



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/19/2020
LAST REVIEW DATE:
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

ENSPRYNG™ (satralizumab-mwge) subcutaneous injection

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**



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Criteria:

- **Criteria for initial therapy:** Enspryng (satralizumab-mwge) is considered *medically necessary* and will be approved when **ALL** of 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. A confirmed diagnosis of neuromyelitis optica spectrum disorder (NMOSD) who has had at least 1 relapse in the previous 12 month
 4. Individual is anti-aquaporin-4 (AQP4) antibody positive
 5. Attacks of NMOSD consist of at least **ONE** of the following core clinical features:
 - a. Optic neuritis
 - b. Acute myelitis
 - c. Area postrema syndrome (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
 6. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
 - a. Expanded Disability Status Scale (EDSS) score is 6.5 or less
 - b. Hepatitis B screening
 - c. Tuberculosis screening
 - d. Liver transaminases and serum bilirubin
 7. Individual has failure (using stable doses for 8 weeks), intolerance, or has a contraindication to **TWO** the following:
 - a. Azathioprine
 - b. Corticosteroid
 - c. Mycophenolate
 - d. Soliris (eculizumab)
 - e. Uplinza (inebilizumab)
 8. There are **NO** contraindications. Contraindications include:
 - a. Active hepatitis B infection
 - b. Active or untreated latent tuberculosis
 9. Will not be used in an individual with an active infection
 10. Will not be used with live-attenuated or live vaccines

Initial approval duration: 6 months



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- **Criteria for continuation of coverage (renewal request):** Enspryng (satralizumab-mwge) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
 2. Individual's condition has responded while on therapy.
 - a. Response is defined as:
 - i. Prolonged time to relapse
 3. Individual has been adherent with the medication
 4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
 - a. Contraindications or adverse effect.
 - i. Liver toxicity
 - ii. Neutrophil count remains below $1.0 \times 10^9/L$
 5. Will not be used in an individual with an active infection
 6. Will not be used with live-attenuated or live vaccines
 7. There are no significant interacting drugs

Renewal duration: 12 months

- Enspryng (satralizumab-mwge) for all other indications not previously listed is considered **experimental or investigational** and will not be covered when any one or more of the following criteria are met:
1. Lack of final approval from the Food and Drug Administration;
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes;
 3. Insufficient evidence to support improvement of the net health outcome;
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; **or**
 5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, but are not limited to:

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration.

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

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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, that occurs with extension of cervical lesions into the brainstem or from primary brainstem lesions.

Definitions:

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

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

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 LETM, or area postrema syndrome

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- 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

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



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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

Resources:

Enspryng (satralizumab-mwge) product information, revised by manufacturer 08-2020, at DailyMed
<https://dailymed.nlm.nih.gov> accessed 08-20-2020

Glisson CC. Neuromyelitis optica spectrum disorders. In: UpToDate, Gonzalez-Scarano F, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com> (Accessed on September 10, 2020).
