Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCOTH038.1024	**MISCELLANEOUS PRODUCTS** **UPLIZNA®** (inebilizumab injection)
Effective Date: 1/1/2025	**Review/Revised Date**: 07/21, 09/22, 09/23, 08/24 (KN)
Original Effective Date: 01/21	**P&T Committee Meeting Date**: 10/20, 08/21, 10/22, 10/23, 10/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

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®)

For patients established on therapy (within the previous year) for Neuromyelitis Optica Spectrum Disorder (NMOSD):

1. Documentation of positive clinical response to therapy as defined by a reduction in relapses

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS:
May be approved for patients aged 18 years and older

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, a neurologist

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

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.

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:
For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

POSITION STATEMENT:

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).[4] AQP4 autoantibodies are detected in approximately 80% of patients with NMOSD.[5]

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.[24]

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)[5]

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.[5]

Due to the rarity of the condition, comparator trials would not be feasible as thousands of patients would need to be enrolled.[5]

REFERENCE/RESOURCES:

1. Uplizna (inebilizumab) package insert. Gaithersburg, MD: Viela Bio, Inc; Revised June 2020.
2. Inebilizumab In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed September 15, 2022.
3. Inebilizumab In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-

Comp, Inc. Updated periodically. Accessed September 15, 2022.
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, Giglhuber 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.

CODING

Brand Name	Generic Name	Procedure Code
Uplizna®	inebilizumab injection	J1823