About Enspryng

Enspryng™ (satralizumab-mwge) is approved by the U.S. Food and Drug Administration (FDA) for adults living with anti-aquaporin-4 (AQP4) antibody positive neuromyelitis optica spectrum disorder (NMOSD). Enspryng is the first and only subcutaneous treatment option for NMOSD. It can be self-administered every four weeks by a person living with NMOSD or a caregiver, after an initial loading dose and following training from a healthcare provider. Enspryng, which was designed by Chugai, is a humanized monoclonal antibody and the only approved therapy for NMOSD designed to target and inhibit interleukin-6 (IL-6) receptor activity. IL-6 is believed to play a key role in the inflammation associated with NMOSD.
The treatment was designed using novel recycling antibody technology, which allows for longer duration of antibody circulation and subcutaneous dosing every four weeks. Enspryn is a prefilled, injectable treatment that can be self-administered by a person living with NMOSD or a caregiver following training from a healthcare provider.

About NMOSD

NMOSD is a rare, lifelong and debilitating autoimmune disease of the central nervous system, which primarily damages the optic nerve(s) and spinal cord.

Symptoms of NMOSD can include blindness, muscle weakness, paralysis, inability to walk, fatigue and pain.

Although most cases of NMOSD can be confirmed through diagnostic biomarker tests, many people living with NMOSD are misdiagnosed with multiple sclerosis. This is due to overlapping characteristics of the two disorders, including a higher prevalence in women, similar symptoms and the fact that both are relapse-based conditions.
NMOSD is estimated to affect up to 15,000 people in the U.S.

NMOSD can affect individuals of any age, race and gender, but is most common among women in their 30s and 40s, and appears to occur at higher rates in people of African or Asian background. There is some evidence that people of African or Asian descent may also experience a more severe disease course.

Although the exact cause of NMOSD remains unknown, it is believed that IL-6 plays a key role in the disease process. NMOSD is commonly associated with pathogenic antibodies (AQP4) that target and damage a specific cell type, called astrocytes, resulting in inflammatory lesions of the optic nerve(s), spinal cord and brain. AQP4 antibodies are detectable in the blood serum of around 70-80% of NMOSD patients, and these patients tend to experience a more severe disease course.
# About Enspryng Pivotal Trials

Enspryng has been studied in two randomized, controlled Phase III clinical trials, one of the largest pivotal clinical trial programs undertaken for this rare neurological disease, which demonstrated its sustained efficacy and favorable safety profile in adults with AQP4 antibody positive NMOSD throughout the 96-week duration of the clinical trial program.

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<th><strong>SAkuraSky</strong></th>
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<tr>
<td><strong>STUDY DESIGN</strong></td>
<td>Phase III randomized, double-blind, placebo-controlled – Addition to baseline immunosuppressive therapy</td>
<td>Phase III randomized, double-blind, placebo-controlled – Monotherapy</td>
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<td><strong>POPULATION</strong></td>
<td>Males or females aged 12 to 74</td>
<td>Males or females aged 18 to 74</td>
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<td><strong>AQP4-IgG STATUS</strong></td>
<td>AQP4 antibody positive and AQP4 antibody negative</td>
<td>Time to first relapse</td>
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<td><strong>PRIMARY ENDPOINTS</strong></td>
<td>Change in Visual Analogue Scale (VAS) score for pain, Change in Functional Assessment of Chronic Illness Therapy (FACIT) score for fatigue</td>
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<td><strong>SECONARY ENDPOINTS</strong></td>
<td>1:1 ratio of Enspryng or placebo</td>
<td>2:1 ratio of Enspryng or placebo</td>
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<td><strong>EFFICACY RESULTS</strong></td>
<td>Data from the AQP4 antibody positive adult subgroup showed that 91.1% were relapse-free at 96 weeks when treated with Enspryng, compared to 53.3% with placebo. While AQP4 antibody negative patients were included, the results were not statistically significant.</td>
<td>Data from the AQP4 antibody positive adult subgroup showed that 76.5% were relapse-free at 96 weeks when treated with Enspryng, compared to 41.1% with placebo. While AQP4 antibody negative patients were included, the results were not statistically significant.</td>
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<td><strong>SAFETY</strong></td>
<td>In both studies, Enspryng adverse reactions were comparable with placebo groups showing Enspryng has a favorable risk/benefit profile as a monotherapy and when used concurrently with baseline immunosuppressive therapy in people with NMOSD. The most common adverse reactions with Enspryng include:</td>
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<td>• sore throat, runny nose (nasopharyngitis)</td>
<td>• nausea</td>
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<td></td>
<td>• headache</td>
<td>• extremity pain</td>
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<td></td>
<td>• upper respiratory tract infection</td>
<td>• inflammation of the stomach lining (gastritis)</td>
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<td></td>
<td>• rash</td>
<td>• joint pain</td>
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<td></td>
<td>• fatigue</td>
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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.

Important Safety Information

Patients should not take Enspryng if they:

- are allergic to satralizumab-mwge or any of the ingredients in Enspryng
- have an active hepatitis B infection
- have active or untreated inactive (latent) tuberculosis (TB)

Enspryng may cause serious side effects including:

- **Infections.** Enspryng can increase risk of serious infections some of which can be life-threatening. Patients should speak with their healthcare provider if they are being treated for an infection and call right away if there are 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 the body
  - diarrhea, belly pain, or feeling sick
  - burning when urinating or urinating more often than usual

A healthcare provider will check for infection and treat it if needed before starting or continuing to take Enspryng

- A healthcare provider should test for hepatitis and TB before initiating 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 a patient starts Enspryng.

A healthcare provider may recommend that a patient receive a ‘non-live’ (inactivated) vaccine, such as some of the seasonal flu vaccines. If a patient plans to get a ‘non-live’ (inactivated) vaccine it should be given, whenever possible, at least 2 weeks before starting Enspryng.
- **Increased liver enzymes.** A healthcare provider should order blood tests to check patient liver enzymes before and while taking Enspryng. A healthcare provider will dictate how often these blood tests are needed. Patients should complete all follow-up blood tests as ordered by a healthcare provider. A healthcare provider may wait to start Enspryng if liver enzymes are increased

- **Low neutrophil count.** Enspryng can cause a decrease in neutrophil counts in the blood. Neutrophils are white blood cells that help the body fight off bacterial infections. A healthcare provider should order blood tests to check neutrophil counts while a patient is taking Enspryng

- **Serious allergic reactions** that may be life-threatening have happened with other medicines like Enspryng. Patients should call their healthcare provider right away if they have any of these symptoms of an allergic reaction:
  - shortness of breath or trouble breathing
  - swelling of lips, face, or tongue
  - dizziness or feeling faint
  - moderate or severe stomach (abdominal) pain or vomiting
  - chest pain

Before taking Enspryng, patients should tell their healthcare provider about all of their medical conditions, including if they:
- have or think they have an infection
- 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 TB
- have had a recent vaccination or are scheduled to receive any vaccination
- are pregnant, think they might be pregnant, or plan to become pregnant. It is not known if Enspryng will harm one’s unborn baby
- are breastfeeding or plan to breastfeed. It is not known if Enspryng passes into breast milk. Patients should speak with their healthcare provider about the best way to feed one’s baby while on treatment with Enspryng
Patients should **tell their healthcare provider about all the medicines they take**, including prescription and over-the-counter medicines, vitamins and herbal supplements.

The most common side effects of Enspryng include:

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

For more information about the risk and benefit profile of Enspryng, patients should ask their healthcare provider.

Patients may report side effects to the FDA at 1-800-FDA-1088 or [http://www.fda.gov/medwatch](http://www.fda.gov/medwatch). Patients may also report side effects to Genentech at 1-888-835-2555.

Please see the full Prescribing Information for additional Important Safety Information.