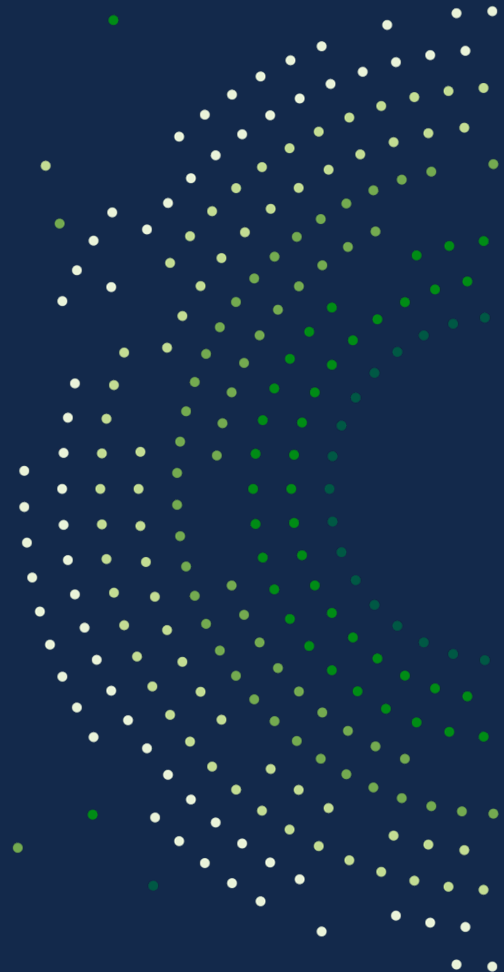


Administration of ENSPRYNG™ (satralizumab-mwge)

Centers for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting

March 2021



ENSPRYNG is a humanized IgG2 monoclonal antibody for the treatment of adult NMOSD patients who are AQP4-IgG positive

ENSPRYNG was FDA-approved on August 14, 2020¹

- The first self-administered subcutaneous and third of only three FDA-approved drugs available for NMOSD¹⁻³
- Humanized IgG2 monoclonal antibody targeting soluble and membrane-bound IL-6 receptor⁴
- Utilizes antibody recycling technology engineered for sustained suppression of IL-6 signaling and its downstream inflammatory effects in periphery and CNS⁴

NMOSD (ICD-10-CM diagnosis code G36.0) is a rare, debilitating autoimmune disorder of the CNS



Optic neuritis⁵



Transverse myelitis⁵



Area postrema syndrome⁶



Acute brainstem syndrome⁷

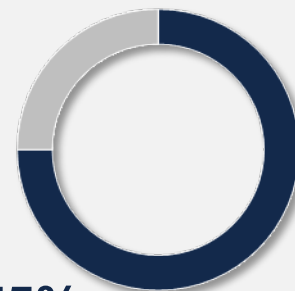


Symptomatic narcolepsy⁸



Cerebral syndrome symptoms⁸

AQP4-IgG is a diagnostic marker of NMOSD⁵



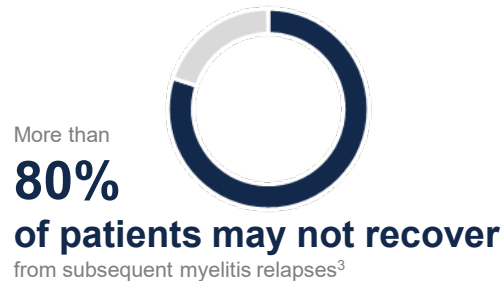
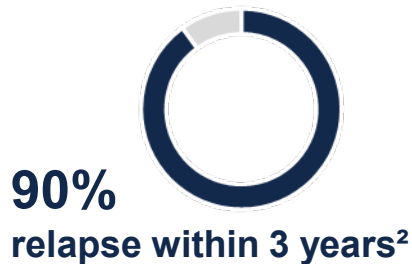
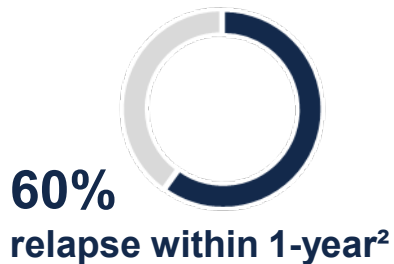
~75% of NMOSD patients are AQP4-IgG positive⁹

IL-6 – Interleukin 6; AQP4-IgG – anti-aquaporin-4 antibody; CNS – Central Nervous System

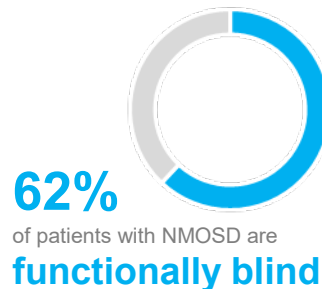
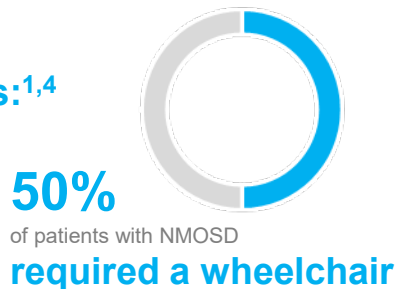
1. ENSPRYNG (satralizumab-mwge) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2020. 2. SOLIRIS (eculizumab) [prescribing information]. Boston, MA: Alexion Pharmaceuticals, Inc.; 2019. 3. UPLIZNA (inebilizumab) [prescribing information]. Gaithersburg, MD: Viela Bio, Inc.; 2020. 4. Heo, Y. Satralizumab: First Approval. *Drugs* 80, 1477–1482 (2020). 5. National Organization for Rare Disorders. Neuromyelitis optica spectrum disorder. <https://rarediseases.org/rare-diseases/neuromyelitis-optica>. Accessed November 2, 2020. 6. Wingerchuk DM et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology*. 2015;85(2):177-189. 7. Cheng C et al. The role of anti-aquaporin 4 antibody in the conversion of acute brainstem syndrome to neuromyelitis optica. *BMC Neurol*. 2016;16(1):203. 8. Kim HJ et al. *Neurology*. 2015;84(11):1165-1173. 9. Wingerchuk DM et al. The spectrum of neuromyelitis optica. *Lancet Neurol*. 2007;6(9):806-815.

NMOSD is characterized by relapses, which often result in hospitalization and can lead to severe, lasting disabilities¹

Prior to the approval of therapies for NMOSD:



Historically,
within 5 years:^{1,4}



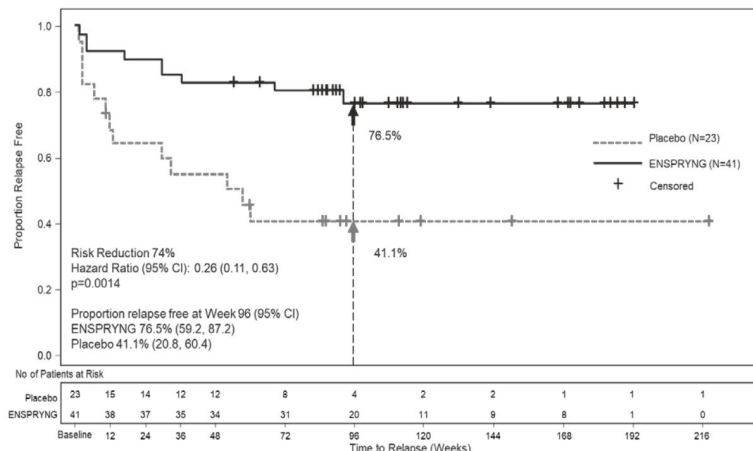
1. Kessler RA, Mealy MA, Levy M. Treatment of neuromyelitis optica spectrum disorder: acute, preventive, and symptomatic. *Curr Treat Options Neurol*. 2016;18(1):2. doi:10.1007/s11940-015-0387-9. 2. Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinshenker BG. The spectrum of neuromyelitis optica. *Lancet Neurol*. 2007;6(9):806-815. 3. Jarius S, Ruprecht, Wildemann B, et al. *J Neuroinflammation*. 2012;9:14. 4. Wingerchuk DM, Weinshenker BG. Neuromyelitis optica: clinical predictors of a relapsing course and survival. *Neurology*. 2003;60(5):848-853.

In adult AQP4-IgG seropositive patients, ENSPRYNG significantly reduced the risk of relapse vs. placebo

Study design

- Randomized, multicenter, double-blind, placebo-controlled trial
- 95 adult patients (64 of whom were AQP4-IgG seropositive)
- Patients were randomized in a 2:1 ratio to receive ENSPRYNG or placebo

Results



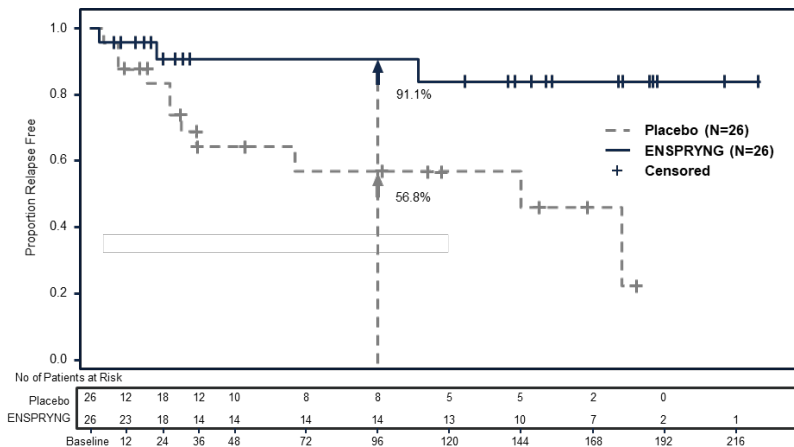
- In the AQP4-IgG positive population, there was a 74% risk reduction and a hazard ratio of 0.26 (95% CI 0.11, 0.63); p = 0.0014
- The proportion of relapse free AQP4-IgG positive patients at week 96 was 76.5% in ENSPRYNG group and 41.1% in the placebo group
- 9 patients (22%) in the ENSPRYNG group and 13 patients (56.5%) in the placebo group experienced a relapse
- Double-blind period was followed by an open-label extension period

In adult AQP4-IgG seropositive patients, ENSPRYNG plus immunosuppressive therapy (IST) significantly reduced the risk of relapse vs. IST alone

Study design

- Randomized, multicenter, double-blind, placebo-controlled trial
- 76 adult patients (52 of whom were AQP4-IgG seropositive)
- Patients were randomized in a 1:1 ratio to receive ENSPRYNG or placebo in addition to immunosuppressive therapy

Results



- In the AQP4-IgG positive population, there was a 78% risk reduction and a hazard ratio of 0.22 (95% CI 0.06, 0.82); $p = 0.0143$
- The proportion of relapse free AQP4-IgG positive patients at week 96 was 91.1% in ENSPRYNG plus IST group and 56.8% in the placebo plus IST group
- 3 patients (11.5%) in the ENSPRYNG plus IST group and 11 patients (42.3%) in the placebo plus IST group experienced a relapse
- Double-blind period was followed by an open-label extension period

The safety profile of ENSPRYNG in the open-label extension period was consistent with the double-blind period

Period:	Placebo ± IST, DB period, pooled data (n=74, PY=100.0)		ENSPRYNG ± IST, DB period, pooled data (n=104, PY=193.7)		OST period* (n=166, PY=437.7)	
Adverse Event	Patients n (%)	Events per 100 PY (95% CI)	Patients n (%)	Events per 100 PY (95% CI)	Patients n (%)	Events per 100 PY (95% CI)
All AEs	64 (86.5)	506.5 (463.4, 552.6)	95 (91.3)	478.5 (448.2, 510.3)	153 (92.2)	418.8 (399.8, 438.4)
Common AEs						
URT ¹	12 (16.2)	26.0 (17.0, 38.1)	20 (19.2)	23.7 (17.4, 31.7)	38 (22.9)	25.1 (20.7, 30.3)
Headache	8 (10.8)	11.0 (5.5, 19.7)	20 (19.2)	18.1 (12.6, 25.1)	27 (16.3)	11.0 (8.1, 14.5)
Nasopharyngitis	8 (10.8)	14.0 (7.7, 23.5)	19 (18.3)	17.0 (7.7, 23.5)	37 (22.3)	20.1 (16.1, 24.8)
UTI	15 (20.3)	32.0 (21.9, 45.1)	18 (17.3)	22.7 (16.5, 30.5)	29 (17.5)	18.5 (14.7, 23.0)
Serious AEs	14 (18.9)	18.0 (10.7, 28.4)	19 (18.3)	15.0 (10.0, 21.5)	35 (21.1)	12.6 (9.5, 16.4)
Severe AEs [†]	7 (9.5)	11.0 (5.5, 19.7)	22 (21.2)	21.7 (15.6, 29.3)	34 (20.5)	15.1 (11.7, 19.2)
AEs leading to treatment discontinuation	5 (6.8)	5.0 (1.6, 11.7)	4 (3.8)	2.6 (0.8, 6.0)	7 (4.2)	1.8 (0.8, 3.6)
Infections [‡]	40 (54.1)	154.9 (131.4, 181.2)	62 (59.6)	113.0 (98.6, 129.0)	109 (65.7)	112.4 (102.7, 122.8)
Serious infections [‡]	6 (8.1)	7.0 (2.8, 14.4)	8 (7.7)	4.1 (1.8, 8.1)	16 (9.6)	3.9 (2.3, 6.2)
Injection-related reactions	7 (9.5)	9.0 (4.1, 17.1)	13 (12.5)	17.0 (11.7, 23.9)	21 (12.7)	12.1 (9.1, 15.8)

Pooled safety analysis from the SakuraSky and SakuraStar studies. *The OST period includes cumulative data from the DB and the OLE up to a CCOD of 7 June 2019. †Severe AEs were defined as incapacitating AEs affecting the patient's ability to work or to perform normal daily activities. ‡MedDRA system order class: infections and infestations.

While hypersensitivity reactions, including fatal anaphylaxis, have occurred with other IL-6 receptor antagonists, there were no deaths and no anaphylactic reactions in any of the arms

AE – adverse event; CCOD – clinical cut-off date; CI – confidence interval; DB – double-blind; IST – immunosuppressants; MedDRA – Medical Dictionary for Regulatory Activities; OLE – open-label extension; OST – overall satralizumab treatment period; PY – patient-years; URTI – upper respiratory tract infection; UTI – urinary tract infection.
 1. Greenberg B, Seze JD, Fox E. et al. Safety of satralizumab in neuromyelitis optica spectrum disorder (NMOSD): Results from the open-label extension periods of SakuraSky and SakuraStar Presentation at: Americas Committee for treatment and research in Multiple Sclerosis (ACTRIMS); September 2020; Virtual

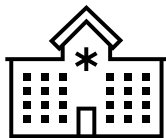
ENSPRYNG – safety information

Contraindications	Warnings and Precautions	Adverse Reactions
<ul style="list-style-type: none">• Known hypersensitivity to satralizumab or any of the inactive ingredients• Active Hepatitis B infection• Active or untreated latent tuberculosis	<ul style="list-style-type: none">• Infections: Delay ENSPRYNG 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 during treatment; interruption of ENSPRYNG may be required.• Decreased Neutrophil Counts: Monitor neutrophils during treatment	<ul style="list-style-type: none">• The most common adverse reactions (incidence at least 15%) are nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea

1. ENSPRYNG (satralizumab-mwge) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2020.

ENSPRYNG injection is available as a pre-filled syringe that must be subcutaneously administered, both in the inpatient and outpatient settings

Inpatient Setting



- In the inpatient setting, utilization of ENSPRYNG will be documented in the “medication administration” and/or “discharge summary” sections of the medical record, as either ENSPRYNG or satralizumab-mwge
- An average of 1.22 doses per patient are anticipated in this setting

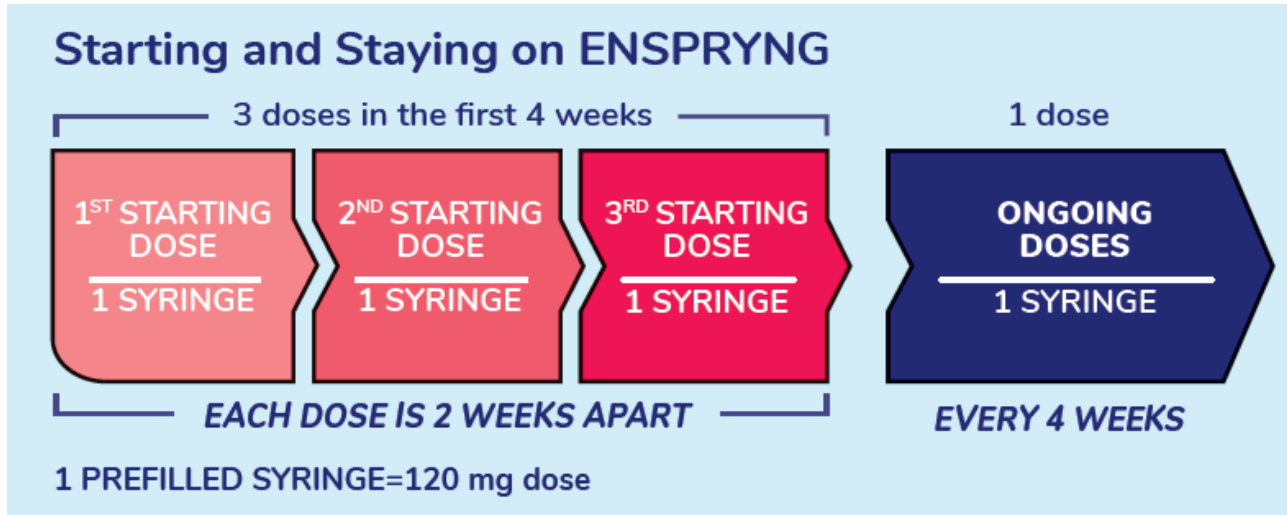
Outpatient Setting



- Once discharged, a patient/caregiver can administer subsequent doses of ENSPRYNG at home (with physician approval and proper training)

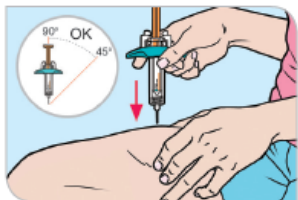
1. ENSPRYNG (satralizumab-mwge) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2020.

After a loading period, ENSPRYNG is dosed every four weeks

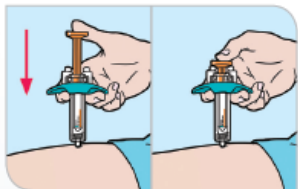


1. ENSPRYNG (satralizumab-mwge) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2020.

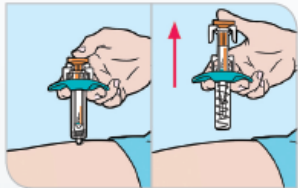
ENSPRYNG can be injected into the lower part of the abdomen or the front and middle of the thighs



- Take the cap off the needle and dispose of it as instructed. Do not touch the needle or let it touch any surfaces
- Hold the barrel of the syringe using your thumb and index finger
- Use your other hand to pinch the skin area you have cleaned
- Use a quick, dart-like motion to insert the needle at an angle between 45 to 90 degrees, doing it just once



- Let go of the pinched skin and slowly inject the medicine by gently pushing the plunger all the way down



- Gently release the plunger and allow the needle to come out of the skin at the same angle it was inserted
- The needle shield should now cover the needle. If not, dispose of the syringe carefully

1. ENSPRYNG (satralizumab-mwge) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2020.

Genentech
A Member of the Roche Group