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P&T Date: 06/05/2025

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. Diagnosis of neuromyelitis optica spectrum disorder (NMOSD)
      i. Prescribed by or in consultation with a neurologist
      ii. Must not be used in combination with Soliris®, Enspryng™, or other medications to treat NMOSD
      iii. Adequate trial and failure of, contraindication, or intolerance to Enspryng
   d. Diagnosis of IgG4 related disease (IgG4-RD)
      i. Confirmation of diagnosis with a score greater than or equal to 20 on the 2019 ACR/EULAR Classification Criteria for IgG4-RD
      ii. Trial and failure, contraindication, or intolerance to prednisone at a dose of a least 30 mg/day
      iii. Trial and failure, contraindication, or intolerance to a steroid sparing agent or rituximab or a rituximab biosimiliar
   e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in WyoBlue Advantage'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)

    - Neuromyelitis optica spectrum disorders 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.

- IgG4 related disease (IgG4-RD)

  - IgG4-RD is a recently established systemic disease that is characteristically associated with elevated serum IgG4 levels and believed to be caused by autoimmune mechanisms. The clinical features of IgG4-RD include systemic distribution; imaging findings of swelling, nodules, and/or wall thickening; high serum IgG4 levels; abundant IgG4-bearing plasma cell infiltration and fibrosis in affected organs; a favorable response to corticosteroid therapy; and coexistence with other IgG4-RD manifestations simultaneously or in a metachronous fashion. The systemic distribution of IgG4-RD seems to be capable of affecting every organ causing issues including autoimmune pancreatitis, Mikulicz's disease, respiratory disease, sclerosing cholangitis, kidney disease, and retroperitoneal fibrosis.

  - High serum IgG4 levels and increased IgG4-bearing plasma cell infiltration in affected organs are the most important characteristic features of IgG4-RD and the major indicators in the diagnostic process. However, because these findings are similar for other inflammatory or malignant conditions, their presence does not necessarily exclude other disorders. In addition, while other clinical, serologic, radiologic, and pathologic features all contribute to the classification of IgG4-RD, none of these approaches alone provides definitive evidence for the diagnosis of patients. Therefore, in 2019, the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) developed an international set of classification criteria for IgG4-RD. The 3 step classification process includes demonstration that a potential IgG4-RD case has involvement of at least 1 of 11 possible organs in a manner consistent with IgG4-RD; exclusion criteria consisting of a total of 32 clinical, serologic, radiologic, and pathologic items that if present eliminates the patient from IgG4-RD classification; and 8 weighted inclusion criteria domains addressing clinical findings, serologic results, radiology assessments, and pathology interpretations. A score on the classification system of greater than or equal to 20 correlates to an IgG4-RD diagnosis with a specificity of 99.2% (95% CI: 97.2%, 99.8%) and a sensitivity of 85.5% (95% CI: 81.9%, 88.5%).

  - The 2015 International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease recommend treatment with 30 – 40 mg/day of prednisone as first-line treatment for remission induction in all patients with active, untreated IgG4-RD. Typically the initial glucocorticoid dose should be maintained for 2 – 4 weeks after which it can be tapered gradually. The goal of induction therapy for many patients is to discontinue glucocorticoid use 3 – 6 months after the start of treatment, however, many clinicians recommend the use of low-dose glucocorticoid maintenance therapy for up to 3 years. Retreatment with glucocorticoids is indicated in patients who relapse off of treatment following successful remission induction.

  - Following a successful course of induction therapy for certain high-risk patients or after a relapse, patients can benefit from maintenance therapy. The introduction of a steroid-sparing agent, such as, azathioprine, mycophenolate mofetil, methotrexate, tacrolimus, cyclophosphamide, or rituximab for continuation in the remission maintenance period can be considered. Patients with multiorgan disease, significantly elevated serum IgG4 concentrations, involvement of the proximal bile ducts, and a history of disease relapse are at higher risk of early recurrence following remission induction and can benefit from addition of steroid sparing agents from the start of glucocorticoid inducation. Patients with organ-threatening IgG4-RD manifestations and those with an elevated risk of relapse will also likely benefit from maintenance therapy in an effort to minimize morbidity.

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Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** 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.*