



Dear Members of the Silver State Scripts Board:

Please see below summary of clinical information for Ajovy® (fremanezumab-vfrm), submitted as part of my request to provide public testimony during the Sept 23<sup>th</sup>, 2021 Silver State Scripts Board meeting.

Ajovy®(fremanezumab-vfrm) is indicated for the preventive treatment of migraine in adult patients. <sup>1</sup>

Fremanezumab is a fully humanized monoclonal antibody that binds the CGRP ligand and blocks it from binding to the CGRP receptor. <sup>2</sup> Fremanezumab is contraindicated in patients with serious hypersensitivity to fremanezumab or to any of the excipients. Reactions have included anaphylaxis and angioedema.<sup>1</sup>

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 quarterly is now available in a triple-pack. 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.<sup>3</sup> Ajovy quarterly is now available in a triple-pack.

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.<sup>4</sup> 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.<sup>5</sup>

Pooled data from three phase 3 trials indicate that treatment with AJOVY over 12 weeks has a cardiovascular safety profile similar to placebo (<2%). In patients with a cardiovascular medical history and with cardiovascular risk factors, no safety signals were detected.<sup>6</sup> In a long-term, open label, and blinded (as to dose) extension study, hypertension occurred in 2% (42/1888) of AJOVY treated patients. There was no worsening of hypertension over 12 months in patients with history or baseline hypertension.<sup>7</sup> During the post-marketing period, hypertension has not been identified as a safety signal.<sup>4</sup> 1.08% of Phase III clinical trial participants (HALO, HALO LTE and FOCUS) reported constipation (24/2209).<sup>4</sup>

Evaluating real-world experience with AJOVY, comparing before and after AJOVY initiation the following statistically significant changes in were observed:

- In an analyses of pharmacy claims, the total annual claims for acute medications, specifically opioids and triptans, as well as the proportions of patients filing claims for these medications decreased.<sup>8</sup>
- In an analysis of linked EMR and claims records, migraine pain intensity decreased significantly, and the majority of patients reported improvements in headache frequency/symptoms.<sup>9</sup>
- Adherence was significantly higher for patients receiving quarterly (84% MPR) versus monthly (79% MPR) AJOVY for 6 months. Most patients who discontinued AJOVY, permanently discontinued all preventive migraine therapy.<sup>10</sup>

Real-world pre/post retrospective studies referenced in the above three bullets suggest associations and not causality. Changes in the outcome of interest

1. AJOVY™ [current prescribing Information] North Wales, PA: Teva Pharmaceuticals USA Inc, 2021.
2. 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.
3. Teva Announces U.S. Launch of Autoinjector for Ajovy® (fremanezumab-vfrm) Injection.Tevapharm.com. April 2020.
4. Teva Data on File
5. Silberstein S, et al. Headache. 2019;59:880-890.
6. Nahas SJ, et al. Neurology Apr 2021, 96 (15 Supplement) 2382.
7. Goadsby PJ, et al. Neurology. 2020;Nov;95(18) e2487-e2499.
8. Seminerio M, Thompson SF, Cohen JM, et al. Neurology.2021;96(15 suppl):4192.
9. Mauskop A, Lamerato L, Casciano J, et al. Presented at Academy of Managed Care Pharmacy (AMCP) Nexus 2021 Virtual; April 13-16, 2021.
10. Tangirala K, Cohen JM, Pandya S, Krasenbaum LJ, Thompson SF, Chen C-C. Neurology. 96(15 suppl):2145.

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

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