Drug Monograph

Drug/Drug Class:	**Ajovy™ (fremanezumab-vfrm) for Injection / Calcitonin Gene-Related Peptide Receptor Antagonist**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Ajovy™ is available as a single-dose prefilled syringe containing 225 mg fremanezumab per 1.5 ml. Distributed by: Teva Pharmaceuticals USA, Inc. North Wales, PA 19454.
Summary of Findings:	In a randomized, double-blind, two-part clinical trial (N=2005), Ajovy™ showed improved efficacy versus placebo at both episodic and chronic migraine endpoints. During the three-month trial the most common adverse reaction with Ajovy™ was injection site reactions. Patients should be monitored closely for hypersensitivity reactions while taking Ajovy™.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☒ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Non-Preferred Agent ☒ Appropriate Indications ☐ No PA Required

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [(2)]

Migraine is a neurological disease that affects as many as 1 in 4 U.S. households. This widespread disease ranks 6th in the world for most disabling illness. While migraine affects women more than men, 18% to 6% respectively, it is still labeled as the 3rd most prevalent disease in the world and is estimated to affect nearly 39 million people in the U.S. alone. A migraine attack is more than just a headache and can present with nausea, vomiting, visual impairments, sensitivity to light and sound to name a few. One treatment option for migraine sufferers is to prevent a migraine using medications prophylactically. There are several prophylactic treatment options available with the newest form being calcitonin gene-related peptide (CGRP) inhibitors. This class of medications act to block the vasodilating CGRP neuropeptide believed to be vital to migraine presentation. To date there are three monoclonal antibodies in this class all of which coming to market in 2018.

Dosage Form(s) [(1)]

Ajovy™ is available as a single-dose prefilled syringe containing 225 mg fremanezumab per 1.5 ml.

Manufacturer [(1)]

Distributed by: Teva Pharmaceuticals USA, Inc. North Wales, PA 19454.

Indication(s) [(1)]

Ajovy™ is indicated for the preventative treatment of migraine in adults.

Clinical Efficacy [(1)] (mechanism of action/pharmacology, comparative efficacy)

Ajovy™ is a humanized monoclonal antibody that binds to the calcitonin gene-related peptide (CGRP) and prevents its binding to the receptor. Ajovy™ is approved for the prevention of migraine in adult patients.

Pharmacokinetics:

	Ajovy™
Volume of Distribution	~6 L
Metabolism	Degraded by enzymatic proteolysis
Excretion	Clearance 0.141 L/day
Half-life	~31 Hours

Efficacy in Preventative Treatment of Episodic or Chronic Migraine

STUDY DESIGN	Two-part, double-blind, randomized, placebo-controlled clinical trial (N=2005).
INCLUSION CRITERIA	Adult patients with a history of episodic migraine as defined by <15 headache days per month or history of chronic migraine as defined by ≥15 headache days per month.
EXCLUSION CRITERIA	The study excluded patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events.
TREATMENT REGIMEN	Patients in part 1 of the study (episodic migraine) were randomized to receive Ajovy™ 675 mg every 3 months, 225 mg monthly or placebo monthly for 3 months. 875 patients were randomized with 791 completing the 3-month study. In the second part of the study (chronic migraine) patients were randomized to randomized to receive a 675 mg starter dose followed by 225 mg monthly, 675 mg every 3 months or placebo. 1130 patients were randomized with 1034 completing the 3-month study.
RESULTS	The two-part clinical trial showed statistically significant improvement for efficacy endpoints compared to placebo in both parts of the study. For part 1 of the study, endpoints were defined by monthly migraine days, ≥50% MDD responders and monthly acute migraine-specific medication days. Both dosages of Ajovy™ showed improvement over placebo in all three categories. In part 2 of the study, efficacy endpoints of change from baseline in monthly average number of headache days of at least moderate severity, change from baseline in monthly number of headache days of at least moderate severity at 4 weeks after 1st dose and change from baseline in monthly average number of days of acute headache medication were analyzed. Once again both dosages of Ajovy™ showed improvement versus placebo in all three efficacy endpoints.
SAFETY	The most common adverse reactions were injection site reactions. These included injections site pain, induration and erythema.

Contraindications (1)

- Ajovy™ is contraindicated in patients with a serious hypersensitivity to fremanezumab-vfrm or to any of the excipients.

Warnings and Precautions [1]

- Ajovy™ has a warning for hypersensitivity reactions. This includes rash, pruritus, drug hypersensitivity and urticaria. While most reactions were not serious, some led to therapy discontinuation and/or corticosteroid treatment. Reactions were reported anywhere between hours after injection and up to 1 month after administration.

Adverse Effects [1]

Most common, ≥ 2%	Ajovy™ 225 mg Monthly	Ajovy™ 625 mg Quarterly	Placebo
Injection Site Reaction	43%	45%	38%

Drug Interactions [1]

- Ajovy™ does not have any known direct drug interactions.

Dosage and Administration [1]

Ajovy™ has two different FDA recommended dosing options:

- 225 mg monthly
- 675 mg every 3 months administered as three consecutive 225 mg injections.

Dosage adjustments/changes should be done by administering the first dose of the new regimen on the next scheduled date of administration.

Cost

BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/DOSE*
Ajovy™	Teva	225 mg/1.5 mL	Monthly or Quarterly	$575
Aimovig™	Amgen	70 mg/mL	Monthly	$575
Emgality™	Eli Lilly	120 mg/mL	Monthly	$575

* Wholesale Acquisition Cost

Conclusion

Ajovy™ is a monoclonal antibody available in injection form that blocks CGRP for use in adults for the preventative treatment of migraine. In a two-part double-blind study (N=2005), Ajovy™ showed statistically significant improvement versus placebo in both episodic and chronic migraine endpoints. The most common adverse reaction during the study was injection site reactions. There are several medications used for the prevention of migraines and multiple factors should be addressed when selecting an appropriate regimen. While Ajovy™ was well tolerated in clinical

trials, the medication is very costly when compared to other medication options that have generic forms available. As with any injectable medication, proper training and ability should be confirmed before starting a patient on Ajovy™. Patients should be monitored for signs and symptoms of hypersensitivity reactions while using this medication.

Recommendation

The Division recommends adding this drug to the CGRP Antagonist clinical edit

References

1) Product Information: Ajovy™ (fremanezumab-vfrm), Teva Pharmaceuticals USA, Inc. North Wales, PA 09/2018.
2) Jazwinder, Chawla MD, Helmi, Lutsep MD et al. Migraine Headache Treatment & Management January 30,2018 Medscape.

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