Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Uplizna™ (inebilizumab)

HCPCS: J1823

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with a neurologist
   d. Must not be used in combination with Soliris®, Enspryng™, or other medications to treat neuromyelitis optica spectrum disorder (NMOSD)
   e. Adequate trial and failure of, contraindication, or intolerance to Enspryng
   f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 1 year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Neuromyelitis optica spectrum disorders (NMOSD) are inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage mainly of the optic nerves and spinal cord. NMOSD is thought to be primarily mediated by the humoral immune system and the autoantibody aquaporin-4 (AQP4) which is released by B-cells and plasma blasts. Serum anti-AQP4 levels have been shown to correlate with disease activity, decrease after immunosuppressive therapy, and remain low during remissions.

- Uplizna is indicated for the treatment of neuromyelitis optica spectrum disorder in adult patients who are anti-AQP4 antibody positive. Uplizna should be started with a loading dose of 300 mg at weeks 0 and 2 followed by 300 mg every 6 months starting from the first infusion thereafter.

- Safety and efficacy were established in the multicenter, double-blind, randomized placebo-controlled, phase 2/3 N-Momentum study of 230 patients with NMOSD. In the trial, 213 of the 230 patients were anti-AQP4 antibody positive. Patients were included if they had a history of at least one attack requiring rescue therapy in the prior year and had an Expanded Disability Status Scale score of less than or equal to 7.5. Patients were randomized to receive 300 mg of Uplizna on day 1 and 15 followed by every 6 months thereafter or placebo in a 3:1 ratio. The primary endpoint was the time to the onset of the first adjudicated relapse on or before day 197. The risk of an NMOSD relapse in the 161 anti-AQP4 antibody positive patients who were treated with Uplizna was reduced by 77% when compared to the placebo treatment group ($p < 0.0001$). There was no evidence of a benefit in patients who were anti-AQP4 antibody negative.

- Uplizna has not been studied and there is no data to support use in combination with other medications used to treat NMOSD, such as Rituxan®, Enspryng, or Soliris.

- No American treatment guidelines are available for neuromyelitis optica spectrum disorders. The European Federation of Neurological Societies published guidelines for the diagnosis and management of neuromyelitis optica in 2010. Long-term treatment options should be initiated as soon as the diagnosis is made to prevent attacks and reduce the risk of permanent disability, but evidence from randomized-controlled trials for any particular medication is lacking. The guidelines recommend azathioprine plus prednisone or rituximab as first-line therapy to prevent attacks. If first-line treatment is ineffective or the patient develops steroid-dependence for clinical remission, alternative immunosuppressive therapies need to be considered. Second-line therapy includes cyclophosphamide, mitoxantrone, methotrexate, IVIG, mycophenolate mofetil, and intermittent plasma exchange. The guidelines have not been updated to include Uplizna, Soliris, or Enspryng.

- While a variety of immunosuppressive therapies are regarded as first-line therapy based on primarily observational or single-arm data, use has fallen out of favor due to lack of efficacy. The most widely prescribed treatments include azathioprine and mycophenolate mofetil. However, if given, they are often prescribed with low doses of corticosteroids to treat the relapse and the steroids are weaned slowly.

- Rituximab targets the CD20 antigen on B-cells and leads to profound B-cell depletion, principally over an antibody-dependent cell cytotoxicity mechanism and decreases attack frequency and severity in patients with NMOSD. Most of the investigations revealed that Expanded Disability Status Score (EDSS) improved significantly in all patients with rituximab treatment after treatment with rituximab and relapse rates decreased by up to 88%. No new or enlarged lesions or pathological gadolinium enhancement was observed in serial brain and spinal cord MRIs, except for those observed concomitantly with clinical relapses and the median length of spinal cord lesions was significantly reduced after therapy. Paradoxical relapses may occur shortly after initiation of rituximab therapy so it is important to allow enough time for the rituximab to become effective. Complete suppression of CD19-positive B-lymphocytes takes one month.

- There are multiple options for the long-term treatment of NMOSD. There an no clinical trials comparing the efficacy of one therapy to another. Choice of therapy should be based on patient characteristics, side effect profiles, cost, and availability.

References:

1. Uplizna [prescribing information]. Gaithersburg, MD; Viela Bio, Inc.; July 2021.
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4. Soliris [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc.; November 2020.
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7. VielaBio. Potential first-line therapy for patients with NMOSD and other diseases sharing the autoantibody pathway. Available at: https://vielabio.com/product-candidates/inebilizumab/. Accessed on February 18, 2020.
8. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in aquaporin-4 positive neuromyelitis optica spectrum disorder. *NEJM*. 2019 May 3. Doi: 10.1056/NEJMoa1900866.
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14. Etemadifar M, Salari M, Mirmosayyeb O, et al. Efficacy and safety of rituximab in neuromyelitis optica: review of evidence. J Res Med Sci. 2017; 22: 18.
15. IPD Analytics. Enspryng (satralizumab-mwge) New Drug Review. September 2020.

Policy History		
#	Date	Change Description
1.9	Effective Date: 04/11/2024	Annual review of criteria was performed, no changes were made
1.8	Effective Date: 04/06/2023	Updated to remove the step through Rituxan or a rituximab biosimilar
1.7	Effective Date: 12/01/2022	Annual review of criteria was performed, no changes were made
1.6	Effective Date: 12/09/2021	Annual review of criteria was performed, no changes were made
1.5	Effective Date: 12/03/2020	Updated to require trail and failure of rituximab or a rituximab biosimilar and Enspryng; removed relapse requirement, EDSS score requirement, and negative TB and Hep B testing requirements; updated renewal period to 1 year at a time and renewal criteria to show clinical benefit

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<tr><td>1.4</td><td>Effective Date: 10/01/2020</td><td>UM medical management system update for BCBSM
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.3</td><td>Effective Date: 08/21/2020</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date: 8/13/2020</td><td>New Policy</td></tr>
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<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.0</td><td>Effective Date: 04/16/2020</td><td>Preliminary drug review
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Uplizna™ (inebilizumab-cdon) HCPCS CODE: J1823

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Uplizna. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation ***Date patient started therapy***: _____

2. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #3) R*eason for Hospital Outpatient administration:* _____

3. Please specify location of administration if hospital outpatient infusion: _____

4. Please provide the NPI number for the place of administration: _____

5. **Initiation AND Continuation of therapy:**

   a. Please check the patient's diagnosis: ☐ Neuromyelitis optica spectrum disorder (NMOSD) ☐ Other: _____

   b. Is the patient aquaporin-4 (AQP4) antibody positive? ☐ Yes ☐ No Comment: _____

   c. Will the patient be receiving Uplizna in combination with Soliris, Enspryng or any other medication to treat NMOSD?
   ☐ Yes ☐ No Comment: _____

   d. What medications has the patient tried and failed?
   ☐ Enspryng
   ☐ Rituximab (Rituxan, truxima, Ruxience, Riabni)
   ☐ Other: _____

6. **Continuation request:** Uplizna start date _____
   a. Has the patient's condition improved while on therapy with Uplizna?
   ☐ Yes ☐ No Comment _____

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	**Physician Signature**	**Date**
Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Concurrent Medical Problems ☐ Prior Therapies
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

8/1/2020; 12/3/2020