Enspryng (satralizumab-mwge) Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
2/1/2024	4/1/2021

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Enspryng® (satralizumab-mwge) Injection for subcutaneous use	Treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Neuromyelitis optica spectrum disorder	Neuromyelitis optica spectrum disorder (NMOSD), also known as Devic disease, is a chronic disorder of the brain and spinal cord dominated by inflammation, of the optic nerves (optic neuritis) and inflammation of the spinal cord (myelitis). Classically, it was felt to be a monophasic illness, consisting of episodes of inflammation of one or both optic nerves and the spinal cord over a short period of time (days or weeks) but, after the initial episode, no recurrence. It is now recognized that most patients satisfying current criteria for NMOSD experience repeated attacks separated by periods of remission. The interval between attacks may be weeks, months or years.(2) Early in the course of the disease, it may be difficult to distinguish between NMOSD and multiple sclerosis because both may cause optic neuritis and myelitis as symptoms. However, the optic neuritis and myelitis tend to be more severe in NMOSD; the brain MRI is more commonly normal, and the spinal fluid analysis does not usually show oligoclonal bands in NMOSD, which are features that help distinguish it from MS.(2) NMOSD can be AQP4 antibody positive or negative. The diagnostic criteria for NMOSD with AQP4 positive diagnosis are as follows: at least 1 core clinical characteristic, a positive test for AQP4-IgG, and exclusion of alternative diagnoses. The core characteristics are as follows(4): 1. Optic neuritis 2. Acute myelitis 3. Area postrema syndrome (episodes 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

	An international consensus panel reached several conclusions in addition to the above criteria to establish a NMOSD diagnosis. First, at least 1 discrete clinical attack of CNS symptoms must occur to establish a diagnosis of NMOSD. Although asymptomatic AQP4-IgG seropositive status may exist for years before clinical NMOSD presentation, the natural history of asymptomatic seropositivity is poorly understood. Second, NMOSD diagnosis is not warranted in asymptomatic patients with NMOSD-compatible MRI lesions because the expected clinical course in such individuals is unknown. Third, no clinical characteristic is pathognomonic of NMOSD. Accordingly, a single clinical manifestation is not diagnostic when AQP4-IgG is not detected. Finally, no single characteristic is exclusionary, but some are considered red flags that signal the possibility of alternative diagnoses. The main clinical red flags concern the temporal course of the syndrome rather than the actual manifestations. Most notably, a gradually progressive course of neurologic worsening over months to years is very uncommon (1%–2%) in NMOSD. However, after thorough investigation for potential competing disorders, the weight of evidence may justify NMOSD diagnosis despite presence of 1 or more red flags.(4) Treatment strategies for attack prevention in NMOSD and multiple sclerosis (MS) differ. Some MS immunotherapies appear to aggravate NMOSD, indicating an imperative for early, accurate diagnosis. Patients with NMOSD who are AQP4-IgG seropositive should be assumed to be at risk for relapse indefinitely and preventive treatment should be considered.(4) Azathioprine and mycophenolate mofetil have been used off label to prevent NMOSD attacks for decades. Their efficacy in NMOSD has been demonstrated in several retrospective studies and case series. In recent years, their use in NMOSD has declined in favor of rituximab owing to their comparative lower efficacy as demonstrated in multiple retrospective studies.(8) Rituximab is one of the most commonly used off-label preventative therapies in NMOSD. Rituximab is a monoclonal antibody (MAB) against CD20-positive B-Cells with include pre B-cell, immature B-cell, and memory B-cell lineage but not plasmablasts or plasma cells. Its exact mechanism of action in NMOSD is unknown but is hypothesized to involve reduction of pathogenic antibody production, dampening of pro-inflammatory cytokines, and decreasing B-cell dependent antigen presentation to T-cells.(8) Eculizumab, ibalizumab, and satralizumab are FDA approved therapies that can be used as add on or monotherapy for NMOSD. Disability in NMOSD is a direct consequence of the relapse. Spontaneous gradual progression of disability like in MS is very rare in NMOSD. Thus, NMOSD relapses are a clinically relevant measure. Amongst secondary end points, disability is very important. The main categories are spinal cord/brainstem related, motor (weakness, spasticity), sensory (numbness and pain), bladder, bowel, sexual function, and vision. EDSS is suitable and well validated in MS research, but cerebellar and cerebral functional scales are not really applicable in NMO, as cognitive and cerebellar dysfunction is limited in NMO. The Optic Spinal Impairment Scale is derived and modified from EDSS. There are no formal psychometrics supporting the scale and it is not widely used. There are numerous vision specific scales, but none are specific for optic neuritis.(5)
EFFICACY (1)	The safety and efficacy of Enspryng for the treatment of adults with NMOSD were established in two studies.(1) Study 1 enrolled 95 adult subjects with NMOSD who were not on concurrent immunosuppressive therapy and randomized them in a 2:1 manner to Enspryng therapy or placebo; of those enrolled, 67% were AQP4 positive. Study 2 enrolled 76 adult subjects with NMOSD who were on concurrent immunosuppressive therapy (most commonly oral corticosteroids [52%] or azathioprine [42%]) and randomized them in a 1:1 manner to Enspryng therapy or placebo; of those enrolled, 68% were AQP4 positive. In both studies, subjects were required to have clinical evidence of relapse in the preceding 12 months and have an

	expanded disability status scale (EDSS) score between 0 and 6.5 in order to meet eligibility criteria. The primary efficacy endpoint for both studies was the time to first confirmed relapse, as determined by a blinded committee that performed the adjudication of relapses.(1) In both studies the time to first confirmed relapse was significantly longer for those treated with Enspryng versus placebo; a 55% risk reduction was observed in Study 1 (hazard ratio 0.45; *p* equal to 0.0184) and a 62% risk reduction was observed in Study 2 (hazard ratio 0.38; *p* equal to 0.0184). AQP4 positive patients had a 74% risk reduction compared to placebo (hazard ratio 0.26; *p* =0.0014) and a 78% risk reduction compared to placebo (hazard ratio 0.22; *p* equal to 0.0143) in Study 1 and Study 2, respectively. Neither study demonstrated benefit in AQP4 negative patients. Among those who were AQP4 positive in Study 1, 76.5% (95% CI: 59.2-87.2) of Enspryng treated patients were relapse free at week 96 compared to 41.1% (95% CI: 20.8-60.4) of those treated with placebo. Among the same subjects in Study 2, 91.1% (95% CI: 68.4-97.7) of Enspryng treated patients were relapse free at week 96 compared to 56.8% (95% CI: 32.1-75.4) of those treated with placebo.
SAFETY (1)	Enspryng is contraindicated in patients with a known hypersensitivity to satralizumab or any of the inactive ingredients, patients with active hepatitis B infection, and patients with active or untreated latent tuberculosis. Patients should be screened for hepatitis B virus and latent tuberculosis before initiation of Enspryng therapy.

REFERENCES

Number	Reference
1	Enspryng prescribing information. Genentech, Inc. March 2022.
2	National Organization for Rare Disorders (NORD). Rare Disease Database. Neuromyelitis Optica Spectrum Disorder. Accessed at Neuromyelitis Optica Spectrum Disorder - NORD (National Organization for Rare Disorders) (rarediseases.org)
3	Kessler RA, Mealy MA, Levy M. Treatment of neuromyelitis optica spectrum disorder: acute, preventive, and symptomatic. Curr Treat Options Neurol. 2016;18(1):2.
4	Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85(2):177-189.
5	The Siegel Rare Neuroimmune Association (SRNA). Neuromyelitis Optica Spectrum Disorder. NMOSD Prognosis & Management. https://wearesrna.org/living-with-myelitis/disease-information/neuromyelitis-optica-spectrum-disorder/prognosis-management/
6	National Multiple Sclerosis Society. Treatments of NMO. https://www.nationalmssociety.org/What-is-MS/Related-Conditions/Neuromyelitis-Optica-(NMO)/Treatments
7	Regulatory workshop on clinical trials designs in neuromyelitis optica spectrum disorders (NMOSD). 16 June 2015.
8	Abboud H, Zheng C, Kar I, Chen CK, Sau C, Serra A. Current and emerging therapeutics for newuromyelitis optica spectrum disorder: Televance to the COVID-19 pandemic. Mult Scler Relat Disord. 2022;44:102249. doi:10.1016/j.msard.2020.102249.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Enspryng	satralizumab-mwge subcutaneous soln pref syringe	120 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Enspryng	Satralizumab-mwge Subcutaneous Soln Pref Syringe	120 MG/ML	1	Syringe	28	DAYS		* NOTE: Loading dose of 3 syringes for the first month is approvable	

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Enspryng	satralizumab-mwge subcutaneous soln pref syringe	120 MG/ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Enspryng	Satralizumab-mwge Subcutaneous Soln Pref Syringe	120 MG/ML	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of neuromyelitis optica spectrum disorder (NMOSD) **AND** 2. The patient is anti-aquaporin-4 (AQP4) antibody positive **AND** 3. The diagnosis was confirmed by at least ONE of the following: A. Optic neuritis **OR** B. Acute myelitis **OR** C. Area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting) **OR** D. Acute brainstem syndrome **OR** E. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions **OR** F. Symptomatic cerebral syndrome with NMOSD-typical brain lesions **AND** 4. The patient has had at least 1 discrete clinical attack of CNS symptoms **AND** 5. Alternative diagnoses (e.g., multiple sclerosis, ischemic optic neuropathy) have been ruled out **AND** 6. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication **AND** 7. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 8. The prescriber has screened the patient for hepatitis B viral (HBV) infection AND BOTH of the following: A. The patient does NOT have an active HBV infection **AND** B. If the patient has had a previous HBV infection or is a carrier for HBV infection the prescriber has consulted with a gastroenterologist or a hepatologist before initiating and during treatment with the requested agent **AND**

Module	Clinical Criteria for Approval
	9. The patient does NOT have active or untreated tuberculosis **AND** 10. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 11. The patient will not be using the requested agent in combination with rituximab, Soliris, or Uplizna for the requested indication **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent (e.g., decreased relapses, improvement or stabilization of vision or paralysis) **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. BOTH of the following: A. The patient does not have active hepatitis B infection **AND** B. If the patient has had a previous HBV infection or is a carrier for HBV infection the prescriber continues to consult with a gastroenterologist or a hepatologist during treatment with the requested agent **AND** 5. The patient does not have active or latent tuberculosis **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. The patient will NOT be using the requested agent in combination with rituximab, Soliris, or Uplizna for the requested indication **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Length of Approval:** 12 months NOTE: may approve initial loading dose of 3 syringes for 1 month and the maintenance dose for the remainder of 12 months