January 12, 2021

Members of the Silver State Scripts Board:

Please see the enclosed summary of clinical information for Ajovy® (fremanezumab-vfrm), submitted as part of my request to provide public testimony during the January 21, 2021 Silver State Scripts Board Pharmacy and Therapeutics Committee.

Ajovy®(fremanezumab-vfrm) is indicated for the preventive treatment of migraine in adult patients.

Fremanezumab is a fully humanized monoclonal antibody that binds the CGRP ligand and blocks it from binding to the CGRP receptor. [1]

Ajovy® may be administered by healthcare professionals, patients, and/or caregivers, subcutaneously as once monthly (225mg) or quarterly (675mg) dosing, given as three 225mg injections. The Ajovy® autoinjector became available on 4/27/2020. Ajovy® is the only long-acting self-administered subcutaneous anti-CGRP with the option of monthly or quarterly dosing, allowing it to be dosed as few as four times per year either with the autoinjector or the pre-filled syringe.[2]

The FOCUS study examined a subset of 838 adult episodic and chronic migraine patients who previously experienced inadequate response to 2-4 classes of preventive medications. In the FOCUS study primary endpoint analysis, patients treated with fremanezumab experienced a statistically significant reduction in the monthly average number of migraine days for both monthly (-4.1 days, $p<0.0001$) and quarterly (-3.7 days, $p<0.0001$) dosing regimens versus placebo (-0.6 days) over the 12-week assessment period.[3]

Efficacy was sustained in open label period through 6 months of treatment, with 4.7-5.5 monthly average migraine day reductions from baseline. The most common adverse events were injection-site reactions, such as injection-site erythema (6%), and there were low rates of adverse events leading to discontinuation (<1%) and serious adverse events (1%).[4]

Across 24 clinical studies in the Ajovy clinical development program, 4077 patients with migraine have been exposed to Ajovy; no additional safety signals were seen across the exposed population.[6] In Phase IIb and III pooled data (N=2563), adverse events were reported for 48–69% of patients in all treatment groups, most of which were mild to moderate in severity. Serious adverse events, and adverse events leading to discontinuation were infrequent and had similar incidences across all groups.[6]

Pooled data from three phase 3 trials indicate that treatment with Ajovy over 12 weeks has a cardiovascular safety profile similar to placebo (<1%). During the post-marketing period, hypertension has not been identified as a safety signal.[6] 1.08% of Phase III clinical trial participants (HALO, HALO LTE and FOCUS) reported constipation (24/2209).[6]

1. FDA. Clinical Statistical Review, Bethesda, MD: 2018.Fremanezumab-VFRM. Available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed 4/24/2019.
2. Teva Announces U.S. Launch of Autoinjector for Ajovy® (fremanezumab-vfrm) Injection.Tevapharm.com. April 2020.
3. Ferrari MD, et al. *Lancet.* 2019;394(10203):1030-1040.
4. Ashina M, et al. Neurology. Efficacy and Safety of Fremanezumab in Patients With Episodic and Chronic Migraine and Documented Inadequate Response to 2-4 Classes of Migraine Preventive Medications During the Open-label Period of the Phase 3b FOCUS Study 2020; 94(15 Supplement)4379.
5. Teva data on file.
6. Silberstein S, et al. Fremanezumab for the preventive treatment of Migraine Expert Opin Biol Ther. 2019 Aug;19(8):763-771.

Thank you for your time and consideration. Please let me know if you would like a copy of the referenced publications.

Best Regards,

Jennifer Shear

Jennifer Shear, PharmD
Medical Outcomes Liaison, Field Medical Affairs

Cell: 224-325-2628

Jennifer.Shear@tevapharm.com www.tevapharm.com