

# TOMORROW'S POSSIBILITIES START WITH KNOWING TODAY'S TREATMENT OPTIONS

Learn more about ENSPRYNG,  
a treatment option for adults with AQP4+ NMOSD.

## Important Safety Information 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.

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

## Who should not receive ENSPRYNG?

### Do not take ENSPRYNG if you:

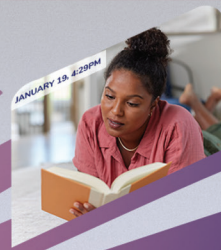
- are allergic to ENSPRYNG or any of the ingredients in ENSPRYNG.
- have an active hepatitis B infection.
- have active or untreated inactive (latent) tuberculosis.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.



  
**ENSPRYNG<sup>®</sup>**  
satralizumab-mwge  
subcutaneous injection 120 mg/mL





MAY 11, 4:29PM



Melissa — diagnosed with NMOSD in 2016

## Table of Contents

- 4 Understanding NMOSD
- 6 What Is ENSPRYNG?
- 8 Clinical Trials — Overview & Results
- 12 Self-injecting ENSPRYNG
- 14 Discover ENSPRYNG Stories
- 16 Additional Important Safety Information
- 18 Talking With Your Doctor
- 20 ENSPRYNG Support Resources
- 22 FAQs
- 24 NMOSD Resources



# Understanding NMOSD

NMOSD (also known as NMO) is a rare inflammatory disease of the central nervous system with unpredictable relapses that may lead to cumulative and permanent damage and disability.

NMOSD occurs when the immune system mistakenly attacks normal tissue of the central nervous system (CNS). Inflammation can result in relapses that may be severe and unpredictable. These relapses are thought to result in vision loss, muscle weakness and paralysis.

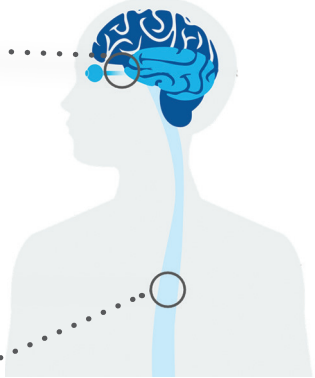
NMOSD mostly impacts nerves of the eyes and other parts of the CNS, which include the brain and spinal cord. Symptoms will be different for each person and depend largely on the location and severity of the inflammation.

To help confirm a NMOSD diagnosis and determine the right treatment, a doctor may order blood tests that look for the presence of specific antibodies to the aquaporin-4 (AQP4) protein, shown as AQP4-IgG.

Some common NMOSD symptoms include:

**Optic nerve-related symptoms:**

- Blurred vision
- Inability to see colors
- Complete vision loss



**Spinal cord-related symptoms:**

- Pain/weakness or paralysis in legs
- Loss of sensation or numbness
- Bladder and bowel control issues

**Other common symptoms:**

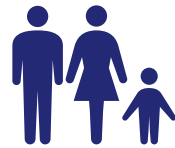
- Spasms
- Persistent nausea
- Uncontrollable vomiting
- Persistent hiccups
- Sleeping problems



NMOSD affects nearly 15,000 people in the United States



It predominantly affects women — up to 9 women are affected for every 1 man affected



It can occur in people in their 30s and 40s, but children and adults can also be affected

**African  
or  
Asian**

NMOSD appears to be more common in people of African or Asian background



80% to 90% of people with NMOSD experience recurring relapses

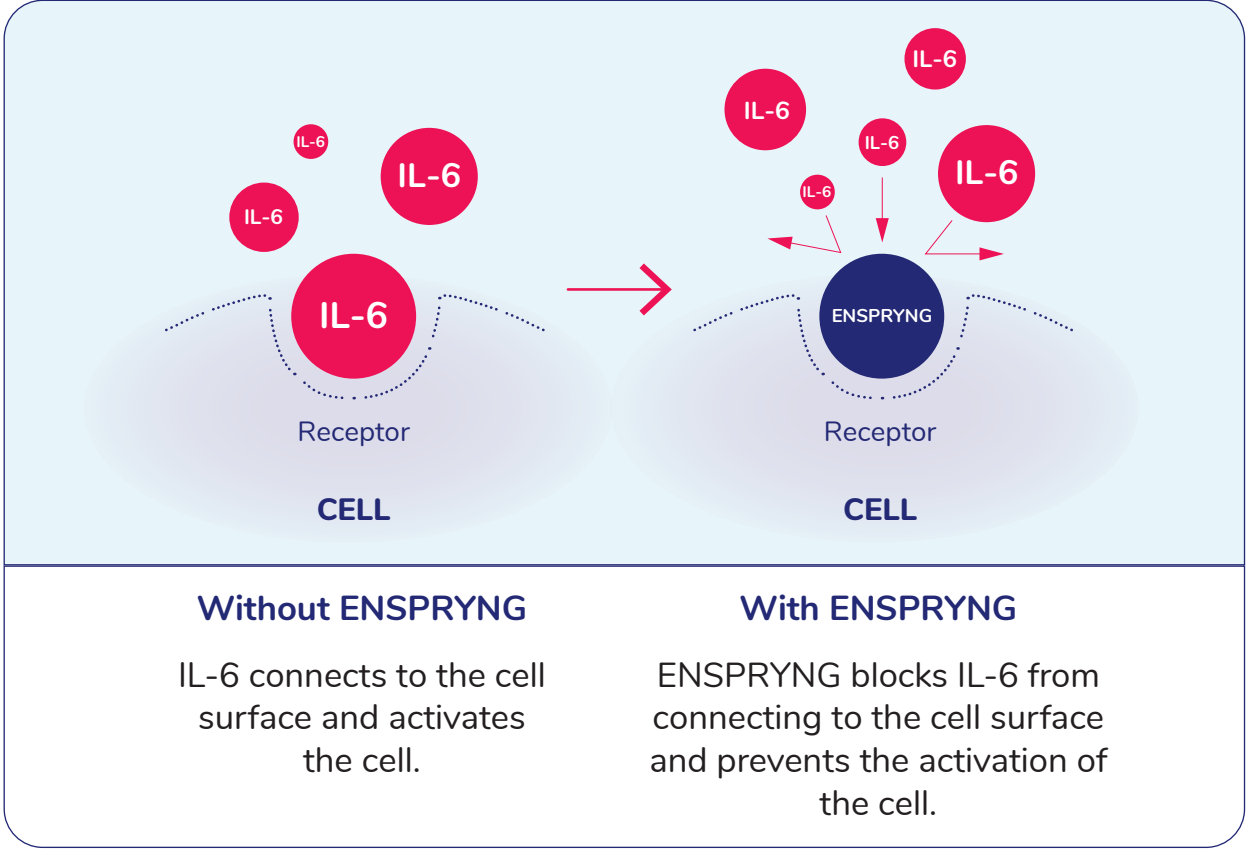


Layla — diagnosed with NMOSD in 2022

**ENSPRYNG<sup>®</sup>**  
satralizumab-mwge  
subcutaneous injection 120 mg/mL

# What Is ENSPRYNG?

ENSPRYNG is a different kind of treatment for NMOSD. ENSPRYNG is the first and only approved NMOSD treatment that is designed to block the action of interleukin 6 (IL-6) — a protein that may play an important role in NMOSD. The exact way ENSPRYNG is believed to work is not known.



Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.

## Why ENSPRYNG might be right for you



ENSPRYNG is proven **effective in reducing the risk of relapse** for adults with AQP4+ NMOSD and has an **established safety profile**<sup>†</sup>

<sup>†</sup>ENSPRYNG may cause serious side effects including: infections, increased liver enzymes, and low neutrophil counts. All required vaccinations should be completed before starting ENSPRYNG. Do not take ENSPRYNG if you are allergic to satralizumab-mwge or any of the ingredients in ENSPRYNG, have an active hepatitis B infection, or have active or untreated inactive (latent) TB.



ENSPRYNG reduced the risk of relapse in **2 clinical studies**, across a **diverse group of patients** from many countries

See pages 8-11 for clinical studies information.



ENSPRYNG is the **only monthly\* self-injection** treatment for NMOSD given under the skin with your doctor's approval and training

\*ENSPRYNG is given every 4 weeks after taking 3 starter doses in your first month of treatment.

### Consider ENSPRYNG if you are:

- Newly diagnosed and receiving NMOSD treatment
- Currently treating with oral immunosuppressive therapies (ISTs) that were used concurrently with ENSPRYNG in Study 2, such as azathioprine, mycophenolate mofetil, or oral corticosteroids
- Uncertain with or not responding well to current therapy

## Important Safety Information (cont.) What is the most important information I should know about ENSPRYNG?

ENSPRYNG may cause serious side effects including:

- **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 usualYour 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.





# Clinical Trials — Overview

ENSPRYNG is the only NMOSD therapy approved based on two clinical trials.

How was ENSPRYNG studied?

ENSPRYNG was studied in two trials. Across each, there were:



A diverse group of patients from around the world



A balanced number of patients in: age, AQP4-IgG status, and severity of disease



Both men and women, with a larger proportion of women

What were the goals of the ENSPRYNG trials?

The goal was to prove that ENSPRYNG alone or ENSPRYNG plus immunosuppressive therapy (IST) could lower the risk of relapse in adults with NMOSD vs. placebo and vs. placebo plus IST. Both trials also measured how many patients were relapse-free at specific points with treatment.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.

STUDY 1

ENSPRYNG alone vs placebo

Excluded patients who were recently taking other treatments before starting the trial.

**95** adult patients were randomly chosen to take ENSPRYNG or placebo  
31 tested AQP4-IgG(-) and 64 tested AQP4-IgG(+)

**41** AQP4-IgG(+) patients received ENSPRYNG

**23** AQP4-IgG(+) patients received placebo

STUDY 2

ENSPRYNG plus IST vs placebo plus IST

Only included patients who were taking certain ISTs (azathioprine, mycophenolate mofetil, or oral corticosteroids) before starting the trial.

**76** adult patients were selected to randomly receive ENSPRYNG plus IST or placebo plus IST  
24 tested AQP4-IgG(-) and 52 tested AQP4-IgG(+)

**26** AQP4-IgG(+) patients received ENSPRYNG plus IST

**26** AQP4-IgG(+) patients received placebo plus IST

ENSPRYNG is only approved for AQP4-IgG(+) adults.

Important Safety Information (cont.)

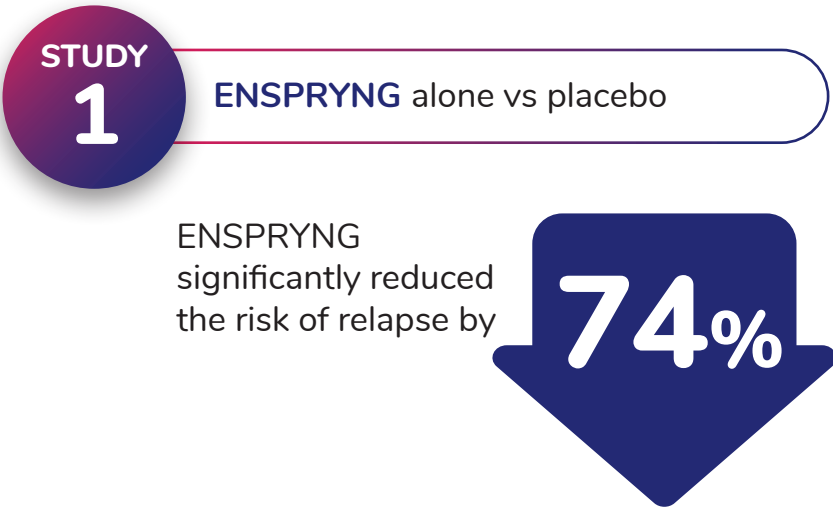
- All required vaccinations should be completed before starting ENSPRYNG. People using ENSPRYNG should not be given ‘live’ or ‘live-attenuated’ vaccines. ‘Live’ or ‘live-attenuated’ vaccines should be given at least 4 weeks before you start ENSPRYNG. Your healthcare provider may recommend that you get 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.
- **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.





# Clinical Trials — Results

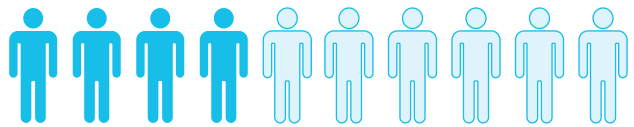
ENSPRYNG reduced the risk of relapse. More AQP4-IgG(+) adult patients were relapse-free at about 2 years (96 weeks) with ENSPRYNG than with placebo.



**8 out of 10**

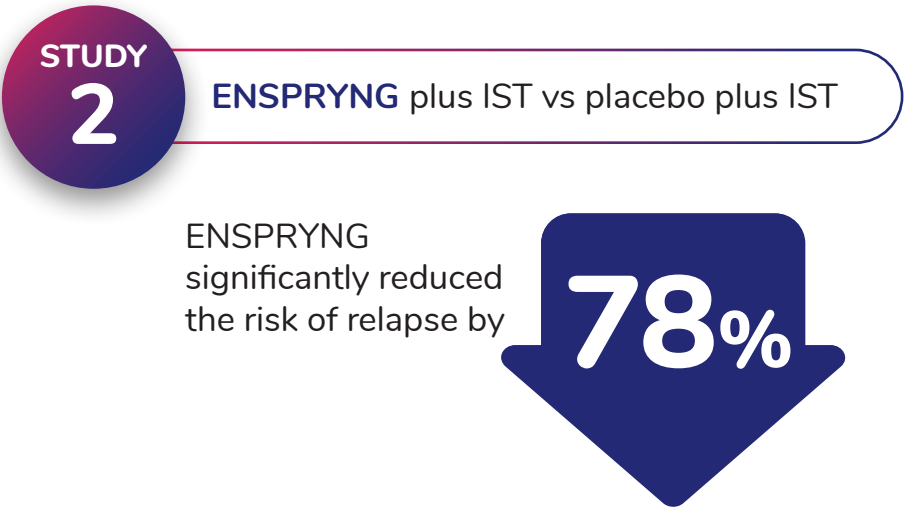
AQP4-IgG(+) patients on ENSPRYNG

**77% of ENSPRYNG patients were relapse-free vs 41% placebo at 96 weeks**



**4 out of 10**

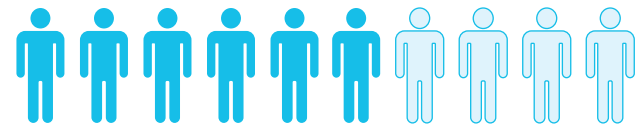
AQP4-IgG(+) patients on placebo



**9 out of 10**

AQP4-IgG(+) patients on ENSPRYNG plus IST

**91% of ENSPRYNG plus IST patients were relapse-free vs 57% placebo plus IST at 96 weeks**



**6 out of 10**

AQP4-IgG(+) patients on placebo plus IST

## Important Safety Information (cont.)

- **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.
- **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



Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.



# Self-injecting ENSPRYNG

ENSPRYNG is a monthly self-injectable treatment that gives you the flexibility to take it where it's convenient for you.

If your healthcare provider determines it is appropriate, and after proper training, you and your caregiver have the ability to administer ENSPRYNG in the comfort of your own home, or even while traveling.

ENSPRYNG is a monthly injection that is given under the skin via a prefilled syringe. It can be stored at room temperature for a total of 8 days, in a row or intermittently, giving you control over where you take it.

Before and while taking ENSPRYNG, your healthcare provider may order tests and monitor you to ensure ENSPRYNG is still appropriate for you.

For reference, scan the QR code or visit [enspryng.com/injection](https://enspryng.com/injection) to watch the training video



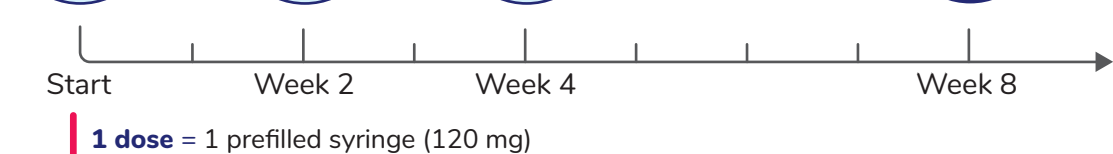
## ENSPRYNG Dosing Schedule

ENSPRYNG is a treatment given every 4 weeks after taking 3 starting doses in the first month of treatment. As an example, if your ongoing dose date falls on a Tuesday, your next ongoing dose date will be four Tuesdays after that.

### Starting and Staying on ENSPRYNG

#### Starting doses

1 dose every 2 weeks for the first 4 weeks



#### Ongoing doses

1 dose every 4 weeks

**If a starting dose is missed,** you should take it immediately, then maintain the 2-week dosing interval from your new starting date until the first 3 doses are complete, and then continue with ongoing doses every 4 weeks.

**If an ongoing dose is missed,** you should take it immediately, wait the 4-week interval from your new starting date, and then continue with ongoing doses every 4 weeks.

Speak with your healthcare provider if you have any questions about how to restart treatment or if it has been more than 8 weeks since your last dose of ENSPRYNG.

## Important Safety Information (cont.)

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.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.





## Discover ENSPRYNG Stories

Meet Cheena.

This is her NMOSD story with ENSPRYNG.

Independent and adventurous, Cheena first attributed her symptoms of NMOSD to soreness from physical activity. As her symptoms became more severe, her doctors struggled to find a diagnosis. Clarity didn't come until she tested positive for the AQP4 antibody.

With each relapse, her symptoms were getting worse. After she began losing her vision, her doctor suggested ENSPRYNG. Her doctor and her discussed the benefits and risks and together decided it might be right for her.

Since beginning ENSPRYNG, Cheena says she's felt more encouraged. As she continues her journey, she feels that the future is bright.



Scan the QR code to read more stories of people living with NMOSD who take ENSPRYNG, or visit [enspryng.com/realpatientstories](https://enspryng.com/realpatientstories)

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.



Cheena — diagnosed with NMOSD in 2021

“My doctor and I know that finding the right medication for me has made all the difference.”

Individual results may vary.

### Important Safety Information (cont.)

- 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. 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, 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.

  
**ENSPRYNG**<sup>®</sup>  
satralizumab-mwge  
subcutaneous injection 120 mg/mL



# Additional Important Safety Information

## Serious side effects

**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

**Increased liver enzymes.** ENSPRYNG can lead to changes in certain blood tests that assess your liver function. Your healthcare provider should order blood tests to check your liver enzymes before and while you receive ENSPRYNG, and will tell you how often you will need to have these blood tests. If your liver enzymes are increased, your healthcare provider may delay starting ENSPRYNG.

**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.

## 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
- moderate or severe stomach (abdominal) pain or vomiting
- dizziness or feeling faint
- chest pain
- swelling of your lips, face, or tongue

## Common side effects

The most common side effects of ENSPRYNG include:

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

## Important considerations

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

- 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. 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, 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.

These are not all of the possible side effects of ENSPRYNG. Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or Genentech at 1-888-835-2555.





# Talking With Your Doctor

Talking about NMOSD with your doctor can be overwhelming. That’s why it’s important to know what you want in a treatment. Asking questions can help you and your doctor be as informed as possible when discussing your treatment options.



## Questions about NMOSD & ENSPRYNG:

- How is ENSPRYNG treatment given?
- What are the risks and benefits of taking ENSPRYNG?
- What is living with NMOSD like long term?
- Can the chance of a relapse be reduced?



Your voice matters when discussing with your doctor the risks and benefits of a treatment.

Scan the QR code to view a printable **Doctor Discussion Guide** to help you prepare for a conversation with your doctor.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.



Kila — diagnosed  
with NMOSD in 2014

“The best plan of action is to educate yourself. You have to be your own advocate.”

## Important Safety Information (cont.)

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

## What are the most common side effects of ENSPRYNG?

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 (arthralgia)





# ENSPRYNG Support Resources

## Support Available to You

Once you are prescribed ENSPRYNG, **ENSPRYNG Access Solutions®** is the place to turn for answers and support. We offer a number of support services, including:



### Patient Navigators

act as your personal guide throughout your treatment with ENSPRYNG



### Clinical Education Managers\*

provide supplemental injection training and NMOSD/ENSPRYNG education (Spanish and English support is available)



### Financial Assistance

committed to helping you find assistance options so you can pay for ENSPRYNG

\*Clinical Education Managers are Genentech employees and do not provide medical advice.

You and your healthcare provider are responsible for completing and submitting all required paperwork to your health insurance plan. Genentech cannot guarantee your plan will cover any treatments.

**Reach out to a Patient Navigator at 844-NSPRYNG (844-677-7964)**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.

Melissa — diagnosed with NMOSD in 2016



“Feeling that I do have some support and don’t have to be my own warrior all the time means a lot to me.”

  
**ENSPRYNG®**  
satralizumab-mwge  
subcutaneous injection 120 mg/mL



## FAQs

Here are some answers to the most frequently asked questions about ENSPRYNG.



Donna — diagnosed with NMOSD in 2014

### Q How do I get started on ENSPRYNG?

**A** ENSPRYNG might be different from other medicines you've taken. You won't pick your prescription up from your local drugstore; instead, a Specialty Pharmacy will deliver ENSPRYNG to your home.

### Q Can I continue with my immunosuppressive therapy while taking ENSPRYNG?

**A** Every person is unique. So your healthcare provider will determine the most appropriate way to use ENSPRYNG, as it has been evaluated alone or with immunosuppressive therapy (IST) such as azathioprine, mycophenolate mofetil, or oral corticosteroids. Talk to your healthcare provider about all your medicines before starting treatment.

### Q What should I do if I experience a relapse while on ENSPRYNG?

**A** Anytime you experience a relapse, you should call your healthcare provider immediately.

### Q How will I or my caregiver learn to give ENSPRYNG injections?

**A** Your healthcare provider should train you on the proper technique for subcutaneous injection, which is an injection into the tissue under the skin. You can also set up a free one-on-one supplemental injection training visit with an ENSPRYNG Clinical Education Manager. Please see the ENSPRYNG Support Resources on page 20 for more information. Once trained and if your healthcare provider determines it is appropriate, you or a caregiver can administer an injection.

### Important Safety Information (cont.)

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.

For more information, go to [www.ENSPRYNG.com](http://www.ENSPRYNG.com) or call 1-844-NSPRYNG.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.

  
**ENSPRYNG<sup>®</sup>**  
satralizumab-mwge  
subcutaneous injection 120 mg/mL



# NMOSD Resources

## Many organizations can help support you on your journey with NMOSD\*

The websites below are sponsored by various advocacy organizations dedicated to providing information and resources specifically to people living with NMOSD and their families, friends, and caregivers. They include:



**Guthy-Jackson Charitable Foundation**  
<https://guthyjacksonfoundation.org/>

**The Sumaira Foundation**  
<https://www.sumairafoundation.org/>

**The Siegel Rare Neuroimmune Association**  
<https://wearesrna.org/about/>

You don't have to navigate NMOSD alone. Explore the resources above to find a support group in your area.

\*There are many organizations and groups for people living with NMOSD. While they are not affiliated with Genentech or ENSPRYNG, these are some of the organizations that may provide useful information about NMOSD. Genentech is not responsible for the accuracy of the information contained on a third-party site and does not recommend or endorse the content provided on the site.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information and Medication Guide in pocket.

Layla — diagnosed with NMOSD in 2022

“It’s really important to have a community of support for a disease like NMOSD because it can be really isolating to go through alone.”





# Important Safety Information

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

## Who should not receive ENSPRYNG?

### Do not take ENSPRYNG if you:

- are allergic to ENSPRYNG or any of the ingredients in ENSPRYNG.
- have an active hepatitis B infection.
- have active or untreated inactive (latent) tuberculosis.

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

### ENSPRYNG may cause serious side effects including:

- **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.

- **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.

- **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.

- **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

## 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. 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, 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.

## What are the most common side effects of ENSPRYNG?

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 (arthralgia)

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.

For more information, go to [www.ENSPRYNG.com](http://www.ENSPRYNG.com) or call 1-844-NSPRYNG.





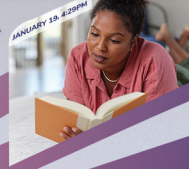
# HEAR MORE FROM OTHERS TAKING ENSPRYNG



Scan the QR code or visit  
[enspryng.com/realpatientstories](https://enspryng.com/realpatientstories)  
to learn about real people like you,  
who are living with AQP4+ NMOSD.

Ask your doctor if  
you're ready to self-inject  
ENSPRYNG today.

ENSPRYNG is a trademark of Chugai Pharmaceutical Co., Ltd., Tokyo, Japan.  
Manufactured by:  
Genentech, Inc., A Member of the Roche Group  
1 DNA Way, South San Francisco, CA 94080-4990  
© 2023 Genentech, Inc. All rights reserved. M-US-00008182(v3.0) 6/23



MAY 11, 4:29PM



  
**ENSPRYNG®**  
satralizumab-mwge  
subcutaneous injection 120 mg/mL



## 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

### 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)

### 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 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)
- 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)

### 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 (incidence at least 15%) are nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea. (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](http://www.fda.gov/medwatch).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2022

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### 1 INDICATIONS AND USAGE

### 2 DOSAGE AND ADMINISTRATION

- 2.1 Assessments Prior to First Dose of ENSPRYNG
- 2.2 Recommended Dosage
- 2.3 Important Administration Instructions
- 2.4 Monitoring to Assess Safety

### 3 DOSAGE FORMS AND STRENGTHS

### 4 CONTRAINDICATIONS

### 5 WARNINGS AND PRECAUTIONS

- 5.1 Infections
- 5.2 Elevated Liver Enzymes
- 5.3 Decreased Neutrophil Counts
- 5.4 Hypersensitivity Reactions

### 6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity

### 8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use

### 11 DESCRIPTION

### 12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

### 13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

### 14 CLINICAL STUDIES

### 16 HOW SUPPLIED/STORAGE AND HANDLING

- 16.1 How Supplied
- 16.2 Storage and Handling

### 17 PATIENT COUNSELING INFORMATION

\* Sections or subsections omitted from the full prescribing information are not listed.



## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

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

### 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)*].

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.



### 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 1.

**Table 1 Recommended Dosage for Delayed or Missed Doses**

<b>Last Dose Administered</b>	<b>Recommended Dosage for Delayed or Missed Doses</b>
Less than 8 weeks during the maintenance period or missed a loading dose	Administer 120 mg by subcutaneous injection as soon as possible, and do not wait until the next planned dose. <u>Maintenance period</u> After the delayed or missed dose is administered, reset the dose schedule to every 4 weeks. <u>Loading period</u> If the second loading dose is delayed or missed, administer as soon as possible and administer the 3 <sup>rd</sup> and final loading dose 2 weeks later. If the third loading dose is delayed or missed, administer as soon as possible and administer the 1 <sup>st</sup> maintenance dose 4 weeks later.
8 weeks to less than 12 weeks	120 mg by subcutaneous injection at 0* and 2 weeks, followed by 120 mg every 4 weeks.
12 weeks or longer	120 mg by subcutaneous injection at 0*, 2, and 4 weeks followed by 120 mg 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. See ENSPRYNG “Instructions for Use” (IFU) 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 a HCP [*see Contraindications (4) and Warning and Precautions (5.4)*].
- Prior to use, remove the prefilled syringe from the refrigerator and allow 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, or contains particles, or if any part of the prefilled syringe appears to be damaged.
- Instruct patients to inject the full amount in the syringe (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. Rotate injection sites with each administration. Do not give injection 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 2.

**Table 2 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 a dosage of 120 mg by subcutaneous injection every 4 weeks.
12 weeks or longer	Restart at a dose of 120 mg by subcutaneous injection at Weeks 0*, 2, and 4, followed by a dosage of 120 mg 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  $1.0 \times 10^9/\text{L}$  and confirmed by repeat testing, ENSPRYNG should be interrupted until the neutrophil count is  $> 1.0 \times 10^9/\text{L}$  [see *Warnings and Precautions* (5.3)].

## 3 DOSAGE FORMS AND STRENGTHS

Injection: 120 mg/mL clear, and colorless to slightly yellow solution in single-dose prefilled syringe.

## 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.

The safety of ENSPRYNG 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 3 and Table 4, respectively. 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 3 Adverse Reactions Occurring in 4 or More Patients Treated with ENSPRYNG and Greater Incidence than Placebo 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 4 Adverse Reactions Occurring in 3 or More Patients Treated with ENSPRYNG and Greater Incidence than Placebo in Study 2**

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

#### Injection-Related Reactions

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.

#### Infections

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.

#### Laboratory Abnormalities

##### *Decreased Neutrophil Count*

Of the patients treated with ENSPRYNG, 10% had neutrophils below  $1 \times 10^9/L$  compared to 9% in placebo in Study 1. In Study 2, 15% patients had neutrophils below  $1 \times 10^9/L$  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.

##### *Decreased Platelet Count*

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  $50 \times 10^9/L$ .



### *Elevated Liver Enzymes*

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.

### *Lipid Abnormalities*

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.

### *Fibrinogen Levels*

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*

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

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 Study 1 and 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.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ENSPRYNG during pregnancy. Healthcare providers are encouraged to register patients and pregnant women 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.

#### 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 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 with an approximate pH of 6. ENSPRYNG is supplied in a single-dose prefilled syringe. Each syringe delivers 1 mL of solution containing 120 mg of satralizumab-mwge, L-arginine (26.1 mg), L-histidine (3.1 mg), poloxamer 188 (0.5 mg), L-aspartic acid (pH adjustment), 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 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 is unknown.

#### **12.3 Pharmacokinetics**

The pharmacokinetics of ENSPRYNG have been characterized both in Japanese and Caucasian healthy volunteers, and in NMOSD patients. The pharmacokinetics in NMOSD patients using the recommended dose were characterized using population pharmacokinetic analysis methods based on a database of 154 patients.

The concentration-time course of ENSPRYNG in patients with NMOSD was accurately described by a two-compartment population pharmacokinetic model with parallel linear and target-mediated (Michaelis-Menten) elimination and first-order subcutaneous 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). Body weight was shown to be a significant covariate, with clearance and  $V_c$  for patients weighing 123 kg (97.5th percentile of the weight distribution) increased by 71.3% and 105%, respectively, compared to a patient weighing 60 kg.

Steady state pharmacokinetics were achieved after the loading period (8 weeks) as follows [mean ( $\pm$ SD)]:  $C_{\min}$ : 19.7 (12.2) mcg/mL,  $C_{\max}$ : 31.5 (14.9) mcg/mL, and AUC: 737 (386) mcg.mL/day.

#### Absorption

The bioavailability of satralizumab-mwge was 85%.

#### 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 in NMOSD patients) is estimated to be 0.0601 L/day. The associated terminal  $t_{1/2}$  is approximately 30 days (range 22 – 37 days) based on data pooled from Study 1 and Study 2.

#### 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 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 Study 1 and Study 2, 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

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 5; Figure 1). There was no evidence of a benefit in the anti-AQP4 antibody negative patients.

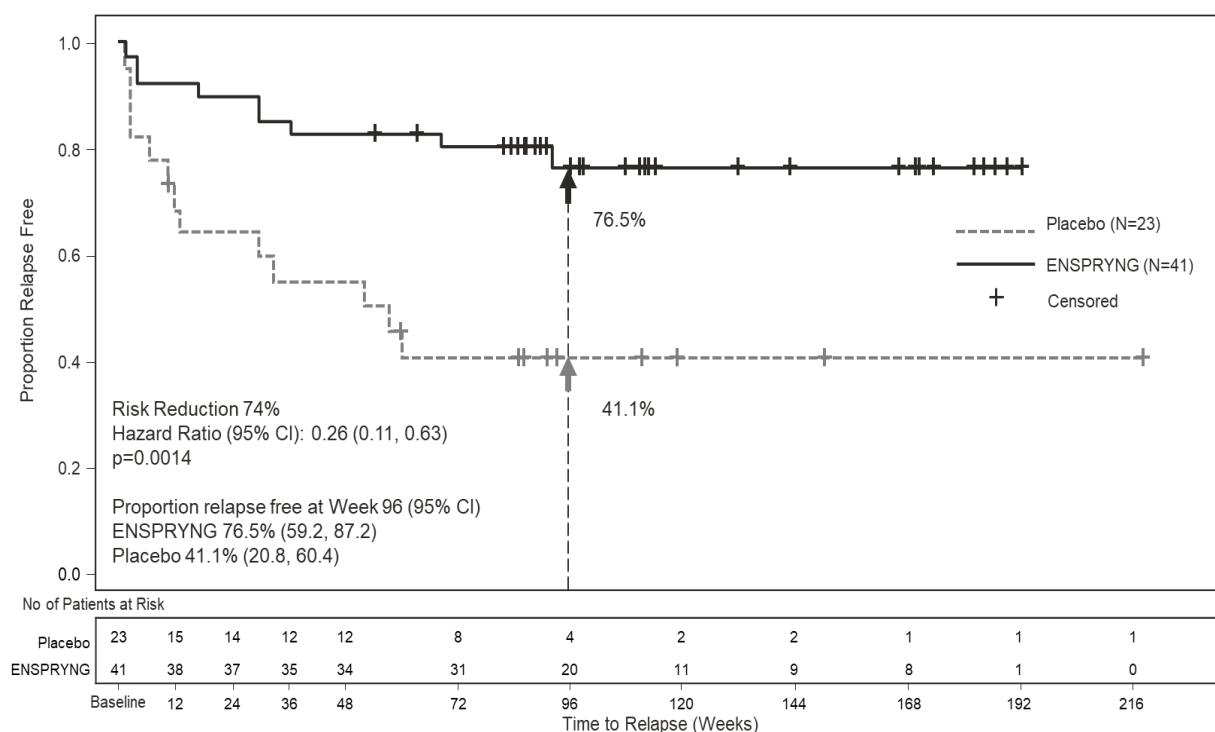
In Study 2, the time to the first CEC-confirmed relapse was significantly longer in patients treated with ENSPRYNG compared to patients who received placebo (risk reduction 62%; hazard ratio 0.38;  $p = 0.0184$ ). In the anti-AQP4 antibody positive population, there was a 78% risk reduction; hazard ratio 0.22;  $p = 0.0143$  (Table 5; Figure 2). There was no evidence of a benefit in the anti-AQP4 antibody negative patients.

**Table 5 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
<b>Time to Clinical Endpoint Committee (CEC)-Determined Relapse (Primary Efficacy Endpoint)</b>				
<b>Number (%) of Patients with Relapse</b>	9 (22)	13 (56.5)	3 (11.5)	11 (42.3)
<b>Hazard Ratio (95% CI)</b>	0.26 (0.11, 0.63)		0.22 (0.06, 0.82)	
<b>p-value</b>	0.0014		0.0143	
<b>Risk Reduction</b>	74%		78%	
<b>Proportion of Protocol Defined Relapse-Free Patients at 96 Weeks</b>	76.5%	41.1%	91.1%	56.8%

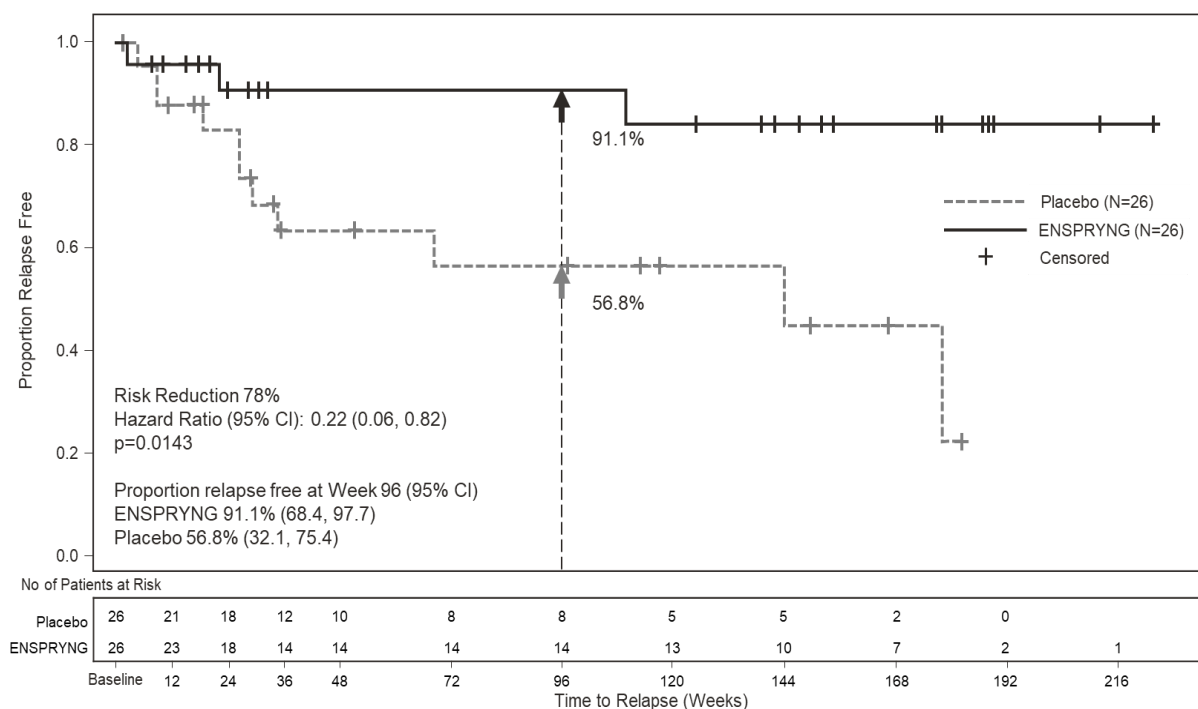
\* IST = immunosuppressant therapy

**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**



## 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 in single-dose prefilled syringe (PFS) with needle safety device.

ENSPRYNG PFS is not made with natural rubber latex. Each ENSPRYNG carton contains one single-dose 120 mg/mL prefilled syringe (NDC 50242-007-01).

### 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.
- Prior to administration, ENSPRYNG, if unopened, can be removed from and returned to the refrigerator, if necessary. The total combined time out of refrigeration should not exceed 8 days at a temperature that does not exceed 30°C (86°F).

## 17 PATIENT COUNSELING INFORMATION

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

### Infections

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)].

### Vaccinations

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].

### Elevated Liver Enzymes

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

### Decreased Neutrophil Counts

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

### Hypersensitivity Reactions

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 from the refrigerator prior to use and allow to sit at room temperature outside of the carton for 30 minutes. Do not warm ENSPRYNG in any other way.

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 disposal, and caution against reuse of these items.

### Pregnancy Exposure Registry

Encourage patients to enroll in the ENSPRYNG Pregnancy Registry if they become pregnant while taking ENSPRYNG. The Registry monitors fetal outcomes of pregnant women 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

ENSPRYNG® is a registered trademark of  
Chugai Pharmaceutical Co., Ltd., Tokyo, Japan  
©2022 Genentech, Inc. All rights reserved.



## 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.

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. 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, 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.
- 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.
- Always inject all of the medicine in the syringe.
- 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
  - swelling of your lips, face, or tongue
  - dizziness or feeling faint
  - moderate or severe stomach (abdominal) pain or vomiting
  - chest pain
- The most common side effects of ENSPRYNG include:
  - sore throat, runny nose (nasopharyngitis)
  - headache
  - rash
  - upper respiratory tract infection
  - fatigue
  - nausea
  - extremity pain
  - 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.
- Protect from light.
- **Do not** freeze or use the syringe if it has been frozen.
- **Do not** shake.
- ENSPRYNG, if unopened, can be removed from and returned to the refrigerator, if needed. The total combined time out of the refrigerator should not be more than 8 days at a temperature that does not go above 86°F (30°C).

#### **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-histidine, poloxamer 188, L-aspartic acid, 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](http://www.ENSPRYNG.com) or call 1-844-NSPRYNG.