

PRIOR AUTHORIZATION POLICY

POLICY: Calcitonin Gene-Related Peptide Inhibitors – Ajovy™ (fremanezumab-vfrm injection for subcutaneous use – Teva)

TAC APPROVAL DATE: 05/29/2019

OVERVIEW

Ajovy, a calcitonin gene-related peptide (CGRP) antagonist, is indicated for the preventive treatment of migraine in adults.¹ Ajovy is a human monoclonal antibody that binds to the CGRP ligand and blocks its binding to the receptor. The recommended dosage of Ajovy is 225 mg injected subcutaneously (SC) once monthly or 675 mg every 3 months (quarterly), which is administered as three consecutive SC injections of 225 mg each. A healthcare professional, patient, and/or caregiver may administer Ajovy.

Disease Overview

Migraine is a common, chronic condition marked by paroxysmal, unilateral attacks of moderate-to-severe throbbing headache which is aggravated by routine physical activity (e.g., walking or climbing stairs) and associated with nausea, vomiting, and/or photophobia and phonophobia.² Migraine headache episodes typically last 4 to 72 hours if untreated. Migraine affects approximately 15% of US adults.³ Migraines have been defined as chronic or episodic. Chronic migraine is described by the International Headache Society as headache occurring on ≥ 15 days/month for > 3 months and has the features of migraine headache on ≥ 8 days/month.² Episodic migraine is characterized by headaches that occur < 15 days/month.⁴ Patients with episodic migraine may transform to chronic migraine over time at a rate of about 2.5% of episodic-migraine patients/year. Potential strategies for preventing migraine transformation include preventing and treating headaches, lifestyle modifications, or effective management of comorbidities (e.g., obesity, obstructive sleep apnea, depression, anxiety). Episodic migraine is more common than chronic migraine; however, chronic migraine is associated with a markedly greater personal and societal burden.

Guidelines

An updated assessment of the **preventive and acute treatment of migraine** by the **American Headache Society** (2018) reaffirms previous migraine guidelines.⁵ Patients with migraine should be considered for preventive treatment when attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks (≥ 4 monthly headache days); contraindication to, failure, overuse, or adverse events with acute treatments; or patient preference. Before developing a preventive treatment plan, the appropriate use (e.g., drug type, route and timing of administration, frequency) of acute treatments should be initiated and coupled with education and lifestyle modifications. All patients with migraine should be offered a trial of acute treatment. Based on the level of evidence for efficacy and the American Academy of Neurology (AAN) scheme for classification of evidence, the following oral treatments have established efficacy and should be offered for migraine prevention: antiepileptic drugs (divalproex sodium, valproate sodium, topiramate [not for women of childbearing potential without a reliable method of birth control]); beta-blockers (metoprolol, propranolol, timolol); and frovatriptan (for short-term preventive treatment of menstrual migraine).⁶ The following treatments are probably effective and should be considered for migraine prevention: antidepressants (amitriptyline, venlafaxine); beta-blockers (atenolol, nadolol); and angiotensin receptor blockers (candesartan).

Four injectable preventive therapies for migraine are mentioned in the AHS consensus statement: Botox[®] (onabotulinumtoxinA injection) and three monoclonal antibodies targeting CGRP (Aimovig, Ajovy[®] [fremanezumab-vfrm injection], and Emgality[®] [galcanezumab-gnlm injection]).⁵ The update notes that a CGRP inhibitor should only be initiated in patients who are diagnosed with migraine, have ≥ 4 migraine headache days per month, and have intolerance or inadequate response to 6-week trials of at least two traditional oral migraine preventive medications. Additional criteria apply depending on the number and severity of monthly headache days. Clinical judgment may result in an emerging treatment being added to one or more established treatments. If initiating treatment with a CGRP inhibitor in a patient already on a preventive treatment, it is appropriate to add the CGRP inhibitor to the existing regimen and make no other changes until the effectiveness of the CGRP inhibitor is determined since the risk of interactions between traditional oral migraine preventive medications and the CGRP inhibitors is minimal or nonexistent. Making a decision regarding continuation of therapy for a CGRP inhibitor requires a trial of the medication for at least 3 months, and treatment should be continued only if benefits can be documented during that time (e.g., reduction in mean monthly headache days of $\geq 50\%$ relative to the pretreatment baseline). Since migraine may improve or remit over time, it is important to reevaluate therapeutic response and, if possible, taper or discontinue treatment if patients no longer meet the criteria for offering preventive treatment. However, once control is established, the decision to discontinue or taper treatment should be a shared decision between patient and clinician.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Ajovy. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ajovy is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Migraine Headache Prevention.** Approve Ajovy for 1 year if the patient meets the following criteria (A, B, C, and D):
 - A)** Patient is ≥ 18 years of age; AND
 - B)** Patient has ≥ 4 migraine headache days per month (prior to initiating a migraine-preventative medication); AND
 - C)** Patient has tried at least two standard prophylactic pharmacologic therapies, each from a different pharmacologic class (e.g., angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, β -blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant), and meets ONE of the following criteria (i, ii, or iii):
 - i.** The patient has had inadequate efficacy to both of those standard prophylactic pharmacologic therapies, according to the prescribing physician; OR
 - ii.** The patient has experienced adverse event(s) severe enough to warrant discontinuation of both of those standard prophylactic pharmacologic therapies, according to the prescribing physician; OR
 - iii.** The patient has had inadequate efficacy to one standard prophylactic pharmacologic therapy and has experienced adverse event(s) severe enough to warrant discontinuation to
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another standard prophylactic pharmacologic therapy, according to the prescribing physician; AND

D) Patient meets ONE of the following (i or ii):

- i. Patient has tried at least one triptan therapy; OR
- ii. Patient has a contraindication to triptan(s) according to the prescribing physician.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ajoyv has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Acute Treatment of Migraine.** Ajoyv has not been studied for the acute treatment of migraine.
2. **Cluster Headache.** Ajoyv has not been found to be effective in in patients with chronic or episodic cluster headache.⁷
3. **Combination Therapy with Aimovig™ (erenumab-aooe injection for subcutaneous use) or Emgality™ (galcanezumab-gnlm injection for subcutaneous use).** Ajoyv, Aimovig, and Emgality are calcitonin gene-related peptide (CGRP) antagonists and have not been studied for use in combination with another agent in the same class.^{8,9}
4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Ajoyv™ injection for subcutaneous use [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2018.
2. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition (beta version). *Cephalalgia*. 2013;33:629-808.
3. MacGregor EA. In the clinic. Migraine. *Ann Intern Med*. 2017;166(7):ITC49-ITC64.
4. Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. *Headache*. 2015;52:103-122.
5. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
6. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78(17):1337-1345.
7. Teva announces update on fremanezumab clinical development for use in episodic cluster headache [press release]. North Wales, PA: Teva Pharmaceuticals USA; April 23, 2019. Available at: https://www.tevapharm.com/news/teva_announces_update_on_fremanezumab_clinical_development_for_use_in_episodic_cluster_headache_04_19.aspx. Accessed on May 22, 2019.
8. Aimovig™ injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2019.
9. Emgality™ injection for subcutaneous use [prescribing information]. Indianapolis, IN: Eli Lilly and Company; September 2018.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	09/19/2018

Calcitonin Gene-Related Peptide Inhibitors – Ajoy PA Policy

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Selected revision	Changed the document name to Calcitonin Gene-Related Peptide (CGRP) Inhibitors – Ajoy PA to take into account the different mechanisms of action of the CGRP inhibitors. Added Emgality to the Condition Not Recommended for Approval for combination therapy with Aimovig.	10/03/2018
Annual revision	No change to criteria.	05/29/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; TAC – Therapeutic Assessment Committee.
