in different anatomic regions, with corresponding MRI requirements. AQP4 positive patients are at risk for relapse and preventative treatment should be considered. Immunosuppresants such as azathioprine, corticosteroids, mycophenolate mofetil, and rituximab have been used historically to prevent attacks.

Inebilizumab (Uplizna™) is Food and Drug Administration (FDA) approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. Inebilizumab binds to CD19, a surface cell antigen on B lymphocytes which results in antibody dependent cellular disruption.

The efficacy of inebilizumab for NMOSD was evaluated in randomized, double-blind, placebo-controlled trial that enrolled 213 patients with anti-APQ4 antibody positive disease and 17 who were negative. Patients were required to have a history of at least one relapse that required treatment in the year prior to screening, or at least 2 relapses that required treatment 2 years prior. Patients had an Expanded Disability Status Scale (EDSS) score of 7.5 or less or a score of 8 if deemed eligible to participate. Inebilizumab was administered as two separate 300 mg intravenous infusions on days 1 and 15. All patients received oral corticosteroids on days 1 through 14 and tapered to day 21 to prevent risk of attack following the first infusion. Of the 161 patients who were treated with inebilizumab who were anti-AQP4 antibody positive, the time to first relapse was significantly longer and the proportion of

patients with relapse by day 197 was less as compared to placebo (11.2% vs 42.3%, HR 0.227). The risk of relapse was reduced by 77% compared to placebo. There was improvement with inebilizumab as compared to placebo in annualized rate of hospitalization, worsening in EDSS score from baseline, and number of active MRI lesions from baseline. There was no difference in change of low-contrast visual acuity binocular score from baseline. The effects could not be determined in subjects who were AQP4 negative due to low enrollment. The most common adverse reactions were urinary tract infection, nasopharyngitis, infusion reaction, arthralgia, headache, and back pain. There was a higher proportion of inebilizumab treated patients that experienced with a reduction from baseline in the total immunoglobulin levels (IgG or IgM) or a neutrophil count below the limit of normal.

POSITION STATEMENT:

Initiation of inebilizumab (Uplizna) **meets the definition of medical necessity** when used to treat **t**he following indications and the indication-specific criteria are met:

1. Neuromyelitis Optica Spectrum Disorder (NMOSD)
    a. Member meets ALL of the following - documentation must be provided:
        i. Member has anti-aquaporin-4 (AQP4) antibody positive disease – lab documentation must be provided
        ii. Member has **ONE** core clinical characteristic of NMOSD and alternative diagnoses have been excluded:
            1. Optic neuritis
            2. Acute myelitis
            3. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting)
            4. Acute brainstem syndrome
            5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
            6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions
        iii. Member has a history of at least 1 relapse in the previous year†
        iv. Member had an inadequate response to a sufficient trial of, or has a contraindication to, rituximab therapy†
    b. Member does not have an active hepatitis B infection
    c. Member does not have active or untreated latent tuberculosis
    d. Inebilizumab will not be used concurrently with an alternative biologic agent for the treatment of NMOSD (e.g., eculizumab, ravulizumab, rituximab, satralizumab, tocilizumab)
    e. Treatment is prescribed by or in consultation with a neurologist
    f. The first dose does not exceed 300 mg, followed by 300 mg two weeks later and the maintenance dosing does not exceed 300 mg every 6 months

Approval duration: 8 months

Continuation of inebilizumab (Uplizna) **meets the definition of medical necessity** when **ALL** of the following are met:

1. An authorization or reauthorization for inebilizumab has been previously approved for the treatment of NMOSD by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
2. The member has a history of beneficial response (e.g., absence or reduction in relapses) to inebilizumab therapy for the treatment of NMOSD – documentation must be provided
3. The member has anti-aquaporin-4 (AQP4) antibody positive disease – lab documentation must be provided
4. Member does not have an active hepatitis B infection
5. Member does not have active or untreated latent tuberculosis
6. Inebilizumab will not be used concurrently with an alternative biologic agent for the treatment of NMOSD (e.g., eculizumab, ravulizumab, rituximab, satralizumab, tocilizumab)
7. Treatment is prescribed by or in consultation with a neurologist
8. The dose does not exceed 300 mg every 6 months

Approval duration: 1 year

[†]Step not required if the member previously received treatment with eculizumab (Soliris), ravulizumab (Ultomiris), or satralizumab (Enspryng)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults who are anti-aquaporin-4 (AQP4) positive
    - Initial dose: 300 mg IV infusion over 90 minutes followed two weeks later by a second 300 mg infusion
    - Subsequent doses: 300 mg starting six months from the first infusion and every 6 months thereafter
- Prior to the first dose, assess the member for hepatitis B, serum immunoglobulins, tuberculosis, and infection.
- Prior to each infusion, assess if there is active infection.
- Administer pre-medication with a corticosteroid, an antihistamine, and an anti-pyretic prior to each infusion.

- Monitor patients during the infusion and for at least one hour after completion.

Dose Adjustments

- None

Drug Availability

- 100 mg/10 mL (10 mg/mL) single dose vial

PRECAUTIONS:

Boxed Warning

Contraindications

- History of life-threatening reaction
- Active hepatitis B infection
- Active or untreated latent tuberculosis

Precautions/Warnings

- Infusion reactions may occur which include headache, nausea, somnolence, dyspnea, fever, myalgia, rash and other symptoms. Administer pre-medication with a corticosteroid, an antihistamine, and an anti-pyretic.
- Infections may occur: delay administration in patients with an active infection until infection has resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation.
- Reduction in immunoglobulins: progressive or prolonged hypogammaglobulinemia or decline in the total and individual immunoglobulins (IgG and IgM) may occur with continued treatment. Monitor levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections.
- Fetal risk due to B-cell lymphopenia and reduction of antibody response in offspring. Use contraception while receiving inebilizumab and for at least 6 months after the last dose.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1823	Injection, inebilizumab-cdon, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

G36.0	Neuromyelitis optica [Devic]

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

RELATED GUIDELINES:

Eculizumab (Soliris), 09-J1000-17

Ravulizumab (Ultomiris), 09-J3000-26

Rituximab products and rituximab hyaluronidase (Rituxan Hycela), 09-J0000-59

Satralizumab (Enspryng), 09-J3000-79

OTHER:

None.

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.;2023. URL www.clinicalpharmacilogy-ip.com Accessed 03/29/24.
2. Cree BA, Bennett JL, Kim HJ et al. Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-MOmentum): a double-blind, randomized placebo-controlled phase 2/3 trial. Lancet. 2019; 394: 1352 – 1363.
3. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 03/29/24.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2023 [2023 July 27]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Uplinza (inebilizumab) [package insert]. Viela Bio, Inc. Gaithersburg (MD): July 2021.
6. Wingerchuck DM, Banwell B, Bennett JL et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85 (2): 177-89.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/10/24.

GUIDELINE UPDATE INFORMATION:

10/01/20	New Medical Coverage Guideline.
11/15/20	Revision to position statement.
01/01/21	Revision: Added HCPCS code J1823 and deleted code J3590.
10/15/21	Review and revision to guideline; consisting of updating references.
07/15/22	Review and revision to guideline; consisting of updating the position statement and references.
09/15/23	Review and revision to guideline; consisting of updating the references.
05/15/24	Review and revision to guideline; consisting of updating the position statement to remove requirement for alternative immunosuppressant therapy.