

Innovation all for the patients



Roche A member of the Roche group

Chugai's Enspryng (Satralizumab) Subcutaneous Injection 120 mg Syringe Approved in Japan for Neuromyelitis Optica Spectrum Disorder

- A treatment option with a novel mechanism of action for anti-aquaporin-4 seropositive neuromyelitis optica spectrum disorder (NMOSD) in both adults and children
- Enspryng, the first drug applying Chugai's proprietary recycling antibody technology, provides convenience for people by subcutaneous injection every four weeks
- The approval was granted based on the results from two global phase III studies where Enspryng showed significantly reduced risk of relapse in people with NMOSD

TOKYO, June 29, 2020 -- [Chugai Pharmaceutical Co., Ltd.](#) (TOKYO: 4519) announced that the new drug application was approved by the Ministry of Health, Labour and Welfare (MHLW) for the pH-dependent binding humanized anti-IL-6 receptor monoclonal antibody, Enspryng® Subcutaneous Injection 120 mg Syringe (generic name: satralizumab) (hereafter, Enspryng) for the prevention of relapses of neuromyelitis optica spectrum disorder (including neuromyelitis optica). Enspryng was granted orphan drug designation in September 2019 and filed in November 2019.

“NMOSD is a chronic autoimmune disease with limited treatment options and high unmet medical needs which causes visual impairment and motor disability in severe unpredictable relapse. Enspryng is an antibody drug with a novel mechanism of action to inhibit the signaling of IL-6, an inflammatory cytokine that is a key driver in NMOSD, and shown to be highly effective in prevention of relapse of NMOSD,” said Dr. Osamu Okuda, Chugai's President and COO. “In addition, Enspryng, which was the first to apply our proprietary recycling antibody technology, can be subcutaneously administered every four weeks for convenience. We are confident that Enspryng will widely contribute to the treatment of people with NMOSD as a new treatment option.”

This approval is based on the results from 2 global phase III clinical studies in patients with NMOSD: SAKuraSky Study (NCT02028884) and SAKuraStar Study (NCT02073279). SAKuraSky is a study to evaluate Enspryng in combination with baseline immunosuppressive treatment, and SAKuraStar is a study to evaluate Enspryng as monotherapy.

Enspryng, created by Chugai, is the pH-dependent binding humanized anti-IL-6 receptor antibody, which was the first to apply our proprietary recycling antibody technology. The drug is believed to prevent relapse of NMOSD by inhibiting IL-6 signal signaling which is a key driver in NMOSD. Enspryng was approved in Canada for the first time in the world. Enspryng is designated as an orphan drug for the treatment of neuromyelitis optica (NMO) and NMOSD in Japan, and for the treatment of the same disease group in Europe and the U.S. In addition, the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for the treatment in December 2018. The application was accepted for

review by the European Medicines Agency and the U.S. FDA in 2019. Regulatory application in Japan was filed in November 2019.

*The description in the Japanese package insert

[INDICATIONS]

Prevention of relapses of NMOSD (including NMO)

[PRECAUTIONS CONCERNING INDICATIONS]

- Enspryng should be used in patients with NMOSD (including NMO)*
 - * “Guidelines for the Management of Multiple Sclerosis and Neuromyelitis Optica, 2017” (Japanese Society of Neurology) should be referred to.
- The data showing efficacy for anti-AQP4 antibody-negative patients are limited. Enspryng should be administered to anti-AQP4 antibody-positive patients.

[DOSAGE AND ADMINISTRATION]

The usual dosage for adults and children is a single dose of 120 mg satralizumab (genetical recombination) administered by subcutaneous injection at weeks 0, 2, and 4, and then once every 4 weeks thereafter.

[PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION]

- If a scheduled dose is missed, administer ENSPRYNG as soon as possible and then according to the original dosing interval from that point onward.
- After a certain period of administration of satralizumab, the frequency of relapse should be investigated. If it is considered that the benefit of satralizumab is not expected (e.g. the frequency of relapse is not decreased), discontinuation of satralizumab administration should be considered.
- In pediatric patients, consideration should be given to the weight of the patient enrolled in the clinical study to determine whether the drug could be administered.

<Reference>

•SAkuraSky study

Results from Phase III SAKuraSky Study for Chugai’s Enspryng in Neuromyelitis Optica Spectrum Disorder Published in The New England Journal of Medicine Online (November 29, 2019)

https://www.chugai-pharm.co.jp/english/news/detail/20191129110000_644.html

•SAkuraStar study

Positive Results from the Second Phase III SAKuraStar Study for Chugai’s Enspryng in Neuromyelitis Optica Spectrum Disorder (NMOSD) Published in The Lancet Neurology (April 24, 2020)

https://www.chugai-pharm.co.jp/english/news/detail/20200424150001_714.html

About neuromyelitis optica spectrum disorder (NMOSD)

NMOSD is an autoimmune disease of the central nervous system characterized by inflammatory lesions in the optic nerves and spinal cord, and cause continual and significant decrease in quality of life due to permanent neurological disability. Patients with NMOSD frequently experience a relapsing disease course with repeated attacks leading to accumulating neurological damage and disability. Symptoms may include

visual impairment, motor disability, pain leading to decreased quality of life. In some cases, attacks of NMOSD result in death. Aquaporin-4 antibodies (AQP4-IgG), pathogenic antibodies, are detected in at least two-thirds of NMOSD people. AQP4-IgG is known to target and damage a specific central nervous cell type called astrocytes, resulting in inflammatory demyelinating lesions of the optic nerve(s), spinal cord and brain¹⁻⁴. The inflammatory cytokine IL-6 is now emerging as an important factor in NMOSD pathogenesis⁵⁻⁹.

Diagnostic criteria introduced in 2006 for NMO were characterized by inflammation of the optic nerve (optic neuritis) and the spinal cord (myelitis). These were revised in 2007 with the definition of NMOSD, proposed for diseases with either optic neuritis or myelitis. In 2015, the definition of NMOSD further revised to include a broader spectrum of diseases. The diagnostic term NMOSD is now widely used¹⁰.

Sources

1. Jarius S, Ruprecht K, Wildemann B et al. Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: A multicentre study of 175 patients. *J Neuroinflammation* 2012;9:14.
2. Lennon VA, Wingerchuk DM, Kryzer TJ et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004;364:2106-12.
3. Marignier R, Bernard-Valnet R, Giraudon P et al. Aquaporin-4 antibody-negative neuromyelitis optica: Distinct assay sensitivity-dependent entity. *Neurology* 2013;80:2194-200.
4. Takahashi T, Fujihara K, Nakashima I et al. Anti-aquaporin-4 antibody is involved in the pathogenesis of NMO: a study on antibody titre. *Brain* 2007;130:1235-43.
5. Chihara N, Aranami T, Sato W et al. Interleukin 6 signaling promotes anti-aquaporin 4 autoantibody production from plasmablasts in neuromyelitis optica. *Proc Natl Acad Sci USA* 2011;108:3701-6.
6. Kimura A, Kishimoto T. IL-6: regulator of Treg/Th17 balance. *Eur J Immunol* 2010;40:1830-5.
7. Lin J, Li X, Xia J. Th17 cells in neuromyelitis optica spectrum disorder: a review. *Int J Neurosci* 2016;126:1051-60.
8. Takeshita Y, Obermeier B, Coteleur AC, et al. Effects of neuromyelitis optica-IgG at the blood-brain barrier in vitro. *Neurol Neuroimmunol Neuroinflamm.* 2016;4(1):e311.
9. Obermeier B, Daneman R, Ransohoff RM. Development, maintenance and disruption of the blood-brain barrier. *Nat Med* 2013;19:1584-96.
10. Wingerchuk DM, Banwell B, Bennett JL et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015;85:177-89.

###