



## PRIOR AUTHORIZATION POLICY

- POLICY:** Migraine – Calcitonin Gene-Related Peptide Inhibitors – Emgality Prior Authorization Policy
- Emgality® (galcanezumab-gnlm subcutaneous injection – Lilly)

**REVIEW DATE:** 05/24/2023; selected revision 08/02/2023

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## **CIGNA NATIONAL FORMULARY COVERAGE:**

### **OVERVIEW**

Emgality, a calcitonin gene-related peptide (CGRP) antagonist, is indicated in adults for the following uses:<sup>1</sup>

- **Episodic cluster headache treatment.**
- **Migraine headache prevention.**

### **Disease Overview**

Migraines have been defined as chronic or episodic. Chronic migraine is described by the International Headache Society as headache occurring on  $\geq 15$  days/month for  $> 3$  months and has the features of migraine headache on  $\geq 8$  days/month.<sup>2</sup> Episodic migraine is characterized by headaches that occur  $< 15$  days/month.<sup>4</sup> Episodic migraine is more common than chronic migraine; however, chronic migraine is associated with a markedly greater personal and societal burden.

Cluster headaches are associated with attacks of severe, strictly unilateral pain which is orbital, supraorbital, temporal, or in any combination of these sites, lasting 15 to 180 minutes.<sup>2</sup> The headaches occur from once every other day to eight times a day. Cluster headache is considered among the most severe of the primary headache disorders because of extreme pain, associated autonomic symptoms, and high attack frequency.<sup>5</sup> In addition, a large proportion of patients with cluster headache have

chronic cluster headache, which features only brief or no remission periods, and may be particularly refractory to medical therapies.

## 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.<sup>6,7</sup> 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 ( $\geq 4$  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**).<sup>13,14</sup>

Five injectable preventive therapies for migraine are mentioned in the AHS consensus statement: Botox<sup>®</sup> (onabotulinumtoxinA subcutaneous injection) and four monoclonal antibodies targeting CGRP (Aimovig<sup>®</sup> [erenumab-aooe subcutaneous injection], Ajovy<sup>®</sup> [fremanezumab-vfrm subcutaneous injection], Emgality, and Vyepti<sup>®</sup> [eptinezumab-jjmr intravenous infusion]).<sup>6,7</sup> The update notes that a CGRP inhibitor should only be initiated in patients who are diagnosed with migraine, have  $\geq 4$  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  $\geq 3$  months for those administered monthly and  $\geq 6$  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  $\geq 50\%$  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.

The **AHS** has published evidence-based guidelines on the **treatment of cluster headache** (2016).<sup>5</sup> The guidelines recommend sumatriptan subcutaneous, zolmitriptan nasal spray, and high flow oxygen for acute treatment. For prophylactic therapy, suboccipital steroid injection has been established as effective for the prophylactic therapy of episodic and chronic cluster headache (Level A). Lithium, verapamil, and melatonin are considered possibly effective for the prophylactic therapy of episodic and chronic cluster headache (Level C). Currently, there is insufficient evidence to make a recommendation for frovatriptan and prednisone (Level U).

## **POLICY STATEMENT**

Prior Authorization is recommended for prescription benefit coverage of Emgality. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

• **Emgality® (galcanezumab-gnlm subcutaneous injection – Lilly) is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):**

## **FDA-Approved Indications**

**1. Episodic Cluster Headache Treatment.** Approve for 6 months if the patient meets the following (A, B, C, and D):

A) Patient is  $\geq$  18 years of age; AND

B) Patient has between one headache every other day and eight headaches per day; AND

C) Patient has tried at least one standard prophylactic (preventive) pharmacologic therapy for cluster headache; AND

Note: Examples of standard prophylactic (preventive) pharmacologic therapies for cluster headache include lithium, verapamil, melatonin, frovatriptan, prednisone, suboccipital steroid injection, topiramate, and valproate.

D) Patient has had inadequate efficacy or has experienced adverse event(s) severe enough to warrant discontinuation of the standard prophylactic (preventive) pharmacologic therapy, according to the prescriber.

**2. Migraine Headache Prevention.** Approve for 1 year if the patient meets the following (A, B, C, D, and E):

- A) Patient is  $\geq$  18 years of age; AND
- B) Patient has  $\geq$  4 migraine headache days per month (prior to initiating a migraine-preventive medication); AND
- C) Patient has tried at least two standard prophylactic (preventive) pharmacologic therapies, each from a different pharmacologic class; AND  
Note: Standard prophylactic (preventive) pharmacologic therapies for migraine include angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, beta-blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant. A patient who has already tried an oral or injectable calcitonin gene-related peptide (CGRP) inhibitor indicated for the prevention of migraine or Botox (onabotulinumtoxinA injection) for the prevention of migraine is not required to try two standard prophylactic pharmacologic therapies.
- D) Patient meets ONE of the following (i, ii, or iii):
  - i. Patient has had inadequate efficacy to both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
  - ii. Patient has experienced adverse event(s) severe enough to warrant discontinuation of both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
  - iii. Patient meets BOTH of the following (a and b):
    - a) Patient has had inadequate efficacy to one standard prophylactic (preventive) pharmacologic therapy; AND
    - b) Patient has experienced adverse event(s) severe enough to warrant discontinuation to another standard prophylactic (preventive) pharmacologic therapy, according to the prescriber; AND
- E) If the patient is currently taking Emgality, the patient has had a significant clinical benefit from the medication, as determined by the prescriber.  
Note: Examples of significant clinical benefit include a reduction in the overall number of migraine days per month or a reduction in number of severe migraine days per month from the time that Emgality was initiated.

## CONDITIONS NOT COVERED

• **Emgality® (galcanezumab-gnlm subcutaneous injection – Lilly) is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

- 1. Acute Treatment of Migraine.** Emgality has not been studied for the acute treatment of migraine.
- 2. Concurrent use with another calcitonin gene-related peptide (CGRP) inhibitor being prescribed for migraine headache prevention.**

Note: CGRP inhibitors that are indicated for migraine headache prevention include Aimovig (erenumab-aooe subcutaneous injection), Ajovy (fremanezumab-vfrm 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.<sup>8-10</sup> Qulipta is an oral CGRP inhibitor for the preventive treatment of migraine in adults.<sup>11</sup>

**3. 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.<sup>12</sup>

**REFERENCES**

1. Emgality® injection for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly; May 2022.
2. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition. *Cephalalgia*. 2018;38:1-211.
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. Robbins MS, Starling AJ, Pringsheim TM, et al. Treatment of cluster headache: the American Headache Society evidence-based guidelines. *Headache*. 2016;56:1093-1106.
6. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
7. Ailani J, Burch RC, Robbins MS, on behalf of the Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021;00:1-19.
8. Aimovig® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; October 2022.
9. Ajovy® subcutaneous injection [prescribing information]. North Wales, PA: Teva; September 2021.
10. Vyepti® intravenous infusion [prescribing information]. Bothell, WA: Lundbeck; October 2022.
11. Qulipta® tablets [prescribing information]. Madison, NJ: AbbVie; April 2023.
12. Nurtec® ODT [prescribing information]. New Haven, CT: Biohaven; April 2022.
13. Micromedex. Merative LP. Available at: <https://www.micromedexsolutions.com/>. Accessed on August 7, 2023. Search terms: lisinopril, verapamil.
14. Clinical Pharmacology. ClinicalKey. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed on August 7, 2023. Search terms: lisinopril, verapamil.

**HISTORY**

Type of Revision	Summary of Changes	Review Date
Annual Revision	<p><b>Migraine Headache Prevention:</b></p> <ul style="list-style-type: none"> <li>• The criterion requiring a trial of at least one triptan was removed.</li> <li>• The criterion for "Patient is NOT taking a calcitonin gene-related peptide (CGRP) inhibitor for migraine headache prevention" and "Patient is switching from a different CGRP inhibitor for migraine headache prevention to Emgality" were removed.</li> <li>• The criterion "Patient is currently taking Emgality and has had a significant clinical benefit from the medication as determined by the prescriber" was changed to "If the patient is currently taking Emgality, the patient has had a significant clinical benefit from the medication as determined by the prescriber".</li> </ul> <p><b>Conditions Not Covered:</b></p>	05/18/2022

	<ul style="list-style-type: none"> <li>• To add clarity, preventive treatment of migraine with Nurtec ODT was moved into its own criterion that cannot be used concurrently with Emgality.</li> <li>• The criterion for combination use with Aimovig, Ajovy, Emgality, and Vyepiti was changed to read "Concurrent use with another CGRP inhibitor indicated for migraine headache prevention".</li> <li>• Qulipta was added to the Note listing CGRP inhibitors that are indicated for migraine headache prevention.</li> </ul>	
Annual Revision	<p><b>Policy Name:</b> The initial descriptor "Migraine" was added to the policy name.</p> <p><b>Migraine Headache Prevention:</b> The note with examples of standard prophylactic (preventive) pharmacologic therapies was expanded to include the statement: Of note, "standard prophylactic (preventive) pharmacologic therapies" do <b>not</b> include oral or injectable CGRP inhibitors.</p>	05/24/2023
Selected Revision	<p><b>Migraine Headache Prevention:</b></p> <ul style="list-style-type: none"> <li>• The note with standard prophylactic (preventive) pharmacologic therapies was changed to remove "Examples of" and to remove the statement: Of note, "standard prophylactic (preventive) pharmacologic therapies" do <b>not</b> include oral or injectable CGRP inhibitors.</li> <li>• A new statement was added: A patient who has already tried an oral or injectable calcitonin gene-related peptide (CGRP) inhibitor indicated for the prevention of migraine or Botox (onabotulinumtoxinA injection) for the prevention of migraine is not required to try two standard prophylactic pharmacologic therapies.</li> </ul>	08/02/2023

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