



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: 12/09/2021**

### **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 an adequate trial of, contraindication, or intolerance to rituximab/rituximab biosimilar and 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 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

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

(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 a 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 are 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.
2. Wilson R, Makuch M, Kienzler AK, et al. Condition-dependent generation of aquaporin-4 antibodies from circulating B cells in neuromyelitis optica. *Brain*. April 2018; 141(4): 1063–74.
3. Cree BAC, 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 Oct 12; 394(10206): 1353 – 63.
4. Soliris [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc.; November 2020.
5. Enspryng [prescribing information]. South San Francisco, CA: Genentech, Inc.; August 2020.
6. Wilson R, Makuch M, Kienzler AK, et al. Condition-dependent generation of aquaporin-4 antibodies from circulating B cells in neuromyelitis optica. *Brain*. April 2018; 141(4): 1063–74.
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.
9. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. *EJN*. 2010; 17: 1019 – 32.
10. Sherman E and Han MH. Acute and chronic management of neuromyelitis optica spectrum disorder. *Curr Treat Options Neurol*. 2015; 17(11): 48 – 62.
11. Gardner J. AstraZeneca spinout wins first FDA approval 2 years after launch. Available at: <https://www.biopharmadive.com/news/viela-bio-uplinza-fda-approval/579750/>. Accessed on June 14, 2020.
12. Nikoo Z, Badihian S, Shaygannejad V, et al. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica spectrum disorder: a randomized clinical trial. *J Neuro*. 2017; 264: 2003 - 9.
13. Damato V, Evoli A, & Iorio R. Efficacy and safety of rituximab therapy in neuromyelitis optica spectrum disorders: a systematic review and meta-analysis. *JAMA Neurol*. 2016; 73: 1342 - 8.
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   |                  |   |      |     |     |     |       |     |      |     |
| 1.6              | Effective Date:<br>12/09/2021                     | Annual review of criteria was performed, no changes were made  |                  |   |      |     |     |     |       |     |      |     |
| 1.5              | Effective Date:<br>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  |                  |   |      |     |     |     |       |     |      |     |
| 1.4              | Effective Date:<br>10/01/2020                     | UM medical management system update for BCBSM <table border="1" data-bbox="483 493 1362 703"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>         | Line of Business | PA Required in Medical Management System (Yes/No) | BCBS | Yes | BCN | Yes | MAPPO | Yes | BCNA | Yes |
| Line of Business | PA Required in Medical Management System (Yes/No) |  |                  |   |      |     |     |     |       |     |      |     |
| BCBS             | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| BCN              | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| MAPPO            | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| BCNA             | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| 1.3              | Effective Date:<br>08/21/2020                     | UM medical management system update for MAPPO and BCNA <table border="1" data-bbox="483 787 1362 997"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table> | Line of Business | PA Required in Medical Management System (Yes/No) | BCBS | No  | BCN | Yes | MAPPO | Yes | BCNA | Yes |
| Line of Business | PA Required in Medical Management System (Yes/No) |  |                  |   |      |     |     |     |       |     |      |     |
| BCBS             | No  |  |                  |   |      |     |     |     |       |     |      |     |
| BCN              | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| MAPPO            | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| BCNA             | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| 1.2              | Effective Date:<br>8/13/2020                      | New Policy   |                  |   |      |     |     |     |       |     |      |     |
| 1.1              | Effective Date<br>08/1/2020                       | UM medical management system update for BCN <table border="1" data-bbox="483 1171 1362 1381"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <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> </tbody> </table>            | Line of Business | PA Required in Medical Management System (Yes/No) | BCBS | No  | BCN | Yes | MAPPO | No  | BCNA | No  |
| Line of Business | PA Required in Medical Management System (Yes/No) |  |                  |   |      |     |     |     |       |     |      |     |
| BCBS             | No  |  |                  |   |      |     |     |     |       |     |      |     |
| BCN              | Yes   |  |                  |   |      |     |     |     |       |     |      |     |
| MAPPO            | No  |  |                  |   |      |     |     |     |       |     |      |     |
| BCNA             | No  |  |                  |   |      |     |     |     |       |     |      |     |
| 1.0              | Effective Date:<br>04/16/2020                     | Preliminary drug review <table border="1" data-bbox="483 1465 1362 1675"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>No</td> </tr> <tr> <td>BCN</td> <td>No</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>                                 | Line of Business | PA Required in Medical Management System (Yes/No) | BCBS | No  | BCN | No  | MAPPO | No  | BCNA | No  |
| Line of Business | PA Required in Medical Management System (Yes/No) |  |                  |   |      |     |     |     |       |     |      |     |
| BCBS             | No  |  |                  |   |      |     |     |     |       |     |      |     |
| BCN              | No  |  |                  |   |      |     |     |     |       |     |      |     |
| MAPPO            | No  |  |                  |   |      |     |     |     |       |     |      |     |
| BCNA             | No  |  |                  |   |      |     |     |     |       |     |      |     |

\* 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>.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.