RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	UPLIZNA™
Generic Name	inebilizumab-cdon
Drug Manufacturer	Viela Bio, Inc.

New Drug Approval

UPLIZNA™ is a CD19-directed cytolytic antibody indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

FDA Approved: June 11, 2020

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).

Epidemiological studies of the uncommon disorder neuromyelitis optica spectrum disorder **(**NMOSD) may be difficult to interpret because of the evolving nature of diagnostic criteria, differences in the definition and accuracy of NMOSD diagnosis, the completeness of case ascertainment, and variability in assays for the disease-specific biomarker aquaporin-4 (AQP4)-IgG.

Efficacy

The efficacy of UPLIZNA™ for the treatment of NMOSD was established in Study 1 (NCT02200770), a randomized (3:1), double-blind, placebo-controlled trial that enrolled 213 patients with NMOSD who were anti-AQP4 antibody positive and 17 who were anti-AQP4 antibody negative.

Patients met the following eligibility criteria:

- A history of one or more relapses that required rescue therapy within the year prior to screening, or 2 or more relapses that required rescue therapy in 2 years prior to screening.
- Expanded Disability Status Scale (EDSS) score of 7.5 or less. Patients with an EDSS score of 8.0 were eligible if they were deemed capable of participating.
- Patients were excluded if previously treated with immunosuppressant therapies within an interval specified for each such therapy.

Of the 213 enrolled anti-AQP4 antibody positive patients, a total of 161 were randomized to receive treatment with UPLIZNA™, and 52 were randomized to receive placebo. The baseline demographic and disease characteristics were balanced between the treatment groups. Females accounted for 94% of the study population. Fifty-two percent of patients were White, 21% Asian, and 9% Black or African American. The mean age was 43 years (range 18 to 74 years). The mean EDSS score was 4.0. The number of relapses in the two years prior to randomization was 2 or more in 83% of the patients.

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All potential relapses were evaluated by a blinded, independent, adjudication committee, who determined whether the relapse met protocol-defined criteria. Patients who experienced an adjudicated relapse in the randomized-controlled period (RCP), or who completed the Day 197 visit without a relapse, exited the RCP.

The primary efficacy endpoint was the time to the onset of the first adjudicated relapse on or before Day 197.

The time to the first adjudicated relapse was significantly longer in patients treated with UPLIZNA™ compared to patients who received placebo (relative risk reduction 73%; hazard ratio: 0.272; $p < 0.0001$). In the anti-AQP4 antibody positive population there was a 77.3% relative reduction (hazard ratio: 0.227, $p < 0.0001$). There was no evidence of a benefit in patients who were anti-AQP4 antibody negative.

Safety

ADVERSE EVENTS

The most common adverse reactions (at least 10% of patients treated with UPLIZNA™ and greater than placebo) were urinary tract infection and arthralgia.

WARNINGS & PRECAUTIONS

- Infusion reactions: Administer premedications prior to infusion. Management recommendations for infusion reactions depend on the type and severity of the reaction. Permanently discontinue UPLIZNA™ if a life threatening or disabling infusion reaction occurs.
- Infections: Delay UPLIZNA™ administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.
- Immunoglobulin levels: Monitor the level of immunoglobulins at the beginning, during, and after discontinuation of treatment with UPLIZNA™ until B-cell repletion. Consider discontinuing UPLIZNA™ if a patient develops a serious opportunistic infection or recurrent infections if immunoglobulin levels indicate immune compromise.
- Fetal Risk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping UPLIZNA™.

CONTRAINDICATIONS

- Previous life-threatening reaction to infusion of UPLIZNA™
- Active hepatitis B infection
- Active or untreated latent tuberculosis

Clinical Pharmacology

MECHANISMS OF ACTION

The precise mechanism by which inebilizumab-cdon exerts its therapeutic effects in NMOSD is unknown but is presumed to involve binding to CD19, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, inebilizumab-cdon results in antibody-dependent cellular cytolysis.

Dose & Administration

ADULTS

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UPLIZNA™ must be diluted in 250 mL of 0.9% Sodium Chloride Injection, USP prior to administration.

UPLIZNA™ is administered as an intravenous infusion titrated to completion, approximately 90 minutes.

The recommended dose is:

- Initial dose: 300 mg intravenous infusion followed two weeks later by a second 300 mg intravenous infusion
- Subsequent doses (starting 6 months from the first infusion): single 300 mg intravenous infusion every 6 months

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

GERIATRICS

Clinical studies of UPLIZNA™ did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

RENAL IMPAIRMENT

No formal clinical studies have been conducted to investigate the effect of renal impairment.

HEPATIC IMPAIRMENT

No formal clinical studies have been conducted to investigate the effect of hepatic impairment.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

100 mg/10 mL (10 mg/mL) solution for injection in a single-dose vial

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