PDL DRUG REVIEW

Proprietary Name: Ajovy®
Common Name: fremanezumab-vfrm
PDL Category: CGRP Inhibitors

Comparable Products	Preferred Drug List Status
Propranolol	Preferred
Topiramate	Preferred

Summary

Pharmacology/Usage: Fremanezumab-vfrm, the active ingredient of Ajovy®, is a humanized IgG2Δ a/kappa monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand that is produced by recombinant DNA. It binds to CGRP ligand and blocks its binding to the receptor.

Indication: For the preventive treatment of migraine in adults.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no adequate data on the developmental risk associated with the use in pregnant women. Ajovy® has a long half-like and this should be taken into consideration for women who are pregnant or plan to become pregnant while using Ajovy®. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Solution in a single-dose prefilled syringe: 225mg/1.5ml. Refrigerate

Recommended Dosage: For subcutaneous use only to be injected into the areas of the abdomen, thigh, or upper arm by healthcare professionals, patients, and /or caregivers. Remove from the refrigerator and allow to sit at room temperature for 30 minutes prior to use, but do not use if Ajovy® has been at room temperature for 24 hours or longer.

There are 2 dosing options available for Ajovy®, including 225mg SC monthly OR 675mg every 3 months (quarterly), which is given as 3 consecutive SC injections of 225mg each. When switching dosage options, administer the first dose of the new regimen on the next scheduled date of administration. No studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of Ajovy®.

Drug Interactions: There were no reported drug interactions with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Ajovy 225mg® monthly/675mg quarterly) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or that the active drug was less than placebo.* The most frequently reported adverse events included injection site reaction (5%/7%). Injection site reactions include multiple related adverse event terms, such as injection site pain, induration, and erythema. In addition, hypersensitivity reactions, including rash, pruritus, drug hypersensitivity, and urticaria, were reported with Ajovy® in clinical trials. While most reactions were mild to moderate, some led to discontinuation of treatment or required corticosteroid treatment. Most reactions were reported within hours to one month after administration. If hypersensitivity occurs, consider discontinuing treatment.

Contraindications: In patients with serious hypersensitivity to the active ingredient or to any of the excipients.

Manufacturer: Teva Pharmaceuticals

Analysis: The safety and efficacy of Ajovy® were assessed in 2 multicenter, randomized, 3-month, double-blind, placebo-controlled studies. Study 1 included adults with a history of episodic migraine (patients with <15 headache days/month) who received Ajovy® 675mg quarterly, Ajovy® 225mg monthly, or placebo monthly over a 3-month treatment period. Patients were allowed to use acute headache treatments during the study, and a subset of patients (21%) was allowed to use one additional concomitant preventive medication. Adults in the study ranged in age from 18 to 70 years (N=875); however, patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism, were excluded. The mean migraine frequency at baseline was about 9 migraine days per month and was similar across treatment groups.

The primary endpoint was the mean change from baseline in monthly average number of migraine days during the 3-month treatment period. Secondary endpoints included the proportion achieving at least a 50% reduction in monthly average number of migraine days, the mean change from baseline in the monthly average number of days of use of any acute headache medication during the 3-month treatment period, and the mean change from baseline in the number of migraine days during the first month of the treatment period.

Results suggested that both monthly and quarterly dosing regimens of Ajovy® demonstrated statistically significant improvements for efficacy endpoints as compared with placebo over the 3-month treatment period. Results can be seen in the table below, which was adapted from the prescribing information.

	Ajovy® 225mg QM (N=287)	Ajovy® 675mg quarterly (N=288)	Placebo (N=290)
Monthly migraine days (MMD)			
Baseline migraine days	8.9	9.2	9.1
Change from baseline	-3.7	-3.4	-2.2
Difference from placebo	-1.5	-1.2	
p-value	<0.001	<0.001	
≥50% MDD Responders			
% Responders	47.7%	44.4%	27.9%
Difference from placebo	19.8%	16.5%	
p-value (NNT)	<0.001 (NNT 6)	<0.001 (NNT 7)	
Monthly acute migraine-specific medication days			
Change from baseline	-3.0	-2.9	-1.6
Difference from placebo	-1.4	-1.3	
p-value	<0.001	<0.001	

With the change from baseline in mean monthly migraine days by treatment, 10% of each Ajovy® group had no change or more migraine days per month as compared with 22% of the placebo group.

Study 2 included adults with a history of chronic migraine (patients with ≥15 headache days per month) who were randomized to Ajovy® 675mg starting dose followed by 225mg monthly, 675mg every 3 months (quarterly) or placebo monthly over a 3-month period. Subjects were allowed to use acute headache treatments throughout the study and a subset of patients (21%) was allowed to use one additional concomitant, preventive treatment. Adults in the study ranged in age from 18 to 70 years (N=1130); however, patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism, were excluded.

The primary endpoint was the mean change from baseline in the monthly average number of headache days of at least moderate severity during the 3-month treatment period. Results suggested that both monthly and quarterly dosing regimens of Ajovy® treatment demonstrated statistically significant improvements for key efficacy outcomes as compared with placebo. Results can be seen in the table below, which was adapted from the prescribing information.

	Ajovy® 225mg QM (N=375) **	Ajovy® 675mg quarterly (N=375)	Placebo (N=371)
Baseline headache days of any severity (used for chronic migraine diagnosis)	20.3	20.4	20.3
Baseline headache days of at least moderate severity (Primary endpoint)	12.8	13.2	13.3
Change from baseline in monthly average # of headache days of ≥moderate severity	-4.6	-4.3	-2.5
Difference from placebo	-2.1	-1.8	
p-value	<0.001	<0.001	
Change from baseline in monthly average # of migraine days in patients	-5.0	-4.9	-3.2
Change from baseline in monthly average # of headache days of ≥moderate severity 4W after 1st dose	-4.6	-4.6	-2.3
% with ≥50% reduction in monthly average # of headache days of ≥moderate severity	40.8%	37.6%	18.1%
Change from baseline in monthly average number of days of acute headache medication	-4.2	-3.7	-1.9

**Patients in this group in this study received a 675mg starting dose

With the mean change from baseline in monthly headache days of at least moderate severity, 15% of the 225mg monthly Ajovy® group had no change or more headache days of at least moderate severity per month as compared with 16% with Ajovy® 675mg quarterly and 26% with placebo.

Place in Therapy: Ajovy® is a subcutaneous injection to be used monthly or quarterly (every 3 months) for the preventive treatment of migraine in adults. In clinical trials compared with placebo, Ajovy® significantly reduced the monthly average number of migraine days, as well as improved response rates, as compared with placebo in adults with chronic or episodic migraines. Ajovy® is the second CGRP antagonist to be approved in 2018, with a prior FDA approval of Aimovig® that carries the same indication as Ajovy®. No comparator studies with Ajovy® and other treatments for the prevention of migraine were found.

There is no evidence at this time to support that Ajovy® is safer or more effective than the currently available, more cost-effective medications. It is therefore recommended that Ajovy® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Ajovy [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; 2018.

[2] Aimovig [package insert]. Thousand Oaks, CA: Amgen, Inc; 2018.