Public Testimony for WV Medicaid-AJOVY® (fremanezumab-vfrm) Injection

Introduction & Purpose	Good day, my name is Fawad Malik and I am a Sr. Medical Outcomes Liaison at Teva Pharmaceuticals. I'm here to provide information about AJOVY®(fremanezumab-vfrm) injection. It is my understanding that you have already reviewed the full prescribing information for AJOVY, so this presentation will also provide additional information that you may not have already reviewed.
Disease Burden of Illness	A top cause of disability in the US, migraine is a complex and widespread neurological disease[1] impacting nearly 1 in 4 US households and most commonly affecting individuals during their most productive years (25-55 yrs. of age).[2] Females of low income classes are at a higher risk of suffering migraine attacks and using emergency services for acute episodes.[3] In the US, 1 out 4 of persons with chronic migraine uses acute medication daily[4] and 15% of all persons with migraine meet the criteria for medication overuse.[5] During the Covid-19 pandemic, healthcare providers request lifting the prior authorization for evidence-based, FDA-approved therapies; patients need to be able to access these medications quickly and easily.[6]
Please refer to the full prescribing information for AJOVY.	
Indication	AJOVY®(fremanezumab-vfrm) is indicated for the preventive treatment of migraine in adult patients.
MOA and Structure	Fremanezumab is a fully humanized IgG2Δa monoclonal antibody that binds the CGRP ligand and blocks it from binding to the CGRP receptor, preventing the activation of the trigeminal vascular system. Two point mutations were introduced into the antibody to increase binding affinity and limit antibody effector function, preventing stimulation of antibody-dependent cell-mediated toxicity (ADCC) and complement dependent cytotoxicity (CDC).[7]
Contraindications Warnings and Precautions	AJOVY is contraindicated in patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients. Hypersensitivity reactions, including rash, pruritus, drug hypersensitivity, and urticaria were reported with AJOVY in clinical trials. Most reactions were mild to moderate, but some led to discontinuation or required corticosteroid treatment. Most reactions were reported from within hours to one month after administration. If a hypersensitivity reaction occurs, consider discontinuing AJOVY and institute appropriate therapy.
Common Adverse Reactions	The most common adverse reactions (≥5% and greater than placebo) were injection site reactions.
Dosing and Administration	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. AJOVY is also available as both an Autoinjector and pre-filled syringe injection. 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.[8]
Clinical trial experience	The HALO clinical trial program included two multicenter, randomized, 12-week, double-blind, placebo-controlled studies and provided the pivotal data presented in the prescribing information.[9,10] Since market approval of AJOVY, data from two additional studies have been made available: FOCUS, a Phase IIIb randomized, 12 week, double-blind, placebo-controlled study in patients who previously had inadequate response to 2-4 classes of preventive therapies, and a long-term extension study.
HALO Pivotal Trials	• Patients treated with AJOVY achieved statistically significant reductions in monthly migraine days (EM) and headache days of at least moderate severity (CM) after accounting for placebo effect (EM: 1.3±0.6 quarterly and 1.5±0.6 monthly; CM 1.8±0.3 quarterly; 2.1±0.3 monthly).[9,10] Efficacy was maintained in subjects on stable doses of *concomitant preventive medication.*[11] • In a secondary endpoint analysis, patients in the EM trial experienced a reduction in their Migraine Disability Assessment Questionnaire (MIDAS) score of 24.6 in monthly (*p*<0.0001*)*, 23.0 in quarterly (p<0.01*)* versus 17.5 in placebo, as compared to baseline.[9] In the CM trial, patients experienced a reduction in their Headache Impact Test (HIT-6) score of 6.8 in monthly (*p<0.0001)*, 6.4 in quarterly (*p*<0.001) versus 4.5 in placebo, as compared to baseline.[10] • In exploratory analysis of pivotal trial data, 1 in 4 patients with episodic migraine taking AJOVY experienced a 75% reduction in monthly average migraine days compared to approximately 1 in 7 patients taking placebo. One in five patients with chronic migraine taking AJOVY experienced a 75% reduction in average headache days compared to approximately 1 in 10 patients taking placebo.[12] • In post hoc analysis of chronic migraine patients participating in HALO trials, separation was observed as early as week 1 between treatment and placebo groups in frequency of headaches of moderate severity.[13] These findings were consistent with observed early effects of AJOVY in the high frequency episodic patient population of the Phase II trial.[14] • Reductions in overuse of acute headache medication were also observed in the post hoc analysis of chronic migraine patients taking AJOVY.[15] In the open label-extension study period, reversion out of medication overuse endured through month 12 in roughly 60% of patients with acute medication overuse at baseline.[16]
FOCUS Study	• 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. Patients were not taking any migraine preventive medications at screening. Chronic migraine and episodic migraine patients were randomized in blinded-fashion 1:1:1 into one of three treatment groups– a quarterly dosing regimen, a monthly dosing regimen or matching placebo.[17] • In the FOCUS study primary endpoint analysis, patients treated with AJOVY 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.[17] • Adverse events with greater than 5% incidence in any group were injection-site erythema: 6% all AJOVY, 5% placebo; Injection-site induration: 4% all AJOVY, 4% placebo; and nasopharyngitis: 4% all AJOVY and 4% placebo. Serious adverse events were rare and did not differ between treatment and placebo groups (1%).[17] • 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%).[18]
Immunogenicity	• Six out of 1,701 (0.4%) AJOVY-treated patients developed low titer, treatment-emergent anti-drug antibody response, in a pooled analysis of Phase II and III immunogenicity data. Of the 6 patients 1 developed anti-AJOVY neutralizing antibodies at Day 84.[7] None of the 6 ADA-positive patients had significant safety consequences of ADA development.[19]
Long-term Safety	• 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.[12] 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.[20] • Pooled data from three phase 3 trials indicate that treatment with AJOVY over 12 weeks has a cardiovascular safety profile similar to

	placebo (<1%). In patients with a cardiovascular medical history and with cardiovascular risk factors, no safety signals were detected. 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.[21] During the post-marketing period, hypertension has not been identified as a safety signal.[12] • 1.08% of Phase III clinical trial participants (HALO, HALO LTE and FOCUS) reported constipation (24/2209).[12]
On-going clinical development	The safety and efficacy of fremanezumab is currently being investigated in fibromyalgia in a phase II randomized controlled trial.[22]
Label Updates	Revised: 1/2020 (Dosage Forms and Strengths: Injection: 225 mg/1.5 mL solution in a single-dose prefilled autoinjector.)[23]

CM= chronic migraine; EM=episodic migraine

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