New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	**Uplizna™ (inebilizumab-cdon) [Viela Bio]**
Dosage Formulations:	100mg/10mL solution in a single-dose vial
FDA Approval Date: **FDB File Date:**	FDA: June 11, 2020 FDB: June 29, 2020
Indication:	For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive
Mechanism of Action:	CD19-directed cytolytic antibody – exact mechanism of action is unknown but believed to cause antibody-dependent cellular cytolysis after Uplizna binds to CD19, which is a cell surface antigen found on pre-B and mature B lymphocytes

Dose/ Administration:	• Initial Dose: 300mg IV infusion followed two weeks later by a second 300mg IV infusion
	• Subsequent Doses: single 300mg IV infusion every 6 months (starting 6 months from the first infusion)
	• Length of infusion is approximately 90 minutes
	• Dilution in 250mg of 0.9% Sodium Chloride Injection is required prior to administration
	• Screenings for Hepatitis B, quantitative serum immunoglobulins and tuberculosis required prior to first dose
	• Prior to every infusion:
	  ○ Determine if there is an active infection
	  ○ Premedicate with a corticosteroid (i.e., IV methylprednisolone 80-125mg 30 minutes prior to Uplizna), an antihistamine (i.e., oral diphenhydramine 25-50mg 30-60 minutes prior to Uplizna), and an antipyretic (i.e., oral acetaminophen 500-650mg 30-60 minutes prior to Uplizna)

Drug Clinical Highlights:	• FDA granted Orphan Drug designation
	• Treatment reduces CD20+ B cell counts in blood by 8 days post-infusion
	• Contraindications include:
	  ○ Previous life-threatening reaction to Uplizna infusion
	  ○ Active hepatitis B infection
	  ○ Active or untreated latent tuberculosis
	• Warning and Precautions include:
	  ○ Infusion reactions including headache, nausea, somnolence, dyspnea, fever, myalgia or rash.
	  ○ Delay administration in those with active infection until resolution of infection.
	  ○ Live-attenuated or live vaccines are not recommended during and after treatment discontinuation, until B-cell repletion.
	  ○ Immunoglobulin levels should be monitored at the beginning, during and after treatment discontinuation, until B-cell repletion.
	  ○ Due to fetal risk, it is recommended females of reproductive age use an effective method of contraception during and 6 months post treatment.
	• The most common adverse reactions reported were urinary tract infections (20%), nasopharyngitis (13%), infusion reaction (12%), joint pain (10%), and headache (10%)
	• Consider risk vs benefit with use of Uplizna and immunosuppressant drugs as this may cause an increased risk of infection
	• Potential for immunogenicity
	• Clinical Trial (N-MOmentum/NCT02200770) – randomized (3:1), double-blind, placebo-controlled trial with 213 anti-AQP4+ and 17 anti-AQP4- NMOSD patients aged 18 years or older.
	  ○ Inclusion criteria:

- One or more relapses (attacks) that required rescue therapy within the year prior to screening or two or more relapses that required rescue therapy in two years prior to screening
- Expanded Disability Status Scale (EDSS) score of ≤7.5 (those with a score of 8 were eligible if they were deemed capable of participating)

- Exclusion criteria: previous treatment with immunosuppressants within an interval specified for each such therapy
- 300mg of Uplizna was administered on days 1, 15 and then every 6 months
- 197-day study

Primary Endpoint: Time to acute attack (the onset of the first adjudicated relapse on or before Day 197)			
	Uplizna (N=161)	**Placebo (N=52)**	**Notes**
Number (%) of patients with relapse	18 (11.2%)	22 (42.3%)	Relative Risk Reduction: 73% Hazard Ratio (95% CI) 0.227 (0.121,0.423) p-value: <0.0001

- No benefit was shown in those who were anti-AQP4 negative
- Secondary outcomes: percentage of patients with worsening EDSS scores
  - 15.5% of Uplizna treated patients vs 33.9% of placebo patients showed a decrease in their EDSS scores (p-value: 0.0049)

Disease State Clinical Highlights:

- Neuromyelitis optica spectrum disorder is a rare, autoimmune disease of the central nervous system. This disorder primarily attacks the optic nerves and spinal cord resulting in inflammation of the optic nerve (optic neuritis) and spinal cord (myelitis) thus leading to accumulating neurological damage and disability. NMOSD was first thought to be a monophasic disease but has been found to be a disease characterized as repeated attacks separated by periods of remission. These periods of remission may be weeks, months or years and is very commonly confused with multiple sclerosis. Within the last 10 years NMOSD became differentiated from multiple sclerosis due to the discovery of the anti-aquaporin-4 antibody that now identifies the disease.
- Incidence/prevalence of disease state: estimated 10,000 patients in the US, with 8,000 cases being anti-AQP4 antibody positive

Price Per Unit (WAC):

- $43,666.67 per 100mg vial
- 300mg dose = $131,000.01 per infusion

Therapeutic Alternatives:

- Goals of current treatment includes suppression of acute attacks along with prevention of future attacks:
  - Acute attacks are commonly treated with high-dose IV methylprednisolone (1 gram daily for 3-5 days), commonly followed by an oral steroid taper of 2-8 weeks
  - Attack prevention therapies include Soliris®, and non-FDA approved therapies such as azathioprine, mycophenolate, or rituximab

	Uplizna	**Soliris**
Mechanism of Action	Anti-CD19 antibody	Monoclonal antibody
Indication	Treatment of neuromyelitis optica spectrum disorder in adults who are aquaporin-4-antibody positive	Treatment of neuromyelitis optica spectrum disorder in adults who are aquaporin-4-antibody positive
Dosage Forms	100mg/10mL IV infusion	300mg/30mL IV infusion
Contraindications	• Previous life-threatening infusion reactions to Uplizna • Active hepatitis B infection • Active or untreated latent tuberculosis	• Black Boxed Warning for serious meningococcal infections
Dose	300mg IV day 1 300mg IV two weeks later 300mg IV every 6 months thereafter	900mg IV weekly x 4 weeks 1,200mg IV on week 5 1,200mg IV every 2 weeks thereafter
WAC	$43,666.67 per vial - Annual cost: $262,000.02	$6,523 per vial - Annual cost: $678,392

Prior Authorization Approval Criteria:	**Must meet the following criteria:** Initial Therapy: • Prescribed by or in consultation with an immunologist, hematologist or other specialist within the treated disease state **AND** • Participants aged 18 years or older **AND** • Documented diagnosis of neuromyelitis optica spectrum disorder (ICD10: G36.0) seropositive for anti-aquaporin-4 (AQP4) antibodies **AND** • Female participants must utilize concurrent birth control methods during and for 6 months post-treatment **AND** • Documented baseline number and frequency of acute attacks • Initial therapy approved for 9 months Continuation of Therapy: • Documented decrease or stabilization in number and frequency of acute attacks **Additional Provider Diagnostic/Monitoring Criteria, if desired:** • Determine if there is an active infection prior to each infusion • Premedicate with a corticosteroid, an antihistamine and an antipyretic • CD20+ B cell counts prior to initiation and as necessary • Screenings for hepatitis B, quantitative serum immunoglobulins and tuberculosis required prior to first dose • Lack of live-attenuated or live vaccines 4 weeks prior to administration • Documented EDSS score of 8 or less
Implication to State Medicaid Program:	Adequate therapeutic trials may include non-FDA approved generic/biosimilar therapies including rituximab, azathioprine or mycophenolate, which may lead to cost savings. LOE: 6.11.2034 Satralizumab (Roche), a monthly subcutaneous interleukin 6 receptor antagonist, indicated for neuromyelitis optica spectrum disorder has a PDUFA of August 2020

References:

1. Uplizna (inebilizumab-cdon) [package insert]. Gaithersburg, MD: Viela Bio; 2020.
2. Soliris (eculizumab) [package insert]. New Haven, CT: Alexion Pharmaceuticals Inc; 2019.
3. Rituxan (rituximab) [package insert]. South San Francisco, CA. Genentech Inc; 2020.
4. CellCept (mycophenolate mofetil) [package insert]. South San Francisco, CA. Genentech Inc; 2019.
5. Azasan (azathioprine) [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; 2019.
6. IPD Analytics. Uplizna (inebilizumab-cdon).
7. Cree BAC, et al/ Inebilizumab for the treatment of neuromyelitis optica spectrum disorder (N-Momentum): a double-blind, randomised placebo-controlled phase 2/3 trial. *The Lancet.* 2019;394(10206):1352-1363. doi: 10.1016/S0140-6736(19)31817-3.
8. Kessler R.A, Mealy M.A, et al. Treatment of Neuromyelitis Optica Spectrum Disorder: Acute, Preventive, and Symptomatic. *Curr Treat Options Neurol.* 2016;18(1):2. doi: 10.1007/s1140-015-0387-9.
9. National Organization for Rare Disorders (NORD) website. Neuromyelitis Optica Spectrum Disorder. https://rarediseases.org/rare-diseases/neuromyelitis-optica/
10. USPDI, Micromedex; 2020.