Drug Monograph

Drug Name: **Uplizna® (inebilizumab-cdon) injection**
Drug Class: **CD19-Directed Cytolytic Antibody**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms:	Uplizna is available as single-dose vial containing 100 mg of inebilizumab-cdon for intravenous infusion.
Manufacturer:	Manufactured by: Viela Bio, Inc., Gaithersburg, MD 20878.
Summary of Findings:	The efficacy of Uplizna for the treatment of neuromyelitis optica spectrum disorder was demonstrated in one randomized, double-blind, placebo-controlled study that enrolled 213 patients with NMOSD who were anti-AQP4 antibody positive. The primary measure of efficacy was the time to the onset of the first adjudicated relapse on or before day 197. The time to relapse was significantly longer in patients treated with Uplizna compared to patients who received placebo (relative risk reduction 73%; p<0.0001)

Status Recommendation:	☒ Clinical Edit ☐ Open Access	☐ PA Required ☐ PDL
Type of PA Criteria:	☒ Appropriate Indications ☐ No PA Required	☐ Non-Preferred ☐ Preferred

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [1,2]

Neuromyelitis optica spectrum disorder (NMOSD), a rare autoimmune disorder, is a chronic disorder of the brain and spinal cord dominated by inflammation of the optic nerve and spinal cord. In the early stages, NMOSD is easily confused with multiple sclerosis symptoms. NMOSD affects approximately 1-10 per 100,000 individuals. Characteristic symptoms of NMOSD include optic neuritis (inflammation of the optic nerve leading to pain inside the eye and rapidly followed by loss of clear vision) or myelitis.

Dosage Form [3]

Uplizna is available as single-dose vial containing 100 mg of inebilizumab-cdon for intravenous infusion.

Manufacturer [3]

Manufactured by: Viela Bio, Inc., Gaithersburg, MD 20878.

Indication(s) [3]

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

Clinical Efficacy [3,4,5] (mechanism of action/pharmacology, comparative efficacy)

Uplizna is an anti-CD19 monoclonal antibody directed against pre-B and mature B-cell lymphocytes, which express the cell surface antigen CD19. Following binding to CD19, Uplizna causes antibody-dependent cellular cytolysis.

Pharmacokinetics:

Volume of Distribution	2.95L
Metabolism	Degraded by proteolytic enzymes widely distributed in the body
Excretion	0.19L/day
Half-life	18 days

Clinical Trials Experience

STUDY 1 DESIGN	Randomized, double-blind, placebo-controlled study (n=213)
INCLUSION CRITERIA	• Men and women ≥18 years with diagnosis of NMO/NMOSD • Confirmation of NMO/NMOSD status:

	○ AQP4-IgG sero-positive NMO/NMOSD with at least one attack requiring rescue therapy in the last year or two attacks requiring rescue therapy in the last 2 years ○ AQP4-IgG sero-negative NMO with at least one attack requiring rescue therapy in the last year or two attacks requiring rescue therapy in the last 2 years • Able and willing to give written informed consent and comply with the requirements of the study protocol • Expanded Disability Severity Scale (EDSS) ≤7.5 (8 in special circumstances) • Men and women of reproductive potential must agree to use a highly effective method of birth control from screening to 6 months after final dose of the investigational product.
EXCLUSION CRITERIA	• Lactating and pregnant females • Treatment with any investigational agent within 4 weeks of screening • Known history of a severe allergy or reaction to any component of the investigational product formulation or history of anaphylaxis following any biologic therapy • Known active severe bacterial, viral, or other infection or any major episode of infection requiring hospitalization • History of alcohol, drug, or chemical abuse, or a recent history of such abuse <1 year prior to randomization • Receipt of the following at any time prior to randomization: Alemtuzumab, Total lymphoid irradiation, Bone marrow transplant, T-cell vaccination therapy • Receipt of rituximab or any experimental B-cell depleting agent within 6 months prior screening and B-cells below the lower limit of normal • Receipt of intravenous immunoglobulin (IVIG) within 1 month prior to randomization • Receipt of any of the following within 3 months prior to randomization: Natalizumab, Cyclosporin, Methotrexate, Mitoxantrone, Cyclophosphamide, Tocilizumab, Eculizumab • History of Hepatitis B and/or Hepatitis C (Hep B/C at screening) • Known history of a primary immunodeficiency (congenital or acquired) or an underlying condition such as human immunodeficiency virus (HIV) infection • History of malignancies, apart from squamous cell or basal cell carcinoma of the skin treated with documented success of curative therapy >3 months prior to randomization • Any concomitant disease other than NMO/NMOSD that required treatment with oral or intravenous steroids at doses over 20 mg a day for over 21 days
TREATMENT REGIMEN	Patients were randomized 3:1 to receive Uplizna (n=161) 300 mg intravenously on day 1 and 15 or placebo (n=52).
RESULTS	The primary measure of efficacy was the time to the onset of the first adjudicated relapse on or before day 197. The time to 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)
SAFETY	Discussed in the Adverse Effects section below.

Contraindications [3,4]

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

Warnings and Precautions [3,4]

- 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.
- 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.
- 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.
- 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.

Adverse Effects [3,4]

Most common, ≥5 %	(n = 161) %
Urinary tract infection	11
Arthralgia	10
Headache	8
Back pain	7

Drug Interactions [3,4]

- Concomitant usage of Uplizna with immunosuppressant drugs, including systemic corticosteroids may increase risk of infection. Consider the risk of additive immune system effects when co-administering immunosuppressive therapies with Uplizna.

Dosage and Administration [3,4]

- Hepatitis B virus, quantitative serum immunoglobulins, and tuberculosis screening is required before the first dose
- Prior to every infusion: Determine if there is an active infection and premedicate with a corticosteroid, an antihistamine, and an antipyretic
- Uplizna must be diluted in 250 mL of 0.9% Sodium Chloride Injection, 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
- Monitor patients closely during the infusion and for at least one hour after completion of the infusion.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost**/Year
Inebilizumab-cdon	Uplizna	Viela Bio, Inc	300 mg IV every 2 weeks x2 doses, then 300 mg every 6 months	$262,000
Satralizumab	Enspryng	Genentech, Inc.	120 mg SubQ every 2 weeks x3 doses, then 120 mg every 4 weeks	$175,385

** Wholesale Acquisition Cost

Conclusion

Uplizna, a CD19-directed cytolytic antibody, is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 antibody positive. The safety and efficacy of Uplizna was demonstrated in one randomized, double-blind, placebo-controlled clinical trial that enrolled 213 patients with NMOSD. The trial demonstrated that patients randomized to Uplizna had a significantly longer onset of first relapse compared to placebo. The most common adverse reactions (>10%) were urinary tract infection and arthralgia.

Recommendation

The MO Healthnet Division recommends adding this drug to the current Rare Disease: NMOSD clinical edit.

References

1) Neuromyelitis Opitca Spectrum Disorder. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/neuromyelitis-optica/. Accessed January 14, 2021.
2) Neuromyelitis Optica (NMS). National Multiple Schlerosis Society. https://www.nationalmssociety.org/What-is-MS/Related-Conditions/Neuromyelitis-Optica-(NMO). Accessed January 15, 2021.
3) Product Information: Uplizna (inebilizumab) 2020. Viela Bio, Inc., Gaithersburg, MD 20878.
4) Inebilizumab: Drug Information. Lexi-Drugs. Wolters Kluwer Clinical Drug Information Inc.
5) A Double-masked, Placebo-controlled Study With Open-label Period to Evaluate the Efficacy and Safety of MEDI-551 in Adult Subjects With Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorders. NCT02200770. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02200770?term=02200770&draw=2&rank=1. Accessed January 14, 2021.

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