HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ENSPRYNG safely and effectively. See full prescribing information for ENSPRYNG.

ENSPRYNG® (satralizumab-mwge) injection, for subcutaneous use
Initial U.S. Approval: 2020

----------RECENT MAJOR CHANGES----------

Indication and Usage (1.2)	10/2026
Dosage and Administration (2.2)	10/2026
Dosage and Administration (2.3)	6/2026

INDICATIONS AND USAGE

ENSPRYNG is an interleukin-6 (IL-6) receptor antagonist indicated for:
- the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. (1.1)
- the treatment of thyroid eye disease (TED) regardless of TED activity or duration in adult patients. (1.2)

DOSAGE AND ADMINISTRATION
- Hepatitis B virus, tuberculosis, and liver transaminase screening is required before the first dose. (2.1)
- Prior to every use, determine if there is an active infection. (2.2)
- The recommended loading dosage of ENSPRYNG is:
- NMOSD: for the first three administrations is 120 mg by subcutaneous injection at Weeks 0, 2, and 4, followed by a maintenance dosage of 120 mg every 4 weeks. (2.2.1)
- TED: for body weight 40-100kg; for the first three administrations is 120 mg by subcutaneous injection at Weeks 0, 2, and 4, followed by a maintenance dosage of 120 mg every 4 weeks. For body weight >100 kg: for the first three administrations is 180 mg by subcutaneous injection at Weeks 0, 2, and 4, followed by a maintenance dosage of 180 mg every 4 weeks (2.2.2)
- See Full Prescribing Information for important preparation and administration instructions. (2.3)

DOSAGE FORMS AND STRENGTHS
- Injection: 120 mg/mL in a single-dose prefilled syringe (3)
- Injection: 120 mg/mL in a single-dose prefilled autoinjector (3)
- Injection: 180 mg/1.5 mL in a single-dose prefilled autoinjector (3)

CONTRAINDICATIONS
- Known hypersensitivity to satralizumab or any of the inactive ingredients (4)
- Active Hepatitis B infection (4)
- Active or untreated latent tuberculosis (4)

WARNINGS AND PRECAUTIONS
- 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. (5.1)
- Elevated Liver Enzymes: Monitor ALT and AST levels during treatment; interruption of ENSPRYNG may be required. (5.2)
- Decreased Neutrophil Counts: Monitor neutrophils during treatment. (5.3)

ADVERSE REACTIONS
- The most common adverse reactions in patients with NMOSD (incidence at least 15%) are nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea. (6.1)
- The most common adverse reactions in patients with TED (incidence at least 5%) are upper respiratory tract infection, and alanine aminotransferase increased. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 10/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Neuromyelitis Optica Spectrum Disorder (NMOSD)

ENSPRYNG is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

1.2 Thyroid Eye Disease (TED)

ENSPRYNG is indicated for the treatment of thyroid eye disease (TED) regardless of TED activity or duration in adult patients.

2 DOSAGE AND ADMINISTRATION

2.1 Assessments Prior to the First Dose of ENSPRYNG

Hepatitis B Virus Screening

Prior to initiating ENSPRYNG, perform Hepatitis B virus (HBV) screening. ENSPRYNG is contraindicated in patients with active HBV confirmed by positive results for surface antigen [HBsAg] and anti-HBV tests. For patients who are negative for HBsAg and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment with ENSPRYNG *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Tuberculosis Screening

Prior to initiating ENSPRYNG, evaluate for active tuberculosis and test for latent infection. For patients with active tuberculosis or positive tuberculosis screening without a history of appropriate treatment, consult infectious disease experts before initiating treatment with ENSPRYNG *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Liver Transaminase Screening

Liver transaminases and serum bilirubin should be assessed prior to initiation of treatment with ENSPRYNG *[see Warnings and Precautions (5.2)]*.

Caution should be exercised when considering initiation of ENSPRYNG treatment in patients whose aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels are greater than 1.5 times the upper limit of normal (ULN).

Vaccinations

Because vaccination with live-attenuated or live vaccines is not recommended during treatment with ENSPRYNG, administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of ENSPRYNG for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ENSPRYNG for non-live vaccines *[see Warnings and Precautions (5.1)]*.

2.2 Recommended Dosage

For subcutaneous use only.

Prior to every use of ENSPRYNG, advise patients to consult with their healthcare professional (HCP) if they suspect an active infection, including localized infections. In case of active infection, delay use of ENSPRYNG until the infection is resolved *[see Warnings and Precautions (5.1)]*.

Recommended Dosage for NMOSD

The recommended loading dosage of ENSPRYNG for the first three administrations is 120 mg by subcutaneous injection at Weeks 0, 2, and 4, followed by a maintenance dosage of 120 mg every 4 weeks.

Recommended Dosage for TED

The recommended dose is based on the patient's body weight, as shown in Table 1.

Table 1 ENSPRYNG Dosing Regimen Based on Body Weight for TED

Body Weight*	**40 kg to less than or equal to 100 kg**	**Greater than 100 kg**
Loading Dose Every 2 weeks for the first three administrations. Weeks 0*, 2 and 4	120 mg	180 mg
Maintenance Dose From week 8 and every 4 weeks thereafter	120 mg	180 mg

* Dosing is based on actual body weight.
** "0 weeks" refers to time of the first administration.

The safety and effectiveness of ENSPRYNG have not been established in TED patients weighing less than 40 kg.

Missed Dose

If a dose of ENSPRYNG is missed for any reason other than increases in liver enzymes *[see Dosage and Administration (2.4)]*, administer as described in Table 2.

Table 2 Recommended Dosage for Delayed or Missed Doses

Last Dose Administered	**Recommended Dosage for Delayed or Missed Doses**
Less than 8 weeks during the maintenance period or missed a loading dose	Administer the recommended dose *[see Recommended Dose (2.2.1 and 2.2.2)]* by subcutaneous injection as soon as possible, and do not wait until the next planned dose. Maintenance period After the delayed or missed dose is administered, reset the dose schedule to every 4 weeks. Loading period

	If the second loading dose is delayed or missed, administer as soon as possible and administer the 3rd and final loading dose 2 weeks later. If the third loading dose is delayed or missed, administer as soon as possible and administer the 1st maintenance dose 4 weeks later.
8 weeks to less than 12 weeks	Administer the recommended dose by subcutaneous injection at 0* and 2 weeks, followed by the recommended dose every 4 weeks.
12 weeks or longer	Administer the recommended dose by subcutaneous injection at 0*, 2, and 4 weeks followed by the recommended dose every 4 weeks.

* "0 weeks" refers to time of the first administration after the missed dose.

2.3 Important Administration Instructions

- ENSPRYNG is intended for patient self-administration by subcutaneous injection under the guidance of a health care professional (HCP). After proper training in subcutaneous injection technique, a patient may self-inject ENSPRYNG or the patient's caregiver may administer ENSPRYNG, if the HCP determines that it is appropriate. Refer patients and/or caregivers to the ENSPRYNG "Instructions for Use" (IFU) for the prefilled syringe or the IFU for the autoinjector, as appropriate, for more detailed instructions on the preparation and administration of ENSPRYNG.
- Patients or caregivers should seek immediate medical attention if the patient develops symptoms of a serious allergic reaction and should not administer further doses until evaluated by an HCP *[see Contraindications (4) and Warning and Precautions (5.4)]*.
- Prior to use, remove ENSPRYNG from the refrigerator and allow it to sit at room temperature outside of the carton for 30 minutes. Do not warm ENSPRYNG in any other way.
- Inspect visually for particulate matter and discoloration prior to administration. ENSPRYNG solution should be clear and colorless to slightly yellow. Do not use ENSPRYNG if the solution is cloudy, discolored, contains particles, or if the prefilled syringe or the autoinjector appears to be damaged or has been dropped.
- Instruct patients who are prescribed the prefilled syringe to inject the full amount (1 mL), which provides 120 mg of ENSPRYNG, according to the directions provided in the IFU.
- Administer ENSPRYNG by subcutaneous injection in the abdomen or thigh. Do not inject into the 2-inch (5 cm) area around the navel. Rotate injection sites with each administration. Each injection must be at least 1 inch (2.5 cm) away from the most recent injection site. Do not inject into moles, scars, or areas where the skin is tender, bruised, red, hard, or not intact.

2.4 Safety Monitoring During Treatment

Liver Transaminases

Monitor ALT and AST levels every 4 weeks for the first 3 months of treatment with ENSPRYNG, followed by every 3 months for one year, and thereafter as clinically necessary *[see Warnings and Precautions (5.2)]*.

If an ALT or AST elevation of greater than 5 times the ULN occurs, discontinue ENSPRYNG as follows:

- If associated with any bilirubin elevation, discontinue ENSPRYNG, and reinitiation is not recommended.
- If not associated with any bilirubin elevation above the ULN, when the ALT or AST level has returned to the normal range and following a benefit-risk assessment of the patient, treatment with ENSPRYNG can be restarted per the schedule in Table 3.

Table 3 Recommended Dosage for Restart of Treatment After Liver Transaminase Elevation

Last Dose Administered	Recommended Dosage for Restart of Treatment
Less than 12 weeks	Restart at the recommended dosage by subcutaneous injection every 4 weeks *[see Recommended Dose (2.2.1 and 2.2.2)]*.
12 weeks or longer	Restart at the recommended dosage by subcutaneous injection at Weeks 0*, 2, and 4, followed by recommended dosage every 4 weeks.

* "0 weeks" refers to time of the first administration after the missed dose.

If treatment is restarted, the liver parameters must be closely monitored, and if any subsequent increase in ALT/AST and/or bilirubin above the ULN is observed, ENSPRYNG should be discontinued, and another reinitiation is not recommended.

Neutrophil Counts

Monitor neutrophils 4 to 8 weeks after initiation of therapy and thereafter at regular clinically determined intervals. If the neutrophil count is below 1.0×10^9/L and confirmed by repeat testing, ENSPRYNG should be interrupted until the neutrophil count is > 1.0×10^9/L *[see Warnings and Precautions (5.3)]*.

3 DOSAGE FORMS AND STRENGTHS

ENSPRYNG is a clear, and colorless to slightly yellow solution available as:

- Injection: 120 mg/mL in single-dose prefilled syringe.
- Injection: 120 mg/mL in single-dose autoinjector.
- Injection: 180 mg/1.5 mL in single-dose autoinjector

4 CONTRAINDICATIONS

ENSPRYNG is contraindicated in patients with:

- A known hypersensitivity to satralizumab or any of the inactive ingredients *[see Warnings and Precautions (5.4)]*
- Active Hepatitis B infection *[see Warnings and Precautions (5.1)]*
- Active or untreated latent tuberculosis *[see Warnings and Precautions (5.1)]*

5 WARNINGS AND PRECAUTIONS

5.1 Infections

An increased risk of infections, including serious and potentially fatal infections, has been observed in patients treated with IL-6 receptor antagonists, including ENSPRYNG.

The most common infections reported in a randomized clinical trial of patients treated with ENSPRYNG who were not on other chronic immunosuppressant therapies (Study 1), and that occurred more often than in patients receiving placebo, were nasopharyngitis (12%) and cellulitis (10%). The most common infections in patients who were on an additional concurrent immunosuppressant, and that occurred more often than in patients receiving placebo, were nasopharyngitis (31%), upper respiratory infection (19%), and pharyngitis (12%).

Delay ENSPRYNG administration in patients with an active infection, including localized infections, until the infection is resolved.

Hepatitis B Virus (HBV) Reactivation

Risk of HBV reactivation has been observed with other immunosuppressant therapies. Patients with chronic HBV infection were excluded from clinical trials. Perform HBV screening in all patients before initiation of treatment with ENSPRYNG. Do not administer ENSPRYNG to patients with active hepatitis. For patients who are chronic carriers of HBV [HBsAg+] or are negative for HBsAg and positive for HB core antibody [HBcAb+], consult liver disease experts before starting and during treatment with ENSPRYNG.

Tuberculosis

Tuberculosis has occurred in patients treated with other interleukin-6 receptor antagonists. Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating ENSPRYNG. Consider anti-tuberculosis therapy prior to initiation of ENSPRYNG in patients with a history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Consult infectious disease experts regarding whether initiating anti-tuberculosis therapy is appropriate before starting treatment. Patients should be monitored for the development of symptoms and signs of tuberculosis with ENSPRYNG, even if initial tuberculosis testing is negative.

Vaccinations

Live or live-attenuated vaccines should not be given concurrently with ENSPRYNG because clinical safety has not been established. Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of ENSPRYNG for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ENSPRYNG for non-live vaccines.

5.2 Elevated Liver Enzymes

Mild and moderate elevations of liver enzymes have been observed in patients treated with ENSPRYNG at a higher incidence than in patients receiving placebo *[see Adverse Reactions (6.1)]*.

ALT and AST levels should be monitored every 4 weeks for the first 3 months of treatment, followed by every 3 months for one year, and thereafter, as clinically indicated *[see Dosage and Administration (2.4)]*.

5.3 Decreased Neutrophil Counts

Decreases in neutrophil counts were observed in patients treated with ENSPRYNG at a higher incidence than placebo *[see Adverse Reactions (6.1)]*.

Neutrophil counts should be monitored 4 to 8 weeks after initiation of therapy, and thereafter at regular clinically determined intervals *[see Dosage and Administration (2.4)]*.

5.4 Hypersensitivity Reactions

Hypersensitivity reactions, including rash, urticaria, and fatal anaphylaxis, have occurred with other interleukin-6 receptor antagonists.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Infections *[see Warnings and Precautions (5.1)]*
- Elevated Liver Enzymes *[see Warnings and Precautions (5.2)]*
- Decreased Neutrophil Counts *[see Warnings and Precautions (5.3)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

Adverse Reactions

Neuromyelitis Optica Spectrum Disorder (NMOSD)

The safety of ENSPRYNG in NMOSD was evaluated in two randomized, placebo-controlled clinical trials [Study 1 evaluated ENSPRYNG without concurrent immunosuppressive therapy (IST) and Study 2 evaluated ENSPRYNG with concurrent IST], which included 41 anti-AQP4 seropositive patients treated with ENSPRYNG in Study 1 and 26 anti-AQP4 seropositive patients treated with ENSPRYNG in Study 2 *[see Clinical Studies (14)]*. In the double-blind, controlled period, the median exposure time on ENSPRYNG treatment was approximately 2 years in Study 1 and approximately 3 years in Study 2. The median exposure time on placebo treatment was approximately 1 year in both Study 1 and Study 2.

Adverse reactions that occurred in Study 1 and Study 2 in more than 5% of patients treated with ENSPRYNG, and at a greater incidence than in patients who received placebo, are shown in Table 4 and Table 5. The most common adverse reactions (15% or greater with ENSPRYNG in either) were nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea.

Table 4 Adverse Reactions Occurring in 4 or More Patients Treated with ENSPRYNG and Greater Incidence than Placebo in Patients with NMOSD in Study 1

Adverse Reaction	ENSPRYNG (N = 41) %	PLACEBO (N = 23) %
Rash	17	0
Arthralgia	17	0
Pain in extremity	15	9
Fatigue	15	4
Nausea	15	9
Nasopharyngitis	12	4
Pruritus	10	0
Depression	10	0
Cellulitis	10	0
Neutropenia	10	4
Blood creatine phosphokinase increased	10	4
Fall	10	4

Table 5 Adverse Reactions Occurring in 3 or More Patients Treated with ENSPRYNG and Greater Incidence than Placebo in Patients with NMOSD in Study 2

Adverse Reaction	ENSPRYNG + IST (N = 26) %	PLACEBO + IST (N = 26) %
Nasopharyngitis	31	15
Headache	27	12
Upper respiratory tract infection	19	12
Gastritis	15	0
Arthralgia	12	0
Pharyngitis	12	8

Thyroid Eye Disease (TED)

The safety of ENSPRYNG in TED was evaluated in two phase III randomized, double-masked, placebo-controlled, multicenter clinical trials (Study 3 and Study 4) which included 131 patients treated with ENSPRYNG.

Adverse reactions that occurred in Study 3 and Study 4 in more than 5% of patients treated with ENSPRYNG, and at a greater incidence than in patients who received placebo, are shown in Table 6.

Table 6 Adverse Reactions Occurring in 5% or More of Patients Treated with ENSPRYNG and Greater Incidence than Placebo in Patients with TED (Study 3 and Study 4 Pooled Analysis)

Adverse Reaction	ENSPRYNG (N = 131) %	PLACEBO (N = 124) %
Upper respiratory tract infection	5.3	2.4
Alanine aminotransferase increased	5.3	0.8

Neutropenia was also reported with less than 5% occurrence.

Injection-Related Reactions

NMOSD

In Study 1 and Study 2, injection-related reactions were reported in 9% of patients treated with ENSPRYNG compared with 8% in patients receiving placebo. These reactions in the ENSPRYNG-treated patients were predominantly mild to moderate in severity, and most occurred within 24 hours after the injection. The most commonly reported systemic symptom was diarrhea. The reported local injection site reactions were pruritus, injection site reaction, and skin mass.

TED

In Study 3 and Study 4, injection-related reactions (IRR) were predominantly mild to moderate in severity. No serious IRRs were reported. The most frequently reported systemic symptoms were fatigue and headache, and the most commonly reported local injection site reaction was pruritus. The majority of these events did not require dose interruption or treatment discontinuation, with the exception of two cases (pruritus and injection site reaction) that resulted in the discontinuation of treatment. IRRs were generally self-limiting and resolved without specific treatment.

In an open label trial in healthy adults, in which a single injection of 180 mg/1.5 mL by autoinjector was compared to two injections of 60 mg/0.5 mL and 120 mg/1 mL by prefilled syringe, the most commonly reported local injection site reactions were erythema, edema, induration, and pain. All local injection site reactions were mild to moderate in severity and most were resolved within 24 hours.

Infections

NMOSD

In Study 1, the rate of patients with infections was 51 patients/100 patient-years (95% CI: 32, 78) in patients treated with ENSPRYNG compared with 108 patients/100 patient-years (95% CI: 52, 199) in patients receiving placebo. The rate of patients with serious infections was 5 patients/100 patient-years (95% CI: 1, 14) in patients treated with ENSPRYNG compared with 4 patients/100 patient-years (95% CI: 0, 21) in patients receiving placebo.

In Study 2, the rate of patients with infections was 168 patients/100 patient-years (95% CI: 100, 265) in patients treated with ENSPRYNG compared with 143 patients/100 patient-years (95% CI: 83, 229) in patients treated with placebo. The rate of patients with serious infections was 4 patients/100 patient-years (95% CI: 1, 15) in patients treated with ENSPRYNG compared with 10 patients/100 patient-years (95% CI: 2, 28) in patients receiving placebo.

TED

In Study 3 and Study 4 the rate of infections was lower in patients treated with ENSPRYNG [94.08 events/100 PY (95% CI: 71.07,122.17)] compared with patients receiving placebo [113.92 events/100 PY (95% CI: 86.93,146.64)]. The rate of serious infections was 0.00 events/100 PY (95% CI: 0,6.2) in patients treated with ENSPRYNG compared with 1.90 events/100 PY (95% CI: 0.05,10.58) in patients receiving placebo.

Laboratory Abnormalities

Decreased Neutrophil Count

NMOSD

Of the patients treated with ENSPRYNG, 10% had neutrophils below 1×10^9/L compared to 9% in placebo in Study 1. In Study 2, 15% of patients had neutrophils below 1×10^9/L compared to 4% in placebo. There was one patient in Study 1 treated with ENSPRYNG with neutrophil counts $< 0.5 \times 10^9$/L, and one patient in Study 2 discontinued ENSPRYNG because of neutropenia.

TED

In Study 3 and Study 4, decreased neutrophil counts through Week 24 were observed in 28.2% of patients treated with ENSPRYNG compared with 9.7% of patients receiving placebo. Of these patients in the ENSPRYNG group, 2.3 % had neutrophil count decreased below 1×10^9/L compared to no patients in the placebo group. The decreased neutrophil counts were not associated with serious infections.

Decreased Platelet Count

NMOSD

In Study 1, a shift in platelet count decreases from normal at baseline to below the lower limit of normal (LLN) occurred in 26% of patients treated with ENSPRYNG compared to 5% of patients receiving placebo. In Study 2, decreases in platelet counts from normal at baseline to below the LLN occurred in 35% of patients treated with ENSPRYNG and in 17% of patients receiving placebo. None of the patients had a decrease in platelet count to less than 50×10^9/L.

TED

In Study 3 and Study 4, decreases in platelet count through Week 24 were reported in 8.4 % of patients treated with ENSPRYNG compared to 2.4% of patients receiving placebo. All decreases in the ENSPRYNG group were characterized by a platelet counts in the range of below the LLN to 75×10^9/L. In the placebo group, two patients experienced decreases in platelet counts to the range of <LLN to 75×10^9/L, and one patient experienced a decrease in platelet count to the range of <75 to 50×10^9/L. None of the patients had a decrease in platelet count to less than 50×10^9/L, and decreases were not associated with bleeding events.

Elevated Liver Enzymes

NMOSD

In Study 1, increases from normal at baseline to above ULN in ALT or AST occurred in 43% and 25% of patients treated with ENSPRYNG, respectively, compared to 13% and 9% of patients receiving placebo. In Study 2, increases from normal at baseline to above the ULN in ALT or AST occurred in 8% and 8% of patients treated with ENSPRYNG, respectively, compared to 12% and 19% of patients receiving placebo.

In Study 1 and Study 2 combined, elevations of ALT or AST greater than 3 times the ULN occurred in 3% of patients treated with ENSPRYNG, compared to no patients treated with

placebo. These elevations were not associated with increases in total bilirubin. One patient receiving ENSPRYNG in Study 2 had an elevation of ALT above 5 times the ULN, which was observed 4 weeks after initiation of therapy, normalizing 78 days after discontinuation of ENSPRYNG.

TED

In Study 3 and Study 4, elevations in ALT or AST through Week 24 occurred in 25.2% and 11.5% of patients treated with ENSPRYNG respectively, compared with 7.3% and 4.8% of patients receiving placebo. The majority of elevations were characterized by an elevation above ULN to 3 X ULN. One patient (0.8%) in the placebo group experienced an AST elevation of >3 to 5 X ULN. No transaminase elevations of > 5 to 20X ULN or > 20 X ULN were reported. Most events of ALT and AST elevation resolved without requiring dose modification or discontinuation of ENSPRYNG.

Elevations in ALT or AST were not associated with increase in total bilirubin. Overall post-baseline, liver function tests abnormalities were infrequent, predominantly of low grade and, with no evidence of drug-induced liver injury or hepatotoxicity.

Lipid Abnormalities

NMOSD

In Study 1 and Study 2, elevations in total cholesterol above 7.75 mmol/L (300 mg/dl) occurred in 12% and 15% of patients treated with ENSPRYNG, respectively, compared to no patients receiving placebo.

Elevations in triglycerides above 3.42 mmol/L (300 mg/dl) occurred in 27% and 12% of patients treated with ENSPRYNG in Study 1 and Study 2, respectively, compared to 13% and 8% of patients receiving placebo.

TED

In Study 3 and Study 4, increases in total cholesterol through Week 24 were reported in 19.8% of patients treated with ENSPRYNG compared with 9.7% of patients receiving placebo. Elevations in cholesterol above 7.75 mmol/L were observed in 9.2% of these patients treated with ENSPRYNG compared with 2.4% of corresponding patients receiving placebo.

Increases in triglycerides were through Week 24 reported in 33.6% of patients treated with ENSPRYNG compared with 27.4 % of patients receiving placebo. Elevations in triglycerides above 3.42 mmol/L were observed in 1.5% of patients treated with ENSPRYNG compared with 3.2% of patients receiving placebo. The elevations in lipid parameters did not require treatment discontinuation

Fibrinogen Levels

NMOSD

In Study 1, the median percent reduction in fibrinogen was 38% in patients treated with ENSPRYNG compared to 5% in patients receiving placebo. In Study 2, the median percent reduction in fibrinogen level was 33% in patients treated with ENSPRYNG compared to 0% in patients receiving placebo.

Complement Levels

NMOSD

In Study 1, the median percent reduction in the C3 and C4 components of complement was 23% and 50% in patients treated with ENSPRYNG, respectively, compared to 0% and 1% patients receiving placebo. In Study 2, the median percent reduction in the C3 and C4 components of complement was 20% and 53% in patients treated with ENSPRYNG, respectively, compared to 0% and 1% in patients receiving placebo.

Body Weight

NMOSD

In the pool of Studies 1 and 2, body weight increases of at least 7% from baseline occurred in 28% of patients treated with ENSPRYNG compared to 8% of patients receiving placebo.

Body weight increases of at least 15% from baseline occurred in 4% of patients treated with ENSPRYNG compared to 4% of patients receiving placebo.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of anti-satralizumab-mwge antibodies in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

In NMOSD Study 1 and NMOSD Study 2, anti-drug-antibodies (ADAs) were observed in 73% and 38% of patients receiving ENSPRYNG in the double-blind period, respectively. The ability of these ADAs to neutralize satralizumab-mwge binding is unknown. Patients with higher body weight and lower exposure were more likely to develop ADAs (irrespective of treatment with IST). Exposure was lower in ADA positive patients. Although anti-satralizumab-mwge antibody development was not found to affect the efficacy of ENSPRYNG in these patients, the available data are too limited to make definitive conclusions. Immunogenicity does not have a clinically-relevant impact on safety. Based on the available information, neither dose interruption nor modification is warranted in those patients who develop ADAs.

In TED Study 3 and TED Study 4, anti-drug-antibodies (ADAs) were observed in 44.8% and 39.1% of patients receiving ENSPRYNG, respectively. The ability of these ADAs to neutralize satralizumab-mwge binding is unknown. ADA incidence is similar in the 120 mg (50 of 119, 42%) and 180 mg (5 of 12, 41.7%) dose groups. Exposure was lower in ADA positive patients. Immunogenicity does not appear to have a clinically-relevant impact on safety, efficacy or PD.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women with NMOSD exposed to ENSPRYNG during pregnancy. Healthcare providers are encouraged to register NMOSD patients and pregnant women with NMOSD are encouraged to register themselves by calling 1-833-277-9338.

Risk Summary

There are no adequate data on the developmental risk associated with the use of ENSPRYNG in pregnant women. In an animal reproduction study, no adverse effects on maternal animals or fetal development were observed in pregnant monkeys and their offspring, with administration of satralizumab-mwge at doses up to 50 mg/kg/week *(see Data)*.

In the U.S. general population, the estimated background risk of major birth defect and miscarriage in clinically recognized pregnancies is 2 – 4% and 15 – 20%, respectively. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. ENSPRYNG should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Clinical Considerations

Fetal/neonatal adverse reactions

Monoclonal antibodies are increasingly transported across the placenta as pregnancy progresses, with the largest amount transferred during the third trimester. Risks and benefits should be considered prior to administering live or live-attenuated vaccines to infants exposed to ENSPRYNG in utero *[see Warnings and Precautions (5.1)]*.

Data

Animal Data

Weekly subcutaneous administration of satralizumab-mwge (0, 2, or 50 mg/kg) to monkeys throughout pregnancy resulted in no adverse effects on postnatal development of the offspring; however, immune function was impaired in offspring at both doses. Plasma exposures (C_{ave}) in dams at the low and high doses were approximately 3 and 100 times, respectively, that in humans at the recommended monthly maintenance dose of 120 mg.

8.2 Lactation

Risk Summary

No information is available on the presence of satralizumab-mwge in human milk, the effects of the satralizumab-mwge on the breastfed infant, or the effects of the satralizumab-mwge on milk production. Satralizumab-mwge was excreted in the milk of lactating monkeys administered satralizumab-mwge throughout pregnancy. Human IgG is excreted in human milk and the potential for absorption in the infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ENSPRYNG and any potential adverse effects on the breastfed infant from ENSPRYNG or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of ENSPRYNG did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently from younger patients. However, population pharmacokinetic analyses in patients with NMOSD and TED did not show that age affected the pharmacokinetics of satralizumab-mwge *[see Clinical Pharmacology (12.3)]*. In general, caution should be used when dosing the elderly, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant diseases or other drug therapy.

11 DESCRIPTION

Satralizumab-mwge is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody based on a human IgG2 framework. Each light chain and heavy chain consists of 214 and 443 amino acids, respectively. Satralizumab-mwge is a glycoprotein with an approximate molecular weight of 143 kDa and is produced by recombinant DNA technology in Chinese hamster ovary cells. The binding of satralizumab-mwge to the IL-6 receptor is pH-sensitive.

ENSPRYNG (satralizumab-mwge) injection for subcutaneous administration is supplied as a sterile, clear, colorless to slightly yellow solution with no preservative, and with an approximate pH of 6. ENSPRYNG is supplied in a single-dose 1 mL prefilled syringe with a needle safety device or a single-dose 1 mL or 1.5 mL autoinjector that contains a prefilled syringe.

Each prefilled syringe delivers 1 mL of solution containing 120 mg satralizumab-mwge, L-arginine (26.1 mg), L-aspartic acid (pH adjustment), L-histidine (3.1 mg), poloxamer 188 (0.5 mg), and Water for Injection, USP.

Each prefilled autoinjector delivers either:

- 1 mL of solution containing 120 mg satralizumab-mwge, L-arginine (26.1 mg), L-aspartic acid (pH adjustment), L-histidine (3.1 mg), poloxamer 188 (0.5 mg), and Water for Injection, USP.
- 1.5 mL of solution containing 180 mg satralizumab-mwge, L-arginine (39.2 mg), L-aspartic acid (pH adjustment), L-histidine (4.65 mg), poloxamer 188 (0.75 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which satralizumab-mwge exerts therapeutic effects in NMOSD and TED is unknown but is presumed to involve inhibition of IL-6-mediated signaling through binding to soluble and membrane-bound IL-6 receptors.

12.2 Pharmacodynamics

The relationship between any of the pharmacodynamic effects of ENSPRYNG and clinical outcomes in NMOSD and TED is unknown.

12.3 Pharmacokinetics

The pharmacokinetics of ENSPRYNG have been characterized in healthy volunteers, and in NMOSD and TED patients. Population pharmacokinetic analyses were performed on databases

of 154 NMOSD patients and 131 TED patients. ENSPRYNG's pharmacokinetics was best described by a two-compartment population pharmacokinetic model with parallel linear and target-mediated (Michaelis-Menten) elimination and first-order SC absorption. ENSPRYNG clearance and volume parameters allometrically scaled by body weight (through power function with the fixed power coefficient of 0.75 and 1 for clearance and volume parameters, respectively)

The pharmacokinetics of satralizumab-mwge following administration of ENSPRYNG by prefilled syringe or autoinjector were comparable.

In patients with NMOSD using the recommended dose, steady state pharmacokinetics were achieved after the loading period (8 weeks) as follows [mean (±SD)]: C_{min}: 19.7 (12.2) mcg/mL, C_{max}: 31.5 (14.9) mcg/mL, and AUC: 737 (386) mcg.day/mL.

In patients with TED using the recommended dose, steady state pharmacokinetics were achieved after the loading period (8 weeks) as follows (mean (±SD)): C_{min}: 17.7 (9.64) mcg/mL, C_{max}: 28.7 (11.3) mcg/mL and AUC: 666 (301) mcg.day/mL.

Absorption

The median time to maximum concentration (T_{max}) at steady state was approximately 6 days based on population pharmacokinetic analyses. The bioavailability of satralizumab-mwge was 85%. In healthy subjects, the bioavailability of satralizumab was comparable following a single subcutaneous injection with the auto-injector and the prefilled syringes.

Distribution

Satralizumab-mwge undergoes biphasic distribution. The central volume of distribution was 3.46 L and the peripheral volume of distribution was 2.07 L. The inter-compartmental clearance was 0.336 L/day.

Elimination

The total clearance of satralizumab-mwge is concentration-dependent. Linear clearance (accounting for approximately half of the total clearance at steady state using the recommended dose) is estimated to be 0.0601 L/day. The associated terminal $t_{1/2}$ is approximately 30 days based on data pooled from all studies.

Metabolism

The metabolism of satralizumab-mwge has not been directly studied, as antibodies are cleared principally by catabolism.

Excretion

Monoclonal antibodies, including satralizumab-mwge, are not eliminated via renal or hepatic pathways.

Specific Populations

Population pharmacokinetic analyses in patients with NMOSD or with TED showed that age, gender, and race did not meaningfully influence the pharmacokinetics of satralizumab-mwge.

Patients with Renal or Hepatic Impairment

No formal studies of the effect of renal impairment or hepatic impairment on the pharmacokinetics of satralizumab-mwge were conducted.

Drug Interaction Studies

No formal drug-drug interaction studies have been performed with ENSPRYNG.

Based on population pharmacokinetic analyses of the available data, the impact of commonly used small molecule drugs on the pharmacokinetics of satralizumab-mwge remains inconclusive.

Suppression of IL-6 signaling by treatment with ENSPRYNG, from the low baseline levels seen in NMOSD and TED Studies is expected to have a minor impact on exposure of concomitant medications metabolized by CYP450 enzymes. The clinical significance of this is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies of satralizumab-mwge were not conducted.

Mutagenesis

Genetic toxicology studies of satralizumab-mwge were not conducted. As an antibody, satralizumab-mwge is not expected to interact directly with DNA.

Impairment of Fertility

In monkeys administered satralizumab-mwge (0, 2, 10, or 50 mg/kg) weekly by subcutaneous injection for 26 weeks, no effects on sperm, estrus cycle, or male and female reproductive organs were observed. At the high dose, plasma exposures (C_{ave}) were approximately 100 times that in humans at the recommended monthly maintenance dose of 120 mg.

14 CLINICAL STUDIES

14.1 Clinical Studies in NMOSD

The efficacy of ENSPRYNG for the treatment of NMOSD in adult patients was established in two studies. Study 1 was a randomized (2:1), placebo-controlled trial in 95 patients without concurrent IST (Study 1, NCT02073279) in which 64 patients were anti-AQP4 antibody positive and 31 patients were anti-AQP4 antibody negative.

Study 2 was a randomized (1:1), placebo-controlled trial in 76 adult patients with concurrent IST (Study 2, NCT02028884). Of these, 52 adult patients were anti-AQP4 antibody positive and 24 adult patients were anti-AQP4 antibody negative.

Patients met the following eligibility criteria:

1. Study 1: Clinical evidence of 1 relapse in the previous 12 months
2. Study 2: Clinical evidence of at least 2 relapses in the previous 2 years, at least one of which must have occurred in the previous year
3. EDSS score of 0 to 6.5 (both studies)
4. Study 1: Patients were excluded if previously treated with IST within an interval specified for each such therapy
5. Study 2: One of the following baseline treatments at a stable dose as a monotherapy for 8 weeks prior to baseline: azathioprine, mycophenolate mofetil, oral corticosteroids

In Study 1, 41 anti-AQP4 antibody positive adult patients were randomized to and received ENSPRYNG and 23 received placebo. Females accounted for 76% of the ENSPRYNG group

and 96% of the placebo group. The remaining baseline demographic characteristics were balanced between the treatment groups. The mean age was 44 years. Fifty percent were White, 22% were Black or African-American, and 20% were Asian. The mean EDSS score was 3.8.

In Study 2, 26 anti-AQP4 antibody positive adult patients were randomized to and received ENSPRYNG and 26 received placebo. All patients were receiving either concurrent azathioprine (42%), oral corticosteroids (52%), or mycophenolate mofetil (6%) during the trial. The baseline demographic and disease characteristics were balanced between the treatment groups. Females accounted for 100% of the study population. Forty-six percent of patients were White and 52% were Asian. The mean age was 46 years. The mean EDSS score was 4.0.

All potential relapses were adjudicated by a blinded Clinical Endpoint Committee (CEC). The primary efficacy endpoint for both studies was the time to the first CEC-confirmed relapse.

In Study 1, the time to the first CEC-confirmed relapse was significantly longer in ENSPRYNG-treated patients compared to patients who received placebo (risk reduction 55%; hazard ratio 0.45; $p = 0.0184$). In the anti-AQP4 antibody positive population, there was a 74% risk reduction; hazard ratio 0.26; $p = 0.0014$ (Table 7; Figure 1). There was no evidence of a benefit in the anti-AQP4 antibody negative patients.

In Study 2, the time to the first CEC-confirmed relapse was significantly longer in patients treated with ENSPRYNG compared to patients who received placebo (risk reduction 62%; hazard ratio 0.38; $p = 0.0184$). In the anti-AQP4 antibody positive population, there was a 78% risk reduction; hazard ratio 0.22; $p = 0.0143$ (Table 7; Figure 2). There was no evidence of a benefit in the anti-AQP4 antibody negative patients.

Table 7 Efficacy Results from Study 1 and Study 2 in anti-AQP4 Antibody Positive NMOSD Patients

	Study 1		Study 2	
	ENSPRYNG N=41	**Placebo N=23**	**ENSPRYNG + IST* N= 26**	**Placebo + IST N=26**
Time to Clinical Endpoint Committee (CEC)-Determined Relapse (Primary Efficacy Endpoint)				
Number (%) of Patients with Relapse	9 (22)	13 (56.5)	3 (11.5)	11 (42.3)
Hazard Ratio (95% CI)	0.26 (0.11, 0.63)		0.22 (0.06, 0.82)	
p-value	0.0014		0.0143	
Risk Reduction	74%		78%	
Proportion of Protocol Defined Relapse-Free Patients at 96 Weeks	76.5%	41.1%	91.1%	56.8%

* IST = immunosuppressant therapy

Figure 1 Study 1: Time to First CEC-Determined NMOSD Relapse in the Randomized Controlled Period in the ITT Population Anti-AQP4 Antibody Positive Patients

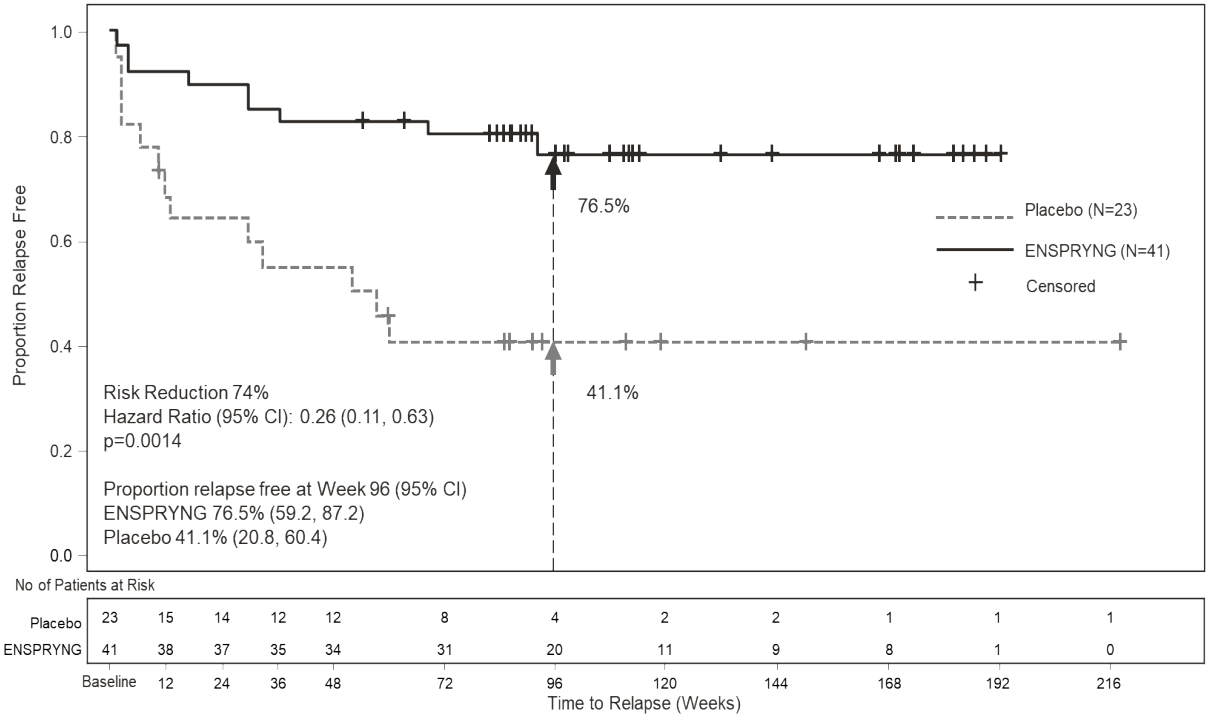
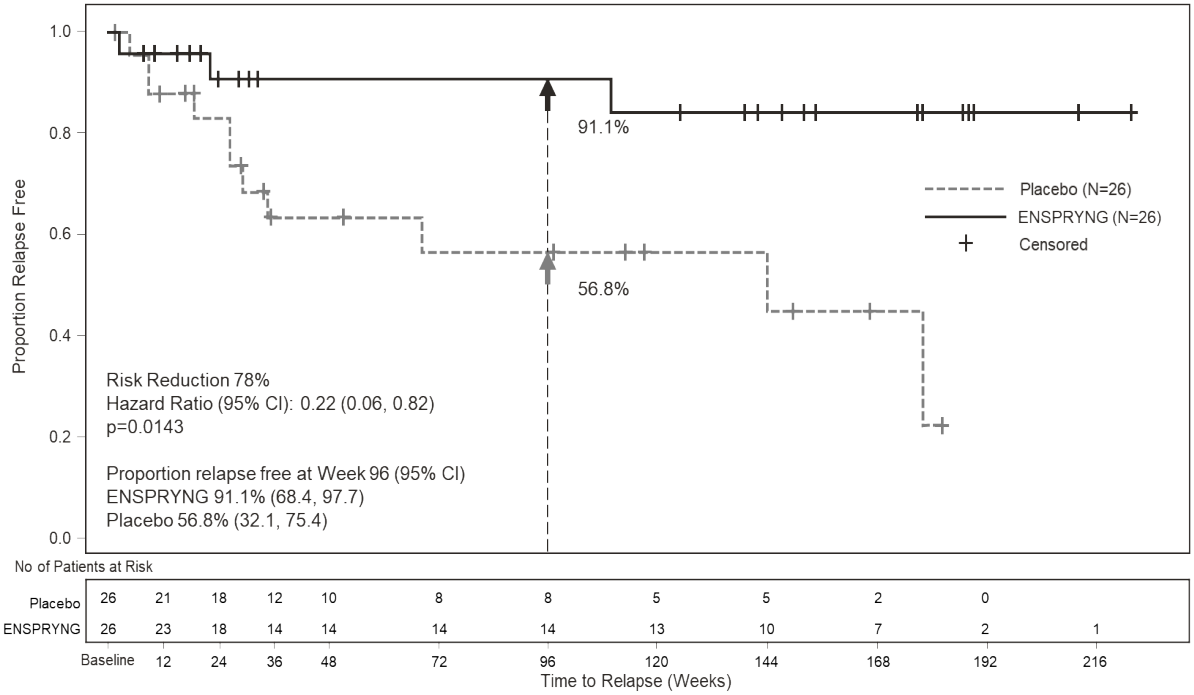


Figure 2 Study 2: Time to First CEC-Determined NMOSD Relapse in the Randomized Controlled Period in the ITT Population Anti-AQP4 Antibody Positive Patients



14.2 Clinical Studies in TED

The efficacy of ENSPRYNG for the treatment of thyroid eye disease (TED) was evaluated in two identical, randomized, double-masked, placebo-controlled, multicenter Phase 3 clinical trials (Study 3, NCT05987423 and Study 4, NCT06106828) in patients with TED. A total of 258 patients were enrolled in the two studies, of whom 255 received at least one dose of study treatment through Week 24 (131 patients received ENSPRYNG). Overall, 238 patients (92.2%) completed the studies through Week 24. Patient age ranged from 19 to 80 years (median age, 49.4 years).

The study population included patients with active, moderate-to-severe TED (76.7%) and patients with inactive TED (23.3%). Patients were required to have either:

- a clinical diagnosis of active TED, defined as a Clinical Activity Score (CAS) ≥3 and proptosis ≥3 mm above normal in the study eye, or

- a clinical diagnosis of stable, chronic inactive TED, defined as CAS <3 and proptosis ≥3 mm above normal.

All patients were required to be euthyroid at baseline or to have mild hypo- or hyperthyroidism (defined as free T3 and free T4 within 50% above or below the normal range at screening). Patients with prior surgical or biologic treatment for TED were excluded. In both studies, patients were randomized to receive ENSPRYNG at the recommended dose *[see Dosage and Administration (2.2)]* or placebo administered by subcutaneous injection at Weeks 0, 2, and 4, followed by dosing every 4 weeks through Week 20.

The primary efficacy endpoint was the proptosis responder rate at Week 24 in the active TED population. A proptosis responder was defined as a patient with a ≥2 mm reduction in proptosis in the study eye from baseline without deterioration (≥2 mm increase in proptosis) in the non-study eye (Table 8). Additional evaluations included signs and symptoms of TED, including orbital pain, gaze evoked orbital pain, eyelid swelling, eyelid erythema, conjunctival redness, chemosis, inflammation, clinical activity score and assessments of quality of life (functional vision and patient appearance). Efficacy results of satralizumab were generally consistent across pre-defined subgroups (e.g., age, gender, ethnicity, race, iris pigmentation, smoking status) for the proptosis responder rate.

Proptosis response in the active TED population at Week 24 was 52.9% in the ENSPRYNG group compared to 23.4% in the placebo group in Study 4. Study 3 did not meet its pre-specified primary efficacy endpoint at Week 24 compared to placebo (Table 8).

Table 8: Primary Efficacy Results at Week 24 in Study 3 and Study 4 among TED Patients

Efficacy Outcomes	Study 3		Study 4	
	Enspryng (n=50)	**Placebo (n=51)**	**Enspryng (n=48)**	**Placebo (n=49)**
Proptosis response in active TED population% (n)	49.0%	31.2%	52.9%	23.4%
Difference 95.03% CI (p-value)	17.9% (-1.6%, 37.3%) (0.07)		28.9% (11.5%, 46.2%) (<0.01)	

Efficacy was also evaluated in the overall TED population, including both active and inactive disease (Table 9). Proptosis response in the overall TED population at Week 24 was 46.9% in the ENSPRYNG group compared to 22.2% in the placebo group in Study 4. The proptosis response in the overall TED population in Study 3 was generally consistent with Study 4.

Table 9 Additional Efficacy Results from Study 4 in TED Patients

Efficacy Outcomes at Week 24	Study 4	
	Enspryng n/N (%) / mean	**Placebo n/N (%) / mean**
Proptosis response in overall TED population at Week 24	30/64 (46.9%)	14/63 (22.2%)
Difference 95.03% CI (p-value)	24.6% 9.4%, 39.8% (<0.01)	
Proportion of patients with Grade ≥ 1 reduction/improvement in diplopia (active population) at Week 24**	17/28 (60.7%)	8/31 (25.8%)
Difference 95.03% CI (p-value)	35.1% 11.0%, 59.3% (<0.01)	
Change in proptosis (mm) in the study eye (active population) at Week 24	48 –1.97mm	49 – 0.96mm
Difference 95.03% CI (p-value)	– 1.02% – 1.67%, 0.36% (<0.01)	

** Results from baseline (Day 1) at Week 24 among participants with diplopia present at baseline

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ENSPRYNG (satralizumab-mwge) injection is available as a sterile, preservative-free, clear, colorless to slightly yellow solution for subcutaneous injection in a single-dose prefilled syringe (PFS) with needle safety device or a single-dose autoinjector.

ENSPRYNG prefilled syringe and autoinjector are not made with natural rubber latex. Each ENSPRYNG carton contains either:

- One single-dose 120 mg/mL prefilled syringe (NDC 50242-007-01)
- One single-dose 120 mg/mL autoinjector (NDC 50242-007-55).
- One single-dose 180 mg/1.5mL autoinjector (NDC 50242-005-01).

16.2 Storage and Handling

- Refrigerate at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.
- ENSPRYNG can be stored out of refrigeration for a maximum of 8 days at a temperature that does not exceed 30°C (86°F). If ENSPRYNG is removed from and returned to the refrigerator, the total combined time out of refrigeration should not exceed 8 days.
- Always keep in the original carton to protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patients to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

<u>Infections</u>

Inform patients that an increased risk of infections, including serious and potentially fatal infections, has been observed in patients treated with IL-6 receptor antagonists, including ENSPRYNG. Instruct patients to contact their healthcare provider immediately when symptoms suggesting infection (e.g., fever, chills, constant cough, or sore throat) appear during treatment *[see Warning and Precautions (5.1)]*.

<u>Vaccinations</u>

Advise patients to complete any required vaccinations at least 4 weeks prior to initiation of ENSPRYNG for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ENSPRYNG for non-live vaccines *[see Warnings and Precautions 5.1]*.

<u>Elevated Liver Enzymes</u>

Inform patients on the importance of liver enzyme testing *[see Warnings and Precautions (5.2)]*.

<u>Decreased Neutrophil Counts</u>

Inform patients on the importance of neutrophil count testing *[see Warnings and Precautions (5.3)]*.

<u>Hypersensitivity Reactions</u>

Inform patients about the signs and symptoms of hypersensitivity reactions and anaphylaxis and advise them to contact their healthcare provider immediately if these symptoms occur *[see Warnings and Precautions (5.4)]*.

Instruction on Injection Technique

Instruct patients and caregivers to read the Instructions for Use before the patient starts using ENSPRYNG, and each time the patient gets a refill as there may be new information they need to know.

Perform the first injection under the guidance of a qualified healthcare professional. If a patient or caregiver is to administer subcutaneous ENSPRYNG, instruct him/her in injection techniques and assess his/her ability to inject subcutaneously to ensure proper administration of subcutaneous ENSPRYNG and the suitability for home use *[see Dosage and Administration (2.3) and Instructions for Use]*.

Instruct patients to remove the prefilled syringe or autoinjector from the refrigerator prior to use and allow it to sit at room temperature outside of the carton for 30 minutes. Do not warm ENSPRYNG in any other way.

Instruct patients to use the syringe or the autoinjector within 5 minutes of removing the cap. Do not remove the cap until ready to inject.

Advise patients not to touch the green needle shield of the autoinjector or put the cap back on after it has been removed, as this may unintentionally activate the autoinjector.

Advise patients to consult their healthcare provider if the full dose is not received.

A puncture-resistant container for disposal of syringes should be used and should be kept out of the reach of children. Instruct patients or caregivers in the technique as well as proper prefilled syringe or autoinjector disposal, and caution against reuse of these items.

Pregnancy Exposure Registry for NMOSD

Encourage patients to enroll in the ENSPRYNG Pregnancy Registry if they become pregnant while taking ENSPRYNG for NMOSD. The Registry monitors fetal outcomes of pregnant women with NMOSD exposed to ENSPRYNG *[see Use in Specific Populations (8.1)]*.

ENSPRYNG® [satralizumab-mwge]

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990

U.S. License No.: 1048

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Chugai Pharmaceutical Co., Ltd., Tokyo, Japan

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MEDICATION GUIDE

ENSPRYNG® (en-spryng)

(satralizumab-mwge)

injection, for subcutaneous use

What is the most important information I should know about ENSPRYNG?

ENSPRYNG may cause serious side effects including:

1. **Infections.** ENSPRYNG can increase your risk of serious infections some of which can be life-threatening. Talk to your healthcare provider if you are being treated for an infection or call them right away if you think you have signs of an infection, with or without a fever, such as:
    - chills, feeling tired, muscle aches, cough that will not go away or a sore throat.
    - skin redness, swelling, tenderness, pain or sores on your body.
    - diarrhea, belly pain, or feeling sick.
    - burning when you urinate or urinating more often than usual.

- Your healthcare provider will check if you have an infection and treat it if needed before you start or continue to take ENSPRYNG.
- Your healthcare provider should test you for hepatitis and tuberculosis (TB) before you start taking ENSPRYNG.
- All required vaccinations should be completed before starting ENSPRYNG. People using ENSPRYNG should not be given 'live' or 'live-attenuated' vaccines. 'Live' or 'live-attenuated' vaccines should be given at least 4 weeks before you start ENSPRYNG. Your healthcare provider may recommend that you get a 'non-live' (inactivated) vaccine, such as some of the seasonal flu vaccines. If you plan to get a 'non-live' (inactivated) vaccine, it should be given, whenever possible, at least 2 weeks before you start ENSPRYNG.

2. **Increased liver enzymes.** Your healthcare provider should order blood tests to check your liver enzymes before and while you are taking ENSPRYNG. Your healthcare provider will tell you how often you will need to have these blood tests. Make sure you get all of your follow-up blood tests as ordered by your healthcare provider. Your healthcare provider will tell you if you need to wait to start ENSPRYNG if your liver enzymes are increased.
3. **Low neutrophil count.** ENSPRYNG can cause a decrease in your neutrophil counts in your blood. Neutrophils are white blood cells that help the body fight off bacterial infections. Your healthcare provider should order blood tests to check your neutrophil count while you are taking ENSPRYNG.

See "What are the possible side effects with ENSPRYNG?"

What is ENSPRYNG?

ENSPRYNG is a prescription medicine used to treat:

- neuromyelitis optica spectrum disorder (NMOSD) in adults who are aquaporin-4 (AQP4) antibody positive.
- thyroid eye disease (TED) no matter how severe it is or how long a person has had it.

It is not known if ENSPRYNG is safe and effective in children.

Do not take ENSPRYNG if you:

- are allergic to satralizumab-mwge or any of the ingredients in ENSPRYNG. See **"What are the ingredients in ENSPRYNG?"** at the end of this Medication Guide for a complete list of ingredients in ENSPRYNG.
- have an active hepatitis B infection.
- have active or untreated inactive (latent) TB.

Before you take ENSPRYNG, tell your healthcare provider about all of your medical conditions, including if you:

- have or think you have an infection. See **"What is the most important information I should know about ENSPRYNG?"**
- have liver problems.
- have ever had hepatitis B or are a carrier of the hepatitis B virus..
- have had or have been in contact with someone with tuberculosis.
- have had a recent vaccination or are scheduled to receive any vaccination.
- are pregnant, think that you might be pregnant, or plan to become pregnant. It is not known if ENSPRYNG will harm your unborn baby.
    - **Pregnancy Registry**: There is a registry for pregnant women who take ENSPRYNG for NMOSD. The purpose of this registry is to check the health of the pregnant mother and her baby. If you are pregnant or become pregnant while taking ENSPRYNG for NMOSD, talk to your healthcare provider about how you can join this pregnancy registry, or you may contact the registry at 1-833-277-9338 to enroll.

- are breastfeeding or plan to breastfeed. It is not known if ENSPRYNG passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take ENSPRYNG.

Tell your healthcare provider about all the medicines you are taking, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take ENSPRYNG?

- ENSPRYNG is provided as a solution in a single-dose, prefilled syringe of 120 mg/mL of satralizumab-mwge, or autoinjector of 120 mg/mL or 180 mg/1.5mL of satralizumab-mwge.
- See the **Instructions for Use** inside the carton for complete instructions for the right way to prepare and inject ENSPRYNG.
- ENSPRYNG is given by an injection under the skin (subcutaneously). If your healthcare provider decides that you or your caregiver can give your injections of ENSPRYNG, you or your caregiver should receive training on the right way to prepare and inject ENSPRYNG.
- Before injecting, wait 30 minutes for the ENSPRYNG prefilled syringe or autoinjector to reach room temperature.
- Use ENSPRYNG within 5 minutes of removing the cap or the needle may clog. Do not remove the cap until ready to inject.
- Always inject all of the medicine in the prefilled syringe or autoinjector.
- The first 3 injections (loading period) of ENSPRYNG are taken 1 time every 2 weeks.
- After this, injection of ENSPRYNG is taken every 4 weeks (maintenance period). Keep taking ENSPRYNG 1 time every 4 weeks for as long as your healthcare provider tells you to.
- If you miss a dose of ENSPRYNG, talk to your health care provider about restarting dosing.

What are the possible side effects of ENSPRYNG?

ENSPRYNG may cause serious side effects, including:

- See **"What is the most important information I should know about ENSPRYNG?"**
- **Serious allergic reactions.** Serious allergic reactions that may be life-threatening have happened with other medicines like ENSPRYNG. Tell your healthcare provider before taking your next dose if you had hives, rash, or flushing after your injection. Seek medical attention right away if you have any symptoms of a serious allergic reaction, such as:
  - shortness of breath or trouble breathing
  - dizziness or feeling faint
  - swelling of your lips, face, or tongue
  - moderate or severe stomach (abdominal) pain or vomiting
  - chest pain

The most common side effects of ENSPRYNG include:

- sore throat, runny nose (nasopharyngitis)
- rash
- fatigue
- extremity pain
- headache
- upper respiratory tract infection
- nausea
- inflammation of the stomach lining (gastritis)
- joint pain

These are not all the possible side effects of ENSPRYNG.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Genentech at 1-888-835-2555.

How should I store ENSPRYNG?

- Store ENSPRYNG in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.
- **Do not** freeze. **Do not** use ENSPRYNG if it has been frozen.
- Do not shake.
- The ENSPRYNG carton can be stored at room temperature up to 86°F (30°C) for up to 8 days.
- If ENSPRYNG is removed from and returned to the refrigerator the total combined time out of the refrigerator should not be more than 8 days.
- Always keep in the original carton to protect from light.
- Keep ENSPRYNG and all medicines out of the reach of children.

General information about the safe and effective use of ENSPRYNG.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ENSPRYNG for a condition for which it was not prescribed. Do not give ENSPRYNG to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about ENSPRYNG that is written for health professionals.

What are the ingredients in ENSPRYNG?
Active ingredient: satralizumab-mwge
Inactive ingredients: L-arginine, L-aspartic acid, L-histidine, poloxamer 188, and Water for Injection.

Manufactured by: **Genentech, Inc.**, A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990
ENSPRYNG® is a registered trademark of Chugai Pharmaceutical Co., Ltd., Tokyo, Japan
U.S. License No.: 1048
For more information, go to www.ENSPRYNG.com or call 1-844-NSPRYNG.

This Medication Guide has been approved by the U.S. Food and Drug Administration

Revised: 10/2026

INSTRUCTIONS FOR USE
ENSPRYNG® (en-spryng)
(satralizumab-mwge)
injection, for subcutaneous use
single-dose prefilled autoinjector

Read this Instructions for Use before you start using the ENSPRYNG autoinjector and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition and treatment.

Your healthcare provider will show you or your caregiver how to use the ENSPRYNG autoinjector the right way. Talk to your healthcare provider if you have questions.

Important information you need to know before injecting ENSPRYNG

- **Do not** use the ENSPRYNG autoinjector until your healthcare provider has trained you or your caregiver on the right way to inject.
- **Do not** use if the expiration (EXP) date has passed.
- **Do not** use if the seals on the carton have been broken.
- **Do not** try to take the autoinjector apart at any time.
- **Do not** remove the cap until you are ready to inject.
- **Do not** use if the autoinjector has been damaged or dropped.
- **Do not** touch or clean the green needle shield.
- **Do not** try to re-use the same autoinjector. Each prefilled autoinjector can be used only one time.
- **Do not** inject through clothing.

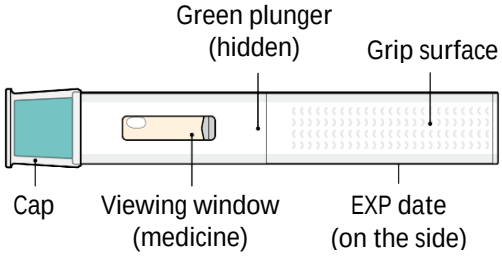
How should I store the ENSPRYNG autoinjector?

- Store ENSPRYNG in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.
- **Do not** freeze. **Do not** use ENSPRYNG if it has been frozen.
- Do not shake.
- The ENSPRYNG carton can be stored at room temperature up to 86°F (30°C) for up to 8 days.
- If ENSPRYNG is removed from and returned to the refrigerator the total combined time out of the refrigerator should not be more than 8 days.
- Always keep in the original carton to protect from light.
- **Keep ENSPRYNG and all medicines out of the reach of children.**

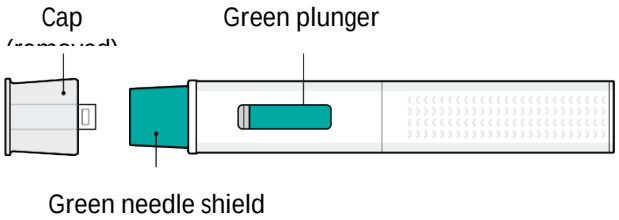
ENSPRYNG autoinjector

Always check that you have the right medicine and dose that your healthcare provider prescribed.

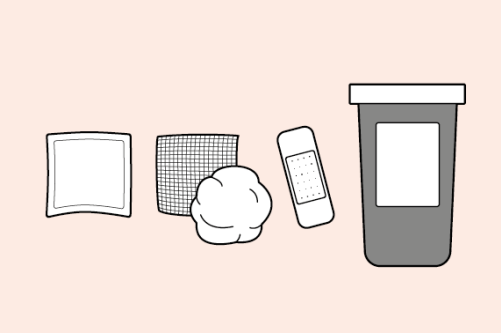
Before use



After use



Prepare to use ENSPRYNG

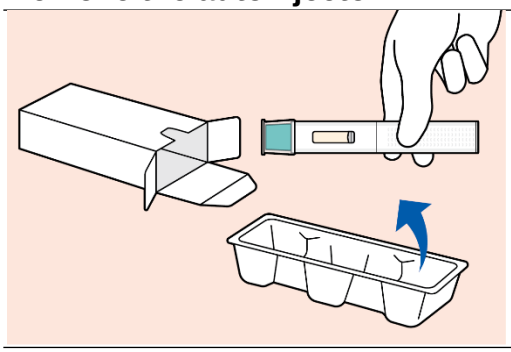


Step 1. Gather supplies needed for your injection.

Included in the carton:
- ENSPRYNG autoinjector

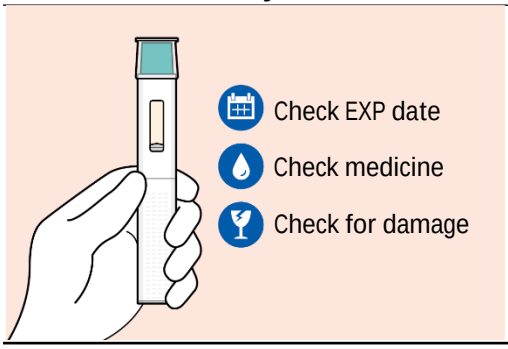
Not included in the carton:
- 1 alcohol pad
- 1 sterile cotton ball or gauze
- 1 small adhesive bandage
- 1 FDA-cleared sharps disposal container (See Step 17 Dispose of the autoinjector)

Remove the autoinjector



Step 2. Take the ENSPRYNG autoinjector carton out of the refrigerator.
Step 3. Open the carton and take the autoinjector out of the tray.

Check the autoinjector



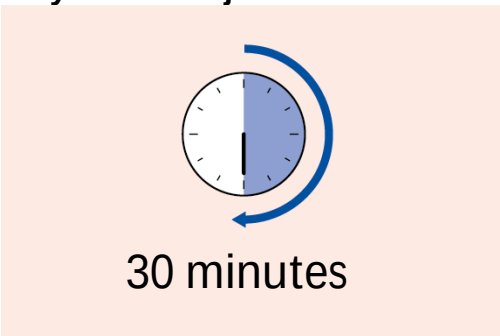
Step 4. Check the expiration (EXP) date on the autoinjector.
- **Do not** inject if the expiration date (EXP) has passed.

Step 5. Check the medicine through the viewing window. The medicine should be clear or slightly yellow. There should be no particles in it.
- **Do not** inject if the medicine looks cloudy, discolored, or has particles in it. You may see small air bubbles. This is normal and you should not try to remove them.

Step 6. Check the autoinjector for any damage.
- **Do not** use if the autoinjector is cracked or broken.

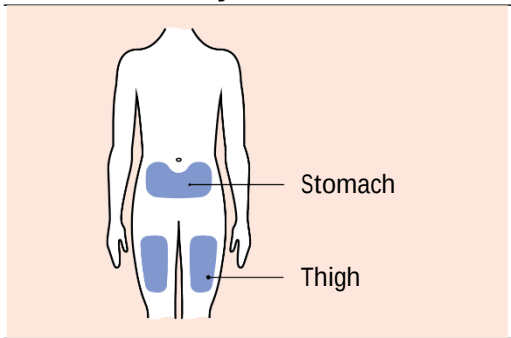
If the expiration date has passed, the autoinjector is damaged or the medicine is cloudy, discolored or has particles in it, do not use. Safely throw away (dispose of) the autoinjector in an FDA-cleared sharps disposal container (See Step 17) and contact your healthcare provider.

Let your autoinjector reach room temperature



Step 7. Place the autoinjector on a clean, flat surface (like a table) for 30 minutes. This allows the medicine to reach room temperature.
If the autoinjector does not reach room temperature, it may take longer to inject the medicine. Injecting cold medicine may feel uncomfortable.
- **Do not** speed up the warming process in any way, such as using a microwave, warm water, or direct sunlight.
- **Do not** remove the cap until you are ready to inject.

Choose the injection site

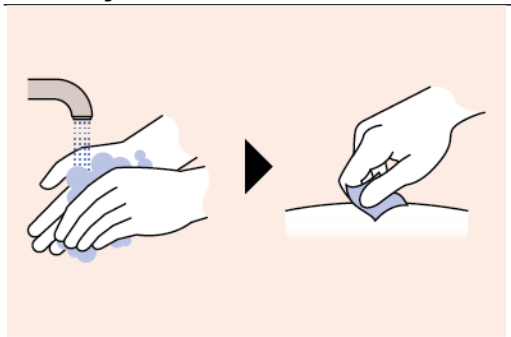


Step 8. You can inject ENSPRYNG in the stomach area (abdomen) or front of the thigh.

- **Do not** inject into the 2 inches (5 cm) area around the belly button.
- **Do not** inject into moles, scars, or areas where the skin is tender, bruised, red, hard, or not intact.

Choose a different injection site for **each new injection. Each injection must be at least 1 inch (2.5 cm) away from area where you last injected.**

Clean your skin

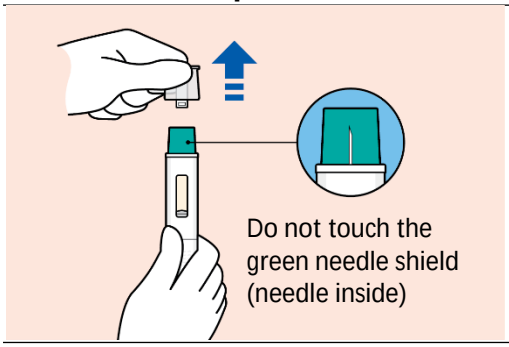


Step 9. Wash your hands with soap and water.

Step 10. Clean the injection site with an alcohol pad and let it air dry.

- **Do not** fan or blow on the area you have cleaned.
- **Do not** touch the injection site again before you inject.

Remove the cap

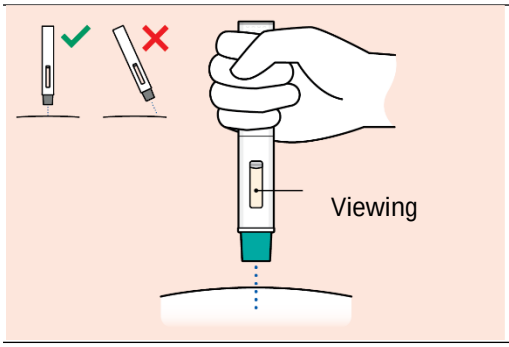


Step 11. Hold the autoinjector with the cap pointing up. Then pull the cap straight off. The needle will remain hidden.
Use the autoinjector within **5 minutes of removing the cap**.

Important: Do not touch the green needle shield. This may cause a needle stick injury.

- **Do not** clean the green needle shield. This may activate the autoinjector.
- **Do not** put the cap back on after it has been removed. This may activate the autoinjector.

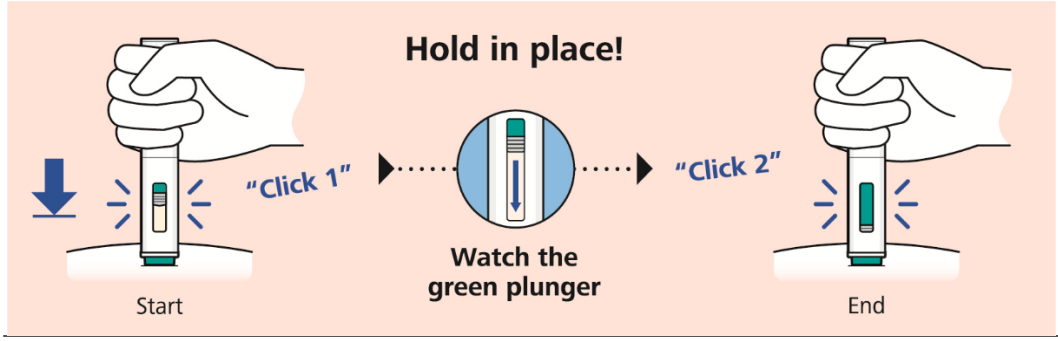
Place onto the skin



Step 12. Hold the autoinjector so that you can **see the viewing window**.
Place the autoinjector flat against the skin with the green needle shield facing down.
You may see drops of liquid. This is normal.

- **Do not** change the angle of the injection.

Push firmly and hold in place



Step 13. **Push firmly and hold down** the autoinjector against the skin.
The **first click** indicates the injection has started.

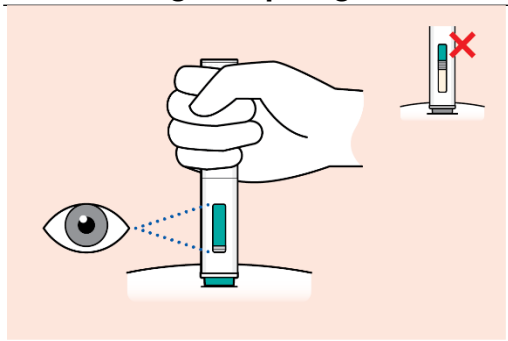
The **green plunger** moves down in the viewing window. It might take **up to 15 seconds** for the green plunger to move all the way down and fill the viewing window.

- **Do not** lift the autoinjector if the green plunger is moving. This may cause a loss of medicine.

Step 14. Keep holding down the autoinjector firmly.
Wait for the second click. This means the injection is done.

Watch the green plunger as it moves down. Or check if the green plunger has already filled the entire viewing window (See Step 15).

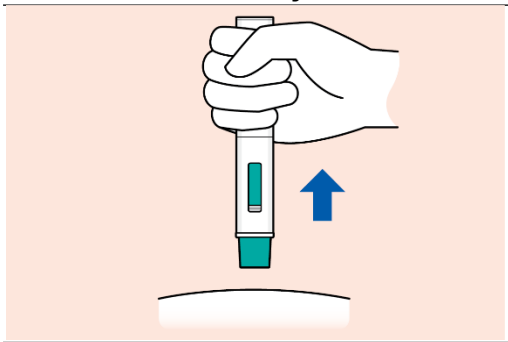
Check the green plunger



Step 15. Before removing the autoinjector from the injection site, check that the green plunger fills the viewing window entirely.

If the green plunger does not fill the viewing window, you may not have received the full dose. Safely throw away (dispose of) the autoinjector in a sharps disposal container (See Step 17) and contact your healthcare provider.

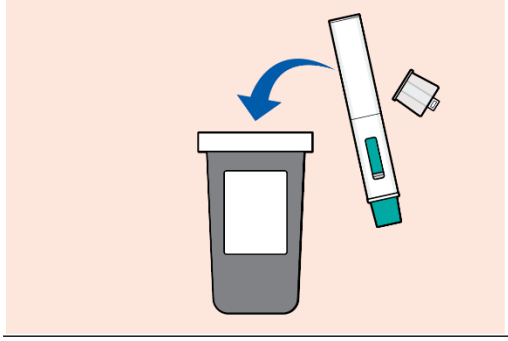
Remove the autoinjector



Step 16. Remove the autoinjector by lifting it straight up from the skin.

The green needle shield will lock into place, covering the needle when the injection is complete.

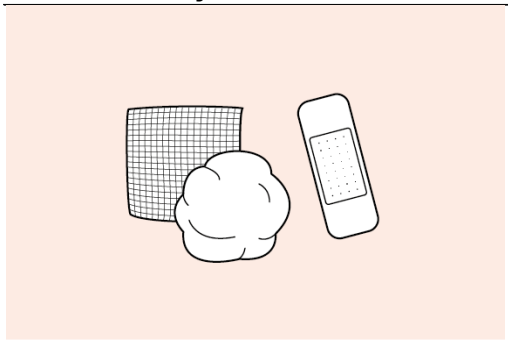
Dispose of the autoinjector



Step 17. Put the used autoinjector and the cap in an FDA-cleared sharps disposal container right away after use.

- **Do not** throw away (dispose of) the autoinjector in your household trash.

Check the injection site



Step 18. There may be a small amount of blood or medicine at the injection site. You can press a cotton ball or gauze on the area. If needed, cover the injection site with a small adhesive bandage.
The injection is now complete.

- **Do not** rub or massage the area where you have injected.

Disposal of the autoinjector

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:
- made of heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.

Do not recycle your used sharps disposal container.

Keep the sharps disposal container out of the reach of children.

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990

U.S. License No.: 1048

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This Instructions for Use has been approved by the U.S. Food and Drug Administration Revised: 10/2026

INSTRUCTIONS FOR USE
ENSPRYNG® (en-spryng)
(satralizumab-mwge)
Injection, for subcutaneous use
single-dose prefilled syringe

Read this Instructions for Use before you start using the ENSPRYNG syringe and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

Your healthcare provider will show you or your caregiver how to use the ENSPRYNG syringe the right way. Talk to your healthcare provider if you have any questions.

Important information you need to know before injecting ENSPRYNG

- **Do not** use the ENSPRYNG prefilled syringe until your healthcare provider has trained you or your caregiver on the right way to inject.
- **Do not** share your ENSPRYNG syringe with other people. You may give them a serious infection or get a serious infection from them.
- **Do not** use if the expiration (EXP) date has passed.
- **Do not** use if the seals on the carton have been broken.
- **Do not** try to take the syringe apart at any time.
- **Do not** take the needle cap off until you are ready to inject ENSPRYNG.
- **Do not** use the syringe if it has been dropped or damaged.
- **Do not** re-use the same syringe. Each prefilled syringe can be used only 1 time.
- **Do not** inject through clothing.

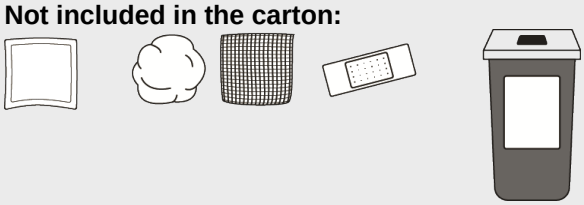
How should I store the ENSPRYNG prefilled syringe?

- Store ENSPRYNG in the refrigerator between 36°F to 46°F (2°C to 8°C) in the original carton to protect from light.
- **Do not** freeze. **Do not** use ENSPRYNG if it has been frozen.
- **Do not** shake.
- The ENSPRYNG carton can be stored at room temperature up to 86°F (30°C) for up to 8 days.
- If ENSPRYNG is removed from and returned to the refrigerator the total combined time out of the refrigerator should not be more than 8 days.
- Always keep in the original carton to protect from light.
- **Keep ENSPRYNG and all medicines out of the reach of children.**

Supplies needed to give your injection
Each ENSPRYNG carton contains:

- 1 prefilled syringe for 1-time use only.

Not included in the carton:



- 1 alcohol pad
- 1 sterile cotton ball or gauze
- 1 small bandage
- 1 FDA-cleared, puncture-resistant sharps container for safe disposal of the needle cap and used syringe. See Step 21 “Disposing of ENSPRYNG” at the end of this Instructions for Use.

Always check that you have the right medicine and dose that your healthcare provider prescribed.

ENSPRYNG prefilled syringe
(See Figure A and Figure B)
Before use:

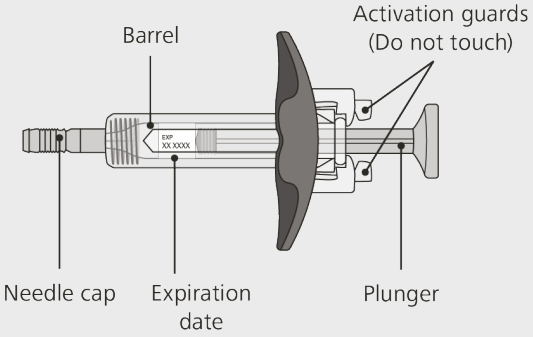


Figure A

After use:

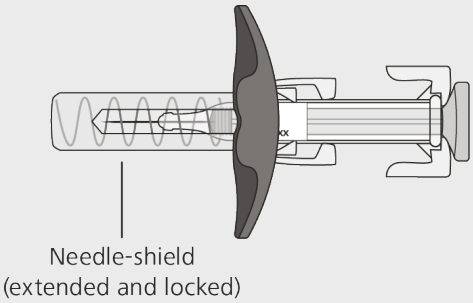


Figure B

The syringe has a needle-shield that automatically covers the needle when the injection is complete.

Prepare to use ENSPRYNG

Step 1. Take the carton containing the syringe out of the refrigerator and place it on a clean, flat work surface (like a table).

Step 2. Check the expiration (EXP) date on the back of the carton **(See Figure C)**. **Do not** use if the expiration date has passed.

Step 3. Check the front of the carton to make sure it is sealed **(Figure C)**. **Do not** use if the seal has been broken.

If the expiration date has passed or the seal is broken, do not use. Then go to Step 21 "Disposing of ENSPRYNG" and contact your healthcare provider.

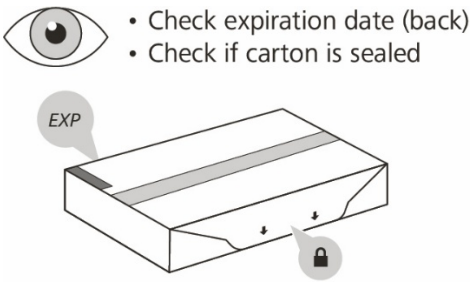


Figure C

Step 4. Open the sealed carton **(See Figure D)**.

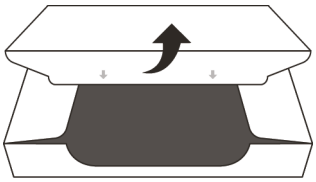


Figure D

Step 5. Carefully lift the syringe out of the carton by holding the barrel **(See Figure E)**.

- **Do not** turn the carton upside down to remove the syringe.
- **Do not** touch the activation guards because this may damage the syringe.
- **Do not** hold the plunger or needle cap.

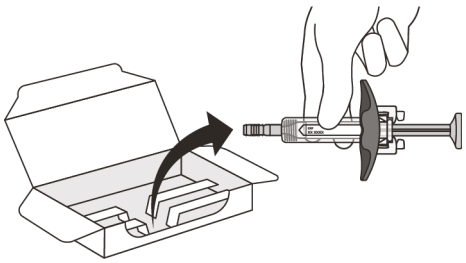


Figure E

Check the syringe

(See Figure F)

Step 6. Check the expiration date on the syringe. **Do not** use the syringe if it has expired.

Step 7. Check the syringe for any damage. **Do not** use if it is cracked or broken.

Step 8. Check that the liquid through the viewing window is clear and colorless to slightly yellow. **Do not** inject the medicine if the liquid is cloudy, discolored, or has particles in it.

- There may be some small air bubbles in the syringe. This is normal and you should not try to remove them.

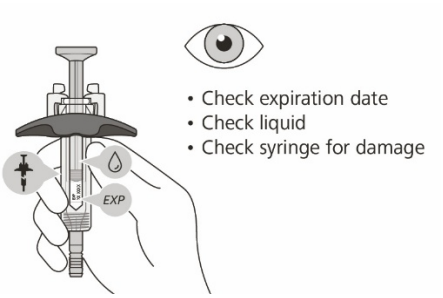


Figure F

If the expiration (EXP) date has passed, the syringe is damaged or the liquid is cloudy, discolored or has particles in it, do not use. Then go to Step 21 “Disposing of ENSPRYNG” and contact your healthcare provider.

Let your syringe reach room temperature

Step 9. After you have checked the syringe, place it on a clean, flat work surface (like a table) for **30 minutes.** This will allow it to reach room temperature. **(See Figure G).**

It is important to let the syringe gently warm to room temperature as injecting cold medicine may feel uncomfortable and make it harder to push.

- **Do not** speed up the warming process in any way, such as using a microwave or placing the syringe in warm water.
- **Do not** remove the needle cover while the syringe is reaching room temperature.

Figure G

Wash your hands

Step 10. Wash your hands with soap and water. **(See Figure H)**.

Figure H

Choose the injection site

Step 11. Choose your injection site in either:

- the lower part of your stomach (abdomen) or
- the front and middle of your thighs. **(See Figure I)**.

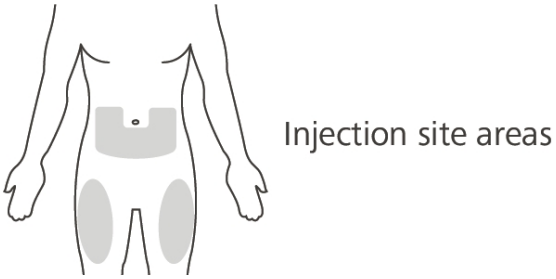


Figure I

- **Do not** inject into the 2-inch (5 cm) area around your belly button.
- **Do not** inject into moles, scars, bruises, or areas where the skin is tender, red, hard or broken.

Choose a different injection site for **each new injection. Choose a different place to inject which is at least 1 inch (2.5 cm) away from the place where you last injected.**

Clean the injection site

Step 12. Wipe the injection site with an alcohol pad and let it air dry **(See Figure J)**.

- **Do not** fan or blow on the area which you have cleaned.
- **Do not** touch the injection site again before you give the injection.

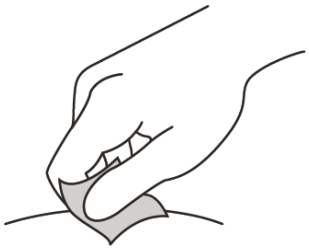


Figure J

Inject ENSPRYNG

Step 13. Hold the barrel of the syringe between your thumb and index finger. With your other hand, pull the needle cap straight off. You may see a drop of liquid at the end of the needle. This is normal and will not affect your dose **(See Figure K)**.

- **Use the syringe within 5 minutes of removing the cap or the needle may clog.**

- **Do not** take the needle cap off until you are ready to inject ENSPRYNG.
- **Do not** put the needle cap back on after it has been removed as this may damage the needle.
- **Do not** touch the needle or let it touch any surfaces after removing the needle cap.

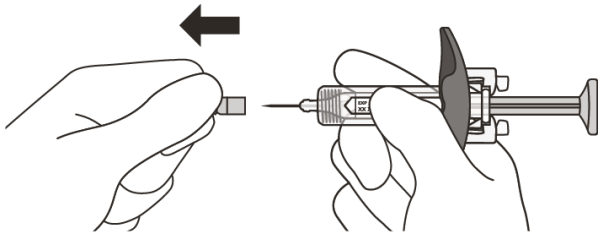


Figure K

Step 14. Throw away the needle cap in a puncture-resistant sharps container immediately. See Step 21 “Disposing of ENSPRYNG”.

Step 15. Hold the barrel of the syringe using your thumb and index finger. With your other hand, pinch the area of skin you have cleaned **(See Figure L).**

Step 16: Use a quick, dart-like motion to insert the needle at an angle between 45° to 90° **(See Figure L).**

- **Do not** insert the needle through clothing.
- **Do not** change the angle of the injection.
- **Do not** insert the needle again.

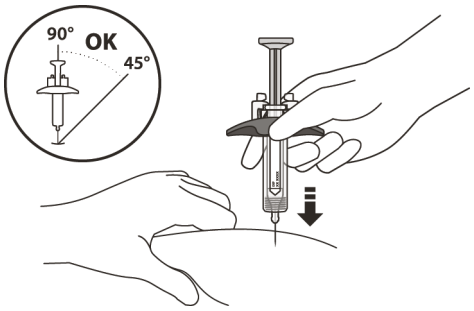


Figure L

Step 17: After the needle is inserted, let go of the pinched skin.

Step 18: Slowly inject all of the medicine by gently pushing the plunger all the way down until it touches the activation guards **(See Figure M).**

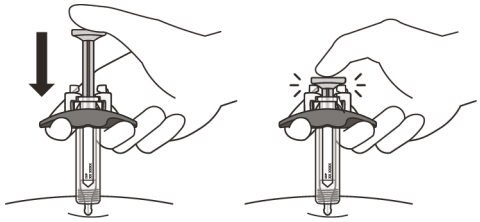


Figure M

Step 19: Gently release the plunger and allow the needle to come out of the skin at the same angle it was inserted **(See Figure N)**.

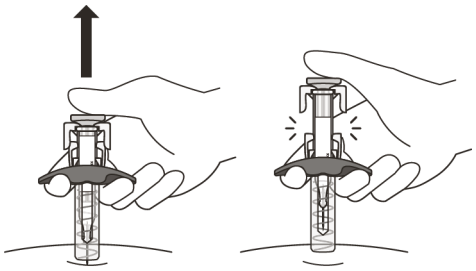


Figure N

- **The needle will now be covered by the needle-shield.** If the needle is not covered, carefully place the syringe into a puncture-resistant sharps container to avoid injury. See Step 21 “Disposing of ENSPRYNG”.

Taking care of the injection site

Step 20: There may be a little bleeding at the injection site. You can press a cotton ball or gauze over the injection site but **do not** rub it. If needed, you may also cover the area you injected with a small bandage. If the medicine gets into contact with your skin, wash the area with water.

Disposing of ENSPRYNG

Step 21: Put your used syringe in an FDA-cleared sharps disposal container immediately after use **(See Figure O)**. **Do not** throw away (dispose of) the syringe in your household trash.

Figure O

- If you **do not** have an FDA-cleared sharps disposal container, you may use a household container that is:
  - made of heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- **Do not** dispose of your used sharps disposal container in trash unless your community guidelines permit this.
- **Do not** recycle your used sharps disposal container.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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