

**Policy and Procedure**

<p align="center"><b>PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCOTH038.1025</b></p>	<p align="center"><b>MISCELLANEOUS PRODUCTS UPLIZNA® (inebilizumab injection)</b></p>
<p><b>Effective Date: 1/1/2026</b></p>	<p><b>Review/Revised Date:</b> 07/21, 09/22, 09/23, 08/24, 08/25, 10/25 (ML)</p>
<p><b>Original Effective Date: 01/21</b></p>	<p><b>P&amp;T Committee Meeting Date:</b> 10/20, 08/21, 10/22, 10/23, 10/24, 10/25</p>
<p><b>Approved by: Oregon Region Pharmacy and Therapeutics Committee</b></p>	

**SCOPE:**

Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**

Medicare Part B

**POLICY CRITERIA:****COVERED USES:**

All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

**REQUIRED MEDICAL INFORMATION:****For ALL REQUESTS:**

1. Dose and frequency must be in accordance with FDA-approved labeling
2. The requested agent must not be given concurrently with another Complement Inhibitor (for example Ultomiris® or Empaveli®), or neonatal Fc receptor blocker (for example, Rystiggo®, Vyvgart®, Vyvgart Hytrulo®)

**For initiation of therapy (new starts) for neuromyelitis optica spectrum disorder (NMOSD), all of the following must be met:**

1. Presence of at least one core clinical characteristic (optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, symptomatic cerebral syndrome with NMOSD-typical brain lesions)
2. Anti-AQP4 antibody positive
3. Documentation that other alternative diagnoses have been excluded (such as multiple sclerosis)
4. Trial and failure, intolerance, or contraindication to rituximab and satralizumab (Enspryng®)

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**For initiation of therapy (new starts) for immunoglobulin G4-related disease (IgG4-RD), all of the following must be met:**

1. Confirmed diagnosis of IgG4-RD
2. Documentation of a history of IgG4-RD affecting at least 2 organ systems/sites
3. Documentation of current or recently experienced IgG4-RD flare requiring initiation or continuation of glucocorticoid treatment

**For patients established on therapy (within the previous year) the following indication-specific criteria must be met:**

1. For neuromyelitis optica spectrum disorder (NMOSD): Documentation of positive clinical response to therapy as defined by a reduction in relapses
2. For immunoglobulin G4-related disease (IgG4-RD): Documentation of positive clinical response to therapy as defined by a reduction in the frequency of disease flares or reduction in need for glucocorticoid treatment

**EXCLUSION CRITERIA:** N/A

**AGE RESTRICTIONS:**

May be approved for patients aged 18 years and older

**PRESCRIBER RESTRICTIONS:**

For NMOSD: Must be prescribed by, or in consultation with, a neurologist

For IgG4-RD: Must be prescribed by, or in consultation with, a rheumatologist, immunologist, endocrinologist, nephrologist, hepatologist

**COVERAGE DURATION:**

Initial authorization will be approved for three months. Reauthorization will be approved for one year.

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*Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.*

*Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.*

*Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.*

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**INTRODUCTION:**

Uplizna® is a humanized monoclonal antibody that binds to the CD19 surface antigen of B cells resulting in depletion of lymphocytes derived from B cell lineage. Evidence suggests that Neuromyelitis Optica Spectrum Disorder (NMOSD) is predominantly a B cell-mediated disorder resulting from pathological autoantibody production, pro-inflammatory cytokine secretion, and B-cell antigen presentation.

**FDA APPROVED INDICATIONS:**

1. For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.
2. For the treatment of immunoglobulin G4-related disease (IgG4-RD) in adult patients.

**POSITION STATEMENT:**

***Neuromyelitis Optica Spectrum Disorder (NMOSD)***

Neuromyelitis Optica Spectrum Disorder (NMOSD), previously known as Devic disease or neuromyelitis optica (NMO), is an autoimmune inflammatory disorder of the central nervous system. It is primarily characterized by recurrent optic neuritis and myelitis often resulting in poor recovery. Aquaporin-4 (AQP4) is a water channel protein that astrocytes in the central nervous system express. Preclinical data indicate that AQP4-IgG triggers the complement cascade, which leads to inflammation and the formation of the membrane attack complex. The membrane attack complex leads to astrocyte destruction and neuronal injury but is not seen in experimental models in the presence of a complement inhibitor. Diagnostic criteria for NMOSD require at least one core clinical characteristic (e.g., optic neuritis, acute myelitis, area postrema syndrome).<sup>4</sup> AQP4 autoantibodies are detected in approximately 80% of patients with NMOSD.<sup>5</sup>

Although off-label, azathioprine and mycophenolate mofetil have been utilized to effectively reduce NMOSD attacks for over 20 years in patients with both AQP4-IgG-positive and -negative patients. They are both considered inferior to rituximab.<sup>24</sup>

There are four monoclonal antibody immunotherapies approved for patients with AQP4-IgG-positive NMOSD which have shown efficacy in the treatment of AQP4-IgG-positive NMOSD, eculizumab, inebilizumab, satralizumab, and ravulizumab. Their targets are as follows:

- Eculizumab: complement protein C5
- Inebilizumab: B cells through the CD19 antigen
- Ravulizumab: complement protein C5
- Satralizumab: Interleukin-6 (IL6)<sup>5</sup>

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Of note, the efficacy of rituximab in reducing NMOSD attacks by over 80% has been demonstrated by multiple studies over the last 15 years with one of the most recent studies resulting in its approval for NMOSD in Japan.<sup>5</sup>

Due to the rarity of the condition, comparator trials would not be feasible as thousands of patients would need to be enrolled.<sup>5</sup>

***Immunoglobulin (Ig) G4-related disease (IgG4-RD)***

IgG4-RD is a fibroinflammatory condition characterized by elevated levels of IgG4 and tumor-like lesions. IgG4-RD can affect any organ, but most commonly affects the pancreas, kidneys, orbital structures, salivary glands, and retroperitoneum.<sup>7</sup>

The standard of care for IgG4-RD is corticosteroids. For those that do not tolerate or lack an appropriate response to steroids, steroid-sparing disease-modifying antirheumatic drugs, such as mycophenolate, azathioprine, methotrexate, may be used.<sup>8</sup>

**REFERENCE/RESOURCES:**

1. Uplizna (inebilizumab) package insert. Dublin (Ireland): Horizon Therapeutics Ireland DAC; 2025 Apr.
2. Inebilizumab In: DRUGDEX® System [Internet database]. Ann Arbor, MI: Merative Micromedex. Updated periodically. Accessed August 8, 2025.
3. Inebilizumab In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed August 8, 2025.
4. Wingerchuk DM, Banwell B, Bennet JL et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015;85(2).
5. Kumpfel T, Gighuber K, Aktas O. Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) – revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. *J Neuro* 2024;271:141-176.
6. Yang X, Zhang S, Feng J et al. Advances in the treatment of neuromyelitis optic spectrum disorder. *The Adv Neurol Disord*. 2025;18:1-13.
7. Floreani A, et al. IgG4-related disease: changing epidemiology and new thoughts on a multisystem disease. *J Transl Autoimmun*. 2020;4:100074.
8. Khosroshahi A, et al. International consensus guidance statement on the management and treatment of IgG4-related disease. *Arthritis Rheumatol*. 2015;67(7):1688–1699.

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**Billing and Coding Table**

<b>HCPCS</b>	<b>Coding Description</b>	<b>Brand Name</b>
J1823	Injection, inebilizumab-cdon, 1 mg	Uplizna®
<b>ADMINISTRATION CODES</b> ◇		
96365	Ther/proph/diag iv inf init	
96366	Ther/proph/diag iv inf addon	
96413	Chemo iv infusion 1 hr	
96415	Chemo iv infusion addl hr	

◇ Coding/Administration Notes:

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.