RXADVANCE
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Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	ENSPRYNG™
Generic Name	satralizumab-mwge
Drug Manufacturer	Genentech, Inc.

New Drug Approval

FDA Approval Date: August 14, 2020

Review Designation: Orphan

Review Type: Type 1 – BLA 761149

Dispensing Restrictions: None

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Neuromyelitis optica spectrum disorder (NMOSD), also known as Devic disease, is a chronic disorder of the brain and spinal cord dominated by inflammation of the optic nerve (optic neuritis) and inflammation of the spinal cord (myelitis). Classically, it was felt to be a monophasic illness, consisting of episodes of inflammation of one or both optic nerves and the spinal cord over a short period of time (days or weeks) but, after the initial episode, no recurrence. It is now recognized that most patients satisfying current criteria for NMOSD experience repeated attacks separated by periods of remission. The interval between attacks may be weeks, months or years. In its early stages, NMOSD may be confused with multiple sclerosis (MS).

NMOSD occurs in individuals of all races. The prevalence of NMOSD is approximately 1-10 per 100,000 individuals and seems to be similar worldwide, although somewhat higher rates have been reported in countries with a higher proportion of individuals of African ancestry. Relative to MS that it mimics, it occurs with greater frequency in individuals of Asian and African descent, but the majority of patients with this illness in Western countries are Caucasian. Individuals of any age may be affected, but typically NMOSD, especially cases seropositive for AQP4-IgG, occur in late middle-aged women. Equal numbers of men and women have the form that does not recur after the initial flurry of attacks, but women, especially those with AQP4-IgG, are four or five times more likely to be affected than men by the recurring (relapsing) form. Children may also be affected by this condition; children more commonly develop brain symptoms at onset and seem to have a higher frequency of monophasic presentation than adults.

Efficacy

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.

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.

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.

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.

Safety

ADVERSE EVENTS

The most common adverse reactions (incidence at least 15%) are nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea.

WARNINGS & PRECAUTIONS

- Infections: Delay ENSPRYNG™ administration in patients with an active infection until the infection is resolved. Vaccination with live or liver attenuated vaccines is not recommended during treatment.
- Elevated Liver Enzymes: Monitor ALT and AST levels during treatment; interruption of ENSPRYNG™ may be required.
- Decreased Neutrophil Counts: Monitor neutrophils during treatment.
- Immunizations: Immunization with live-attenuated or live vaccines is not recommended during therapy. Administer all live or live-attenuated vaccines at least 4 weeks prior, and non-live vaccines at least 2 weeks prior to treatment initiation.

CONTRAINDICATIONS

Hypersensitivity to satralizumab or any component of the formulation; active hepatitis B infection; active or untreated latent tuberculosis.

Clinical Pharmacology

MECHANISMS OF ACTION

Satralizumab is an antagonist of the interleukin-6 (IL-6) receptor. Satralizumab is presumed to inhibit IL-6-mediated signaling through binding to soluble and membrane-bound IL-6 receptors.

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Dose & Administration

ADULTS

- Neuromyelitis optica spectrum disorder: SubQ: Loading dose: 120 mg once every 2 weeks for 3 doses (weeks 0, 2, and 4), followed by maintenance dose: 120 mg once every 4 weeks.
- Dosage for delayed or missed doses (reasons other than increased liver enzymes):
    - Missed loading dose: 120 mg as soon as possible (do not wait until next planned dose). If the second loading dose is delayed or missed, administer as soon as possible and administer the third (final) loading dose 2 weeks later. If the third loading dose is delayed or missed, administer as soon as possible and administer the first maintenance dose 4 weeks later.
    - Missed maintenance dose:

      If <8 weeks since last dose: 120 mg as soon as possible (do not wait until the next planned dose). Reset dose schedule to every 4 weeks after delayed or missed dose administered.

      If 8 to <12 weeks since last dose: 120 mg every 2 weeks for 2 doses (weeks 0 and 2), followed by 120 mg every 4 weeks.

      If ≥ 12 weeks since last dose: 120 mg every 2 weeks for 3 doses (weeks 0, 2, and 4), followed by 120 mg every 4 weeks. Note:

      Note: 'Week 0' refers to time of the first administration after the missed dose.

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing. 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.

RENAL IMPAIRMENT

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

HEPATIC IMPAIRMENT

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied). Use caution in patients with baseline ALT/AST >1.5 × ULN.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: 120 mg/mL in a single-dose prefilled syringe.