BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**PHARMACY COVERAGE GUIDELINE**

# ENSPRYNG™ (satralizumab-mwge) subcutaneous injection Generic Equivalent (if available)

**This Pharmacy Coverage Guideline (PCG):**
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

**Scope**
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

**Instructions & Guidance**
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

## Criteria:

➢ **Criteria for initial therapy:** Enspryng (satralizumab-mwge) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of neuromyelitis optica spectrum disorder (NMOSD)
4. Individual has had at least 1 relapse in the previous 12-months [Note: Criterion may be waived if individual has documented contraindication to rituximab]

ORIGINAL EFFECTIVE DATE: 11/19/2020 | ARCHIVE DATE: | LAST REVIEW DATE: 08/15/2024 | LAST CRITERIA REVISION DATE: 08/15/2024

5. Individual is anti-aquaporin-4 (AQP4) antibody positive

6. Attacks of NMOSD consist of at least **ONE** of the following core clinical features:
    a. Optic neuritis
    b. Acute myelitis
    c. Area postrema syndrome (episodes unexplained intractable hiccups or nausea and vomiting)
    d. Acute brainstem syndrome
    e. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
    f. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

7. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring as clinically appropriate:
    a. Hepatitis B screening
    b. Tuberculosis screening
    c. Liver transaminases and serum bilirubin

8. Individual has failure (trial of at least 3 months), contraindication, intolerance, or is not a candidate for **rituximab** [Note: Criterion may be waived if individual has documented failure of Soliris, Ultomiris, or Uplizna due to lack of efficacy]

9. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

10. There are **NO** FDA-label contraindications such as:
    a. Active hepatitis B infection that is confirmed by positive results for surface antigen (HSsAg) and anti-HBV tests
    b. Active or untreated latent tuberculosis

11. Individual will not be receiving Enspryng in combination with other immunosuppressive drugs (e.g., Actemra, Kesimpta, Ocrevus, Rinvoq, rituximab, Soliris, Ultomiris, Uplizna, etc.)

12. Will not be used in an individual with an active infection including localized infections until the infection is resolved

13. Will not be used with live-attenuated or live vaccines

**Initial approval duration**: 6 months

- **Criteria for continuation of coverage (renewal request):** Enspryng (satralizumab-mwge) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual has a confirmed diagnosis of neuromyelitis optica spectrum disorder (NMOSD) and is anti-aquaporin-4 (AQP4) antibody positive

3. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
    a. Reduction in the number and/or severity of relapses
    b. Decrease in concomitant corticosteroid or immunosuppressive therapy (e.g., azathioprine, mycophenolate, etc.)
    c. Decrease in NMOSD symptoms (e.g., pain, fatigue, improvement in motor function)

4. Individual has been adherent with the medication

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Any bilirubin elevation associated with elevation in transaminases that are five times greater than the upper limit of normal
        ii. Neutrophil count remains below 1.0 x $10^9$/L

7. Individual will not be receiving Enspryng in combination with other immunosuppressive drugs (e.g., Actemra, Kesimpta, Ocrevus, Rinvoq, rituximab, Soliris, Ultomiris, Uplizna, etc.)

8. Will not be used in an individual with an active infection including localized infections until the infection is resolved

9. Will not be used with live-attenuated or live vaccines

**Renewal duration**: 12 months

- If the individual has one or more NMOSD relapse, consider changing disease modifying therapy

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-Cancer Medications**

    2. **Off-Label Use of Cancer Medications**

**PHARMACY COVERAGE GUIDELINE**

# ENSPRYNG™ (satralizumab-mwge) subcutaneous injection Generic Equivalent (if available)

## Description:

Enspryng (satralizumab-mwge) is an interleukin-6 (IL-6) receptor monoclonal antibody antagonist indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. The precise mechanism by which satralizumab-mwge exerts therapeutic effects in NMOSD is unknown but is presumed to involve inhibition of IL-6-mediated signaling through binding to soluble and membrane-bound IL-6 receptors.

NMOSD, previously known as Devic disease or neuromyelitis optica [NMO]) are inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and spinal cord.

NMOSD is distinguished from multiple sclerosis and other central nervous system inflammatory disorders by the presence of the disease-specific AQP4 antibody (also referred to as NMO-immunoglobulin G antibody). AQP4 is a water channel protein that is concentrated in the spinal cord gray matter, periaqueductal and periventricular regions, and astrocytic foot processes of the blood brain barrier. Studies have shown that serum anti-AQP4 titers correlate with disease activity, decrease after immunotherapy, and are low during remission.

NMOSD acute attacks are characterized by bilateral or rapidly sequential optic neuritis (leading to visual loss), acute transverse myelitis (often causing limb weakness and bladder dysfunction), and the area postrema syndrome (with intractable hiccups or nausea and vomiting). The acute attacks may occur over days with variable degrees of recovery that can be weeks to months. It has a relapsing course and management is directed at treating an acute attack and then preventing another attack or prolonging the time to a relapse.

The natural history of NMOSD is a stepwise deterioration from accumulating visual, motor, sensory, and bladder deficits from recurrent attacks. Mortality rate is high in NMOSD, and it is often due to neurogenic respiratory failure, which occurs with extension of cervical lesions into the brainstem or from primary brainstem lesions.

---

## Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

### Neuromyelitis optica spectrum disorder (NMOSD):

**Diagnostic criteria for NMOSD with AQP4-IgG**

1. At least one core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses

**Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status**

1. At least two core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
    a. At least one core clinical characteristic must be optic neuritis, acute myelitis with longitudinally extensive transverse myelitis (LETM), or area postrema syndrome
    b. Dissemination in space (two or more different core clinical characteristics)

c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses

**Core clinical characteristics**
1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: Episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

**Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status**
1. Acute optic neuritis: Requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, **or** (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over more than one-half the optic nerve length or involving optic chiasm
2. Acute myelitis: Requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) **or** ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis
3. Area postrema syndrome: Requires associated dorsal medulla/area postrema lesions
4. Acute brainstem syndrome: Requires associated periependymal brainstem lesions

**Kurtzke Expanded Disability Status Scale (EDSS):**

The EDSS quantifies disability in eight Functional Systems (FS) and allows neurologists to assign a Functional System Score (FSS) in each of these. The Functional Systems are:
- Pyramidal
- Cerebellar
- Brainstem
- Sensory
- Bowel and bladder
- Visual
- Cerebral
- Other

EDSS steps of 1.0-4.5 refer to people who are fully ambulatory. EDSS steps of 5.0-9.5 are defined by the impairment to ambulation.

| Kurtzke Expanded Disability Status Scale | |
|---|---|
| 0.0 | Normal neurological examination |
| 1.0 | No disability, minimal signs in one FS |
| 1.5 | No disability, minimal signs in more than one FS |
| 2.0 | Minimal disability in one FS |
| 2.5 | Mild disability in one FS or minimal disability in two FS |

| | |
|---|---|
| 3.0 | Moderate disability in one FS, or mild disability in three or four FS. Fully ambulatory |
| 3.5 | Fully ambulatory but with moderate disability in one FS and more than minimal disability in several others |
| 4.0 | Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters |
| 4.5 | Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk without aid or rest some 300 meters. |
| 5.0 | Ambulatory without aid or rest for about 200 meters; disability severe enough to impair full daily activities (work a full day without special provisions) |
| 5.5 | Ambulatory without aid or rest for about 100 meters; disability severe enough to preclude full daily activities |
| 6.0 | Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting |
| 6.5 | Constant bilateral assistance (canes, crutches, braces) required to walk about 20 meters without resting |
| 7.0 | Unable to walk beyond approximately five meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day |
| 7.5 | Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; May require motorized wheelchair |
| 8.0 | Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms |
| 8.5 | Essentially restricted to bed much of day; has some effective use of arms retains some self-care functions |
| 9.0 | Confined to bed; can still communicate and eat. |
| 9.5 | Totally helpless bed patient; unable to communicate effectively or eat/swallow |
| 10.0 | Death due to MS |

**Biologic NMOSD therapies:**

| | |
|---|---|
| Interleukn-6 Receptor Antagonist | ENSPRYNG (satralizumab) |
| Compliment 5 inhibitor (C5i) | SOLIRIS (eculizumab) |
| Compliment 5 inhibitor (C5i) | ULTOMIRIS (ravulizumab) |
| Anti-CD19 Monoclonal Antibody | UPLIZNA (inebilizumab) |
| Anti-CD20 Monoclonal Antibody | RIABNI* (rituximab) (off-label) |
| Anti-CD20 Monoclonal Antibody | RITUXAN (rituximab) (off-label) |
| Anti-CD20 Monoclonal Antibody | RUXIENCE* (rituximab)* (off-label) |
| Anti-CD20 Monoclonal Antibody | TRUXIMA* (rituximab)* (off-label) |

** Biosimilar to Rituxan*

## Resources:

Enspryng (satralizumab-mwge) product information, revised by Genentech, Inc. 02-2022. Available at DailyMed https://dailymed.nlm.nih.gov. Accessed May 22, 2024.

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 Nov 1;73(11):1342-1348. doi: 10.1001/jamaneurol.2016.1637.

Glisson CC. Neuromyelitis optica spectrum disorder (NMOSD): Clinical features and diagnosis. In: UpToDate, González-Scarano F, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through April 2024. Topic last updated August 30, 2022. Accessed May 27, 2024.

Glisson CC. Neuromyelitis optica spectrum disorder (NMOSD): Treatment and prognosis. In: UpToDate, González-Scarano F, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through April 2024. Topic last updated April 11, 2024. Accessed May 17, 2024.

Ongphichetmetha T, Jitprapaikulsan J, Siritho S, et al. Efficacy and safety of rituximab in multiple sclerosis and neuromyelitis optica spectrum disorder. *Sci Rep.* 2024;14(1):3503. doi: 10.1038/s41598-024-53838-y.

Tania Kümpfel, Katrin Giglhuber, Orhan Aktas, et al. 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 Neurol*. 2023; 270(7):3341-3368. doi: 10.1007/s00415-023-11634-0.

Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). *J Neurol* 2014; 261:1-16.

Wang Y, Chang H, Zhang X, Yin L. Efficacy of rituximab in the treatment of neuromyelitis optica spectrum disorders: An update systematic review and meta -analysis. *Mult Scler Relat Disord.* 2021 May;50:102843. doi: 10.1016/j.msard.2021.102843.