uplizna™
inebilizumab-cdon

Uplizna® (inebilizumab-cdon): Prescribing Information Overview

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

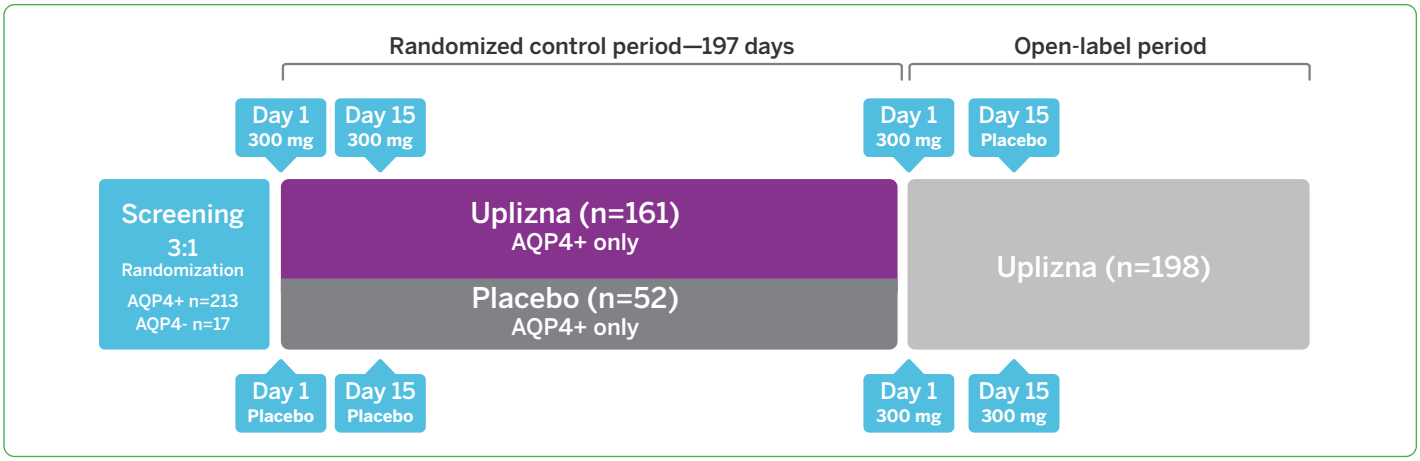
Please see accompanying full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Uplizna is contraindicated in patients with:

- A history of life-threatening infusion reaction to Uplizna
- Active hepatitis B infection
- Active or untreated latent tuberculosis

PIVOTAL NMOSD TRIAL: STUDY DESIGN



- **Randomized, double-blind, placebo-controlled** clinical trial in 213 patients who were anti-AQP4 antibody positive and 17 who were anti-AQP4 antibody negative (N=230)
- **Monotherapy—no use of immunosuppressants during the blinded phase of the trial;** oral or intravenous corticosteroids allowed for pre-medication or as needed for relapses
- **Primary endpoint**—time to onset of first adjudicated NMOSD relapse—all potential relapses evaluated by a blinded, independent Adjudication Committee

TRIAL: PATIENT POPULATION

- **Key inclusion criteria**
  - ≥1 NMOSD relapse in the prior year, or ≥2 relapses in the prior 2 years, requiring rescue therapy
  - An Expanded Disability Status Scale (EDSS) score ≤7.5
- **Patient characteristics**
  - Mean age: 43 years (range 18-74 years); 94% female
  - Ethnic breakdown: 52% White, 21% Asian, 9% Black or African American
  - 83% of the patients had ≥2 relapses in the 2 years prior to randomization
  - Median EDSS score: 4.0 at baseline

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Infusion Reactions: Uplizna can cause infusion reactions, which can include headache, nausea, somnolence, dyspnea, fever, myalgia, rash, or other symptoms. Infusion reactions were most common with the first infusion but were also observed during subsequent infusions. Administer pre-medication with a corticosteroid, an antihistamine, and an anti-pyretic.

Please see accompanying full Prescribing Information.

DOSING

uplizna® inebilizumab-cdon

300 mg intravenous infusion over approximately 90 minutes twice per year after initial dosing

- Hepatitis B virus, quantitative serum immunoglobulins, and tuberculosis screening is required before the first dose
- Administer all immunizations according to guidelines at least 4 weeks prior to initiation of Uplizna

Pre-medication: administer approximately 30-60 minutes prior to each Uplizna infusion

Type of pre-medication	Route of administration	Examples of (or equivalent)	Administration time prior to Uplizna infusion
corticosteroid	intravenous	methylprednisolone 80 mg to 125 mg	30 minutes
antihistamine	oral	diphenhydramine 25 mg to 50 mg	30 to 60 minutes
anti-pyretic	oral	acetaminophen 500 mg to 650 mg	30 to 60 minutes

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

Infections: The most common infections reported by Uplizna-treated patients in the randomized and open-label periods included urinary tract infection (20%), nasopharyngitis (13%), upper respiratory tract infection (8%), and influenza (7%). Delay Uplizna administration in patients with an active infection until the infection is resolved.

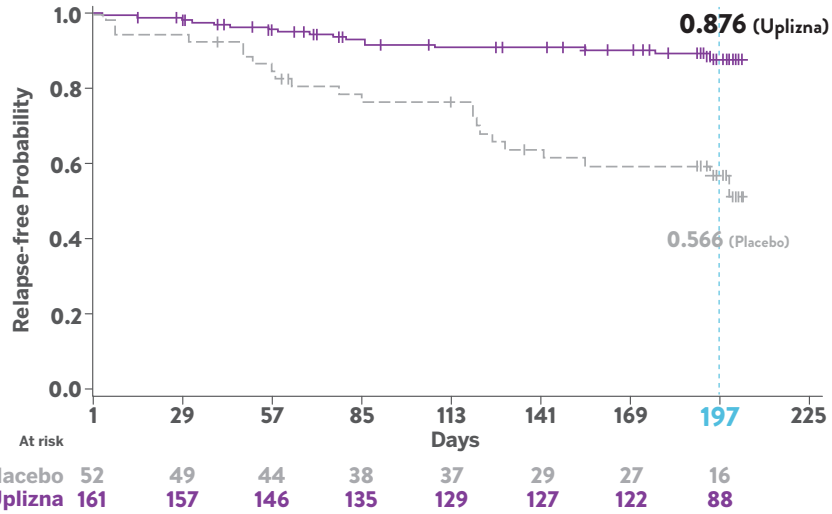
Please see accompanying full Prescribing Information.

RELAPSE REDUCTION

89% of patients on Uplizna were relapse-free at 28 weeks vs 58% for placebo

Significantly longer time to first adjudicated NMOSD relapse for Uplizna vs placebo in the randomized-controlled period (ITT* population; anti-AQP4 antibody positive patients)

KAPLAN-MEIER ESTIMATE: TIME TO FIRST RELAPSE



77% relative reduction in the risk of relapse for Uplizna vs placebo

	Uplizna (n=161)	Placebo (n=52)
No. of events	18 (11.2%)	22 (42.3%)
Hazard Ratio (95% CI†):	0.227 (0.121, 0.423)	
P-value:	<0.0001	

*Intent to treat. | †Confidence interval.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

Increased immunosuppressive effects are possible if combining Uplizna with another immunosuppressive therapy.

The risk of hepatitis B virus (HBV) reactivation has been observed with other B-cell-depleting antibodies. Perform HBV screening in all patients before initiation of treatment with Uplizna. Do not administer to patients with active hepatitis.

Although no confirmed cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in Uplizna clinical trials, JC virus infection resulting in PML has been observed in patients treated with other B-cell-depleting antibodies and other therapies that affect immune competence. At the first sign or symptom suggestive of PML, withhold Uplizna and perform an appropriate diagnostic evaluation.

Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating Uplizna.

Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.

Please see accompanying full Prescribing Information.

REDUCED HOSPITALIZATION

uplizna® inebilizumab-cdon

Uplizna reduced the annualized rate of hospitalization for anti-AQP4 antibody positive patients vs placebo

78% relative reduction in the annualized rate of hospitalization for Uplizna vs placebo (0.11 vs 0.5 for placebo)

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

Reduction in Immunoglobulins: There may be a progressive and prolonged hypogammaglobulinemia or decline in the levels of total and individual immunoglobulins such as immunoglobulins G and M (IgG and IgM) with continued Uplizna treatment. Monitor the level of immunoglobulins at the beginning, during, and after discontinuation of treatment with Uplizna until B-cell repletion especially in patients with opportunistic or recurrent infections.

Please see accompanying full Prescribing Information.

ADVERSE EVENT PROFILE

Adverse reactions in adult patients with NMOSD with an incidence of at least 5% with Uplizna and a greater incidence than placebo		
	Uplizna (n=161) %	**Placebo (n=52) %**
Urinary tract infection	11	10
Arthralgia	10	4
Headache	8	8
Back pain	7	4

Infusion reactions

- Infusion reactions during first course of treatment: 9.3% for Uplizna
- Infusion reactions can include headache, nausea, somnolence, dyspnea, fever, myalgia, rash, or other symptoms
- Infusion reactions were most common with the first infusion but were observed during subsequent infusions
- 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

Immunoglobulins

- Consistent with its mechanism of action, average immunoglobulin levels decreased with Uplizna use
- The proportion of Uplizna-treated patients with IgG levels below the lower limit of normal at year 1 was 6.6% and at year 2 was 13%
- The relationship between reduced immunoglobulin levels and infection has not been assessed with Uplizna

Neutropenia

Neutropenia was generally transient and was not associated with serious infections

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

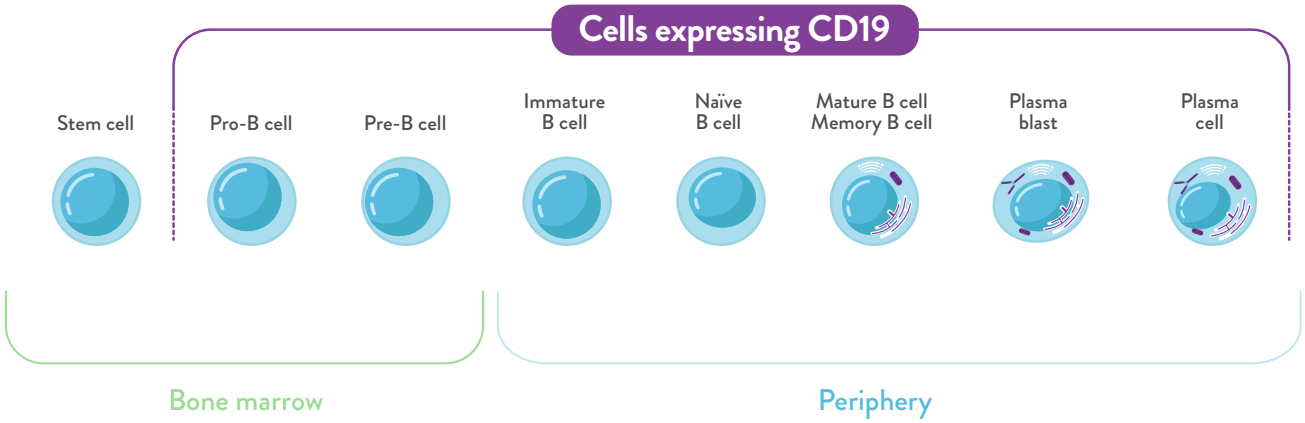
Fetal Risk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping Uplizna.

Please see accompanying full Prescribing Information.

PROPOSED MECHANISM OF ACTION

- Inebilizumab-cdon is a CD19+ B cell-directed humanized IgG1 monoclonal antibody
- Following cell surface binding to CD19+ B lymphocytes, inebilizumab-cdon results in antibody-dependent cellular cytolysis (ADCC)

CD19 is a cell surface antigen present on pre-B and mature B lymphocytes.



- The precise mechanism by which inebilizumab-cdon exerts a therapeutic effect in NMOSD is unknown

B-cell depletion through the randomized-controlled period of the pivotal trial

- B-cell counts were reduced below the lower limit of normal by 4 weeks in 100% of patients treated with Uplizna
- B-cell counts remained below the lower limit of normal in 94% of patients for 28 weeks after initiation of treatment

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (continued)

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

Please see accompanying full Prescribing Information.

NOW FDA APPROVED

for the treatment of adult patients with AQP4+ NMOSD

UPLIZNA AS A MONOTHERAPY REDUCED THE RISK OF RELAPSES

89% of patients on Uplizna were relapse-free through 6.5 months vs 58% for placebo

78% relative reduction in the annualized rate of hospitalization for Uplizna vs placebo (0.11 vs 0.5 for placebo)

Administered as an intravenous infusion until completion (approximately 90 minutes), twice per year after initial dosing

A CD19+ B cell-directed humanized IgG1 monoclonal antibody—CD19 is a cell surface antigen present on pre-B and mature B lymphocytes

Uplizna is contraindicated in patients with: a history of life-threatening infusion reaction to Uplizna, active hepatitis B infection, and active or untreated latent tuberculosis.

VIELAVIPs™
Individualized Personal Support
With You Along Your Journey

Learn more about this complimentary support program at www.VielaVIPs.com

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