New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	**Enspryng™ (satralizumab-mwge) [Roche]**
Dosage Formulations:	120mg/mL in a single-dose prefilled syringe
FDA Approval Date: **FDB File Date:**	FDA: August 14, 2020 FDB: August 23, 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:	Interleukin-6 (IL-6) receptor antagonist – exact mechanism of action is unknown, but thought to involve inhibition of IL-6-mediated signaling through binding to soluble and membrane-bound IL-6 receptors
Dose/ Administration:	• Initial Loading Dose: 120mg subcutaneous injection at weeks 0, 2, and 4. • Maintenance Dose: 120mg subcutaneous injection every 4 weeks following completion of loading dose series. • Prior to initiation screen for hepatitis B, tuberculosis, liver transaminases, and serum bilirubin. • Intended for patient self-administration. The first injection should be performed under the guidance of a qualified health care professional. • Administer subcutaneously in the thigh or abdomen. Rotate sites with each administration. • Prefilled syringe should be removed from the refrigerator and its carton and allowed to sit at room temperature for 30 minutes prior to use. • Unopened syringes can be removed from and returned to a refrigerator if necessary, but a combined total of 8 days at >30°C should not be exceeded.

Drug Clinical Highlights:	• FDA granted Orphan Drug designation.
	• Inhibits IL-6, which increases dramatically in the blood and spinal fluid during autoimmune attacks.
	• Contraindications:
	  ○ Known hypersensitivity to satralizumab or any of its inactive ingredients
	  ○ Active hepatitis B infection
	  ○ Active or untreated latent tuberculosis
	• Warnings and Precautions:
	  ○ Mild to moderate elevations of liver enzymes
	  ○ Decreased neutrophil count and neutropenia
	  ○ Increased risk of infections
	  ○ Hepatitis B reactivation
	  ○ Tuberculosis
	  ○ Live or live-attenuated vaccines should not be given during treatment.
	• The most common adverse reactions reported (≥15%) were nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue, and nausea.
	• Consider risk versus benefit with use of Enspryng and immunosuppressant drugs due to potential increased risk of infection.
	• Potential for immunogenicity.
	• Clinical Trial 1 (NCT02073279) – randomized (2:1), placebo-controlled trial with 64 anti-AQP4+ and 31 anti-AQP4- NMOSD patients 18 years or older.

- Clinical Trial 2 (NCT02028884) – randomized (1:1), placebo-controlled trial with 76 adult NMOSD patients on concurrent immunosuppressive therapy (IST). 52 patients were anti-AQP4+ and 24 were anti-AQP4-.
  - Inclusion Criteria:
    - Diagnosis of either neuromyelitis optica or neuromyelitis optica spectrum disorder
    - At least one documented relapse in the last 12 months (Trial 1)
    - At least two documented relapses in the 2 years before screening, with at least one relapse in the previous 12 months (Trial 2)
    - Expanded Disability Status Scale (EDSS) from 0 to 6.5
    - Mean ages of 44 years (Trial 1) and 46 years (Trial 2)
  - Exclusion Criteria: previous treatment with IST within an interval specified for each category
  - Intervention: 120mg subcutaneous satralizumab or placebo at weeks 0, 2, and 4, and then every 4 weeks thereafter

Primary Endpoint: Time to first Clinical Endpoint Committee (CEC) confirmed relapse				
	Trial 1		**Trial 2**	
	Enspryng (N=41)	**Placebo (N=23)**	**Enspryng + IST (N=26)**	**Placebo + IST (N=26)**
Number (%) of patients with relapse	9 (22%)	13 (56.5%)	3 (11.5%)	11 (42.3%)
Hazard Ratio (95% CI)	0.26 (0.11, 0.63)		0.22 (0.06, 0.82)	
Risk Reduction	74%		78%	
p-value	0.0014		0.0143	
Proportion of Patients Relapse Free at 96 weeks	76.5%	41.1%	91.1%	56.8%

- No benefit was shown in those who were anti-AQP4 negative.

Disease State Clinical Highlights:

- NMOSD is a chronic autoimmune disease that affects the central nervous system and primarily attacks the optic nerves and spinal cord. This results in inflammation of the optic nerve (optic neuritis) and spinal cord (myelitis), which can lead to blindness and impaired mobility. Initially, NMOSD was thought to be a monophasic illness, but is now recognized as a disease that causes repeated attacks with periods of remission in between. Remission periods may last for weeks, months, or even years. Early in the disease process it can be difficult to distinguish NMOSD from multiple sclerosis (MS). The discovery of AQP4 led to greater distinction between NMOSD and MS. AQP4 identifies the disease in at least 72% of patients with over 99% specificity.
- Prevalence of disease state: estimated 10,000 patients in the United States with 8,000 cases being anti-AQP4+.

Price Per Unit (WAC):

- $14,615.39 per 120mg/mL single dose syringe

Therapeutic Alternatives:

- Goals of therapy: suppress acute inflammatory relapse and prevent future relapses
  - Acute attack treatment: typically, methylprednisolone 1g IV daily for 3-5 days followed by an oral steroid taper for 2-8 weeks
  - Attack prevention: therapies include Soliris™, Uplizna™, and non-FDA approved therapies including azathioprine, mycophenolate, and rituximab.

	Enspryng	Uplizna	Soliris
Mechanism of Action	IL-6 receptor antagonist	Anti-CD19 antibody	Monoclonal antibody
Indication	Treatment of NMOSD in adults who are anti-AQP4+	Treatment of NMOSD in adults who are anti-AQP4+	Treatment of NMOSD in adults who are anti-AQP4+
Dosage Forms	120mg/mL prefilled syringe	100mg/10mL IV infusion	300mg/30mL IV infusion
Contraindications	- active hepatitis B infection - active or untreated latent tuberculosis	- active hepatitis B infection - active or untreated latent tuberculosis - previous life-threatening reaction to infusion	- unresolved serious *N. meningitidis* infection - patients not currently vaccinated against *N. meningitidis*
Dose	120mg SC at weeks 0, 2, 4 120mg SC every 4 weeks thereafter	300mg IV day 1 300mg IV two weeks later 300mg IV every 6 months thereafter	900mg IV weekly x4 weeks 1,200mg IV on week 5 1,200mg IV every 2 weeks thereafter
WAC	$14,615.39 per syringe - Annual Cost: $190,000	$43,666.67 per vial - Annual Cost: $262,000	$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, neurologist, 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 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 6 months

Continuation of Therapy:

- Documented decrease or stabilization in number and frequency of acute attacks

Additional Provider Diagnostic/Monitoring Criteria, if desired:

- Screening for hepatitis B, tuberculosis, liver transaminases, and serum bilirubin prior to initiation
- Lack of live or live-attenuated vaccines 4 weeks prior to initiation
- Lack of inactivated vaccines 2 weeks prior to initiation
- Documented EDSS score of 6.5 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: 2036

- Currently there are 55 MO HealthNet patients with NMOSD with an approximated 80% being anti-AQP4 positive. The potential annual budget impact of Enspryng is $8,360,000 compared to $11,528,000 with Uplizna.
- Ravulizumab (Alexion), an intravenous long-acting C5 inhibitor administered every 8 weeks is currently in a Phase III study with expected completion in November 2021. A biosimilar of Soliris is not expected until 2025.

References:

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7. Yamamura T, Kleiter I, Fujihara K, et al. Trial of satralizumab in neuromyelitis optica spectrum disorder. *N Engl J Med*. 2019;381(22):2114-2124. doi: 10.1056/NEJMoa1901747
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