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Coverage Policy Number **IP0504**

Fremanezumab

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for fremanezumab-vfrm subcutaneous injection (**Ajovy®**).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Fremanezumab-vfrm (Ajovy) is considered medically necessary when the following is met:

Migraine Headache Prevention. Individual meets **ALL** of the following criteria:
- A. Age 18 years or older
- B. 4 or more migraine headache days per month (prior to initiating Ajovy)
- C. Documentation of **ONE** of the following (i, ii, or iii):
  - i. Inadequate response following a minimum 8 week trial of **TWO** migraine prevention therapies from different classes of medications including the following:
    - a. Angiotensin receptor blockers or angiotensin converting enzyme inhibitors

b. Antidepressants
c. Antiepileptic drugs
d. Beta-blockers

ii. Contraindication or intolerance to **ALL** of the following: angiotensin receptor blockers/angiotensin converting enzyme inhibitors, antidepressants, antiepileptic drugs, and beta-blockers

iii. Inadequate response, contraindication, or intolerance to a minimum 6 month trial of onabotulinumtoxinA (Botox) for chronic migraine prevention [requires prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Fremanezumab-vfrm (Ajovy) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response (for example, reduction in monthly migraine days or hours or reduction in days requiring acute migraine-specific treatment from the time that Ajovy was started)

Authorization Duration

Migraine Headache Prevention (at a dose of either 225 mg monthly OR 675 mg every 3 months):
Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Acute Treatment of Migraine.** Ajovy has not been studied for the acute treatment of migraine.

2. **Cluster Headache, Treatment or Prevention.** Ajovy has not been found to be effective in a Phase III clinical trial in patients with chronic cluster headache.[7] A trial of Ajovy in episodic cluster headache is on-going.

3. **Concurrent use with another calcitonin gene-related peptide (CGRP) inhibitor being prescribed for migraine headache prevention.** CGRP inhibitors that are indicated for migraine headache prevention include Aimovig (erenumab-aooe subcutaneous injection), Emgality (galcanezumab-gnlm subcutaneous injection), Vyepti (eptinezumab-jjmr intravenous infusion), and Qulipta (atogepant tablets). Ajovy, Aimovig, Emgality, and Vyepti are injectable CGRP inhibitors for migraine prevention and have not been studied for use in combination with another agent in the same class.[8-10] Qulipta is an oral CGRP inhibitor for the preventive treatment of migraine in adults.[11]

4. **Concurrent use with Nurtec® ODT (rimegepant sulfate orally disintegrating tablet) when used as a preventive treatment of migraine.** Nurtec ODT is an oral CGRP inhibitor for the acute treatment of migraine and for the preventive treatment of episodic migraine in adults.[12]

Background

OVERVIEW
Ajovy, a calcitonin gene-related peptide (CGRP) antagonist, is indicated for the **preventive treatment of migraine** in adults.[1]

Disease Overview
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.[3,4] 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** (AHS) [2018; update 2021] reaffirms previous migraine guidelines.[5,6] Patients with migraine should be considered for preventive treatment in the following situations: 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 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). 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**). Additionally, the following treatments are possibly effective and can be considered for migraine prevention: calcium channel blockers (e.g., **verapamil**) and angiotensin converting enzyme inhibitors (e.g., **lisinopril**).[13,14]

Five injectable preventive therapies for migraine are mentioned in the AHS consensus statement: Botox® (onabotulinumtoxinA subcutaneous injection) and four monoclonal antibodies targeting CGRP (Aimovig® [erenumab-aooe subcutaneous injection], Ajovy, Emgality® [galcanezumab-gnlm subcutaneous injection], and Vyepti® [eptinezumab-jjmr intravenous infusion]).[5,6] The update notes that a CGRP inhibitor should only be initiated in patients who are diagnosed with migraine, have ≥ 4 migraine headache days/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 ≥ 3 months for those administered monthly and ≥ 6 months for those administered quarterly. Treatment should be continued only if benefits can be documented during that time (e.g., reduction in mean monthly headache days of ≥ 50% relative to the pretreatment baseline) or a meaningful improvement on a validated migraine-specific patient-reported outcome measure. Since migraine may improve or remit over time, it is important to re-evaluate the therapeutic response and, if possible, taper or discontinue treatment if patient no longer meets the criteria for offering preventive treatment. However, once control is established, the decision to discontinue or taper treatment should be a shared decision between the patient and clinician.

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