09-J3000-79

Original Effective Date: 01/01/21

Reviewed: 05/14/25

Revised: 06/15/25

Subject: Satralizumab (Enspryng)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, severe inflammatory, autoimmune disease of the central nervous system. Clinical core characteristics may include attacks involving optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy, or symptomatic cerebral syndrome. At least one clinical attack is required to establish diagnosis which may be confirmed by the presence of an antibody against the astrocyte water channel aquaporin-4 (AQP4) and exclusion of other diagnoses. When AQP4 is negative or not detected, the diagnosis is more complex and requires more 2 or more clinical characteristics in different anatomic regions, with corresponding MRI requirements. AQP4 positive patients are at risk for relapse and preventative treatment should be considered. Immunosuppresants such as azathioprine, corticosteroids, mycophenolate mofetil, and rituximab have been used historically to prevent attacks.

Satralizumab (Enspryng™) is Food and Drug Administration (FDA) approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. Satralizumab binds to interleukin-6 (IL-6) receptors to inhibit IL-6 mediated signaling.

The efficacy of satralizumab for NMOSD was evaluated in two randomized, double-blind, placebo-controlled trials. One study included patients using satralizumab as monotherapy and the other allowed continuation of baseline immunosuppressive therapy (e.g., azathioprine, mycophenolate mofetil, oral corticosteroids) with satralizumab treatment. Both trials included patients with anti-APQ4 antibody positive disease (n= 64,study one; n= 52, study two). In both studies, patients were required to have clinical evidence of at least one relapse in the year prior to screening and in study two patients also had a minimum of two relapses in the 2 years prior to the study. Patients had an Expanded Disability Status Scale (EDSS) score of 6.5 or less to participate. Satralizumab 120 mg or matching placebo was administered as a subcutaneous injection at week 0, 2, 4, and every 4 weeks thereafter. In study one, of the 41 patients who were treated with satralizumab the time to first relapse was significantly longer and

the proportion of patients with relapse was lower as compared to the 23 patients who received placebo (22% vs 56.5%, HR 0.26). The risk of relapse was reduced by 74% compared to placebo. In study two, of the 26 patients who were treated with satralizumab (combined with immunosuppresants) the time to first relapse was significantly longer and the proportion of patients with relapse was lower as compared to the 26 patients who received placebo (11.5% vs 42.3%, HR 0.22). The risk of relapse was reduced by 78% compared to placebo. Patients with AQP4 negative disease were also enrolled in the trials but there was no benefit found in either study. The most common adverse reactions were nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, nausea, and back pain.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of satralizumab (Enspryng) **meets the definition of medical necessity** when used to treat **t**he following indications and the indication-specific criteria are met:

1. Neuromyelitis Optica Spectrum Disorder (NMOSD)
    a. Member meets **ALL** of the following - documentation must be provided:
        i. Member has anti-aquaporin-4 (AQP4) antibody positive disease - lab documentation must be provided
        ii. Member has **ONE** core clinical characteristic of NMOSD and alternative diagnoses have been excluded:
            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
        iii. Member has a history of at least 1 relapse in the previous year[†]
    b. Member does not have an active hepatitis B infection
    c. Member does not have active or untreated latent tuberculosis

d. Satralizumab will not be used concurrently with an alternative biologic agent for the treatment of NMOSD (e.g., eculizumab and biosimilars, ravulizumab, rituximab, inebilizumab, tocilizumab)

e. Treatment is prescribed by or in consultation with a neurologist

f. The first dose does not exceed 120 mg, followed by 120 mg at week 2 and week 4, and the maintenance dosing does not exceed 120 mg every 4 weeks.

Approval duration: 6 months

Continuation of satralizumab (Enspryng) **meets the definition of medical necessity** when **ALL** of the following are met:

1. An authorization or reauthorization for satralizumab has been previously approved for the treatment of NMOSD by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage
2. The member has a history of beneficial response (e.g., absence or reduction in relapses) to satralizumab therapy for the treatment of NMOSD – documentation must be provided
3. The member has anti-aquaporin-4 (AQP4) antibody positive disease – lab documentation must be provided
4. Member does not have an active hepatitis B infection
5. Member does not have active or untreated latent tuberculosis
6. Satralizumab will not be used concurrently with an alternative biologic agent for the treatment of NMOSD (e.g., eculizumab and biosimilars, ravulizumab, rituximab, inebilizumab, tocilizumab)
7. Treatment is prescribed by or in consultation with a neurologist
8. The dose does not exceed 120 mg every 4 weeks

Approval duration: 1 year

†Not required if the member previously received treatment with eculizumab (Soliris, Bkemv, Epysqli), inebilizumab (Uplizna), or ravulizumab (Ultomiris).

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- For the treatment ofneuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive: 120 mg by subcutaneous injection at weeks 0,2, and 4 followed by a maintenance dosage of 120 mg every 4 weeks.

- Prior to the first dose, hepatitis B virus, tuberculosis, and liver transaminase screening is required. Prior to every use, determine if there is an active infection.

Dose Adjustments

- See prescribing information for missed dose instructions

Drug Availability

- 120 mg/mL in a single-dose prefilled syringe

PRECAUTIONS:

Boxed Warning

- none

Contraindications

- History of known hypersensitivity to satralizumab or any inactive components
- Active hepatitis B infection
- Active or untreated latent tuberculosis

Precautions/Warnings

- Infections: delay administration in patients with an active infection until the infection is resolved. Vaccination with live or live-attenuated vaccines is not recommended during treatment.
- Elevated liver enzymes: monitor ALT and AST levels every 4 weeks for the first 3 months of treatment followed by every 3 months for one year; interruption of treatment may be required.
- Decreased neutrophil counts: monitor neutrophils every 4 to 8 weeks after initiation of treatment and at regular intervals during treatment.
- Hypersensitivity: rash, urticaria, and fatal anaphylaxis has occurred with other interleukin-6 receptor antagonists.

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

G36.0	Neuromyelitis optica [Devic]

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

None

RELATED GUIDELINES:

Eculizumab (Soliris), 09-J1000-17

Inebilizumab (Uplizna), 09-J3000-73

Ravulizumab (Ultomiris), 09-J3000-26

Rituximab products and rituximab hyaluronidase (Rituxan Hycela), 09-J0000-59

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.;2025. URL www.clinicalpharmacilogy-ip.com Accessed 05/01/25.
2. Enspryng (satralizumab) [package insert]. Genentech, Inc. South San Francisco (CA): March 2022.
3. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 05/01/25.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [2025 May 1]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Traboulsee A, Greenberg BM, Bennett JL et al. Safety and efficacy of satralizumab monotherapy in neuromyelitis optica spectrum disorder: a randomised, double-blind, multicenter, placebo-controlled phase 3 trial. Lancet Neurol. 2020; 19: 402-12.
6. Wingerchuck DM, Banwell B, Bennett JL et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015; 85 (2): 177-89.
7. Yamamura T, Kleiter I, Fujihara K et al. Trial of satralizumab in neuromyelitis optica spectrum disorder. N Engl J Med. 2019; 381 (22): 2114 – 24.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

01/01/21	New Medical Coverage Guideline.
10/15/21	Review and revision to guideline consisting of updating references.
07/15/22	Review and revision to guideline consisting of updating the position statement and references.
09/15/23	Review and revision to guideline consisting of updating the references.
05/15/24	Review and revision to guideline; consisting of updating the position statement to remove requirement for alternative immunosuppressant therapy.
08/15/24	Review and revision to guideline; consisting of updating the position statement for NMOSD.
06/15/25	Review and revision to guideline; consisting of updating the position statement for agents not used in combination.