Effective Date **11/1/2023**
Next Review Date… **11/1/2024**
Coverage Policy Number **IP0505**

Galcanezumab

Table of Contents

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 galcanezumab-gnlm subcutaneous injection (**Emgality®**).

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

Medical Necessity Criteria

Galcanezumab-gnlm (Emgality) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Episodic Cluster Headache Treatment.** Individual meets **ALL** of the following criteria:
    A. Age 18 years or older
    B. Has between one headache every other day and eight headaches per day
    C. Documentation of **ONE** of the following (i or ii):
        i. Inadequate response to **ONE** of the following (a or b)
            a. sumatriptan injectable

b. zolmitriptan nasal spray [may require prior authorization]

ii. Contraindication or intolerance to sumatriptan injectable and zolmitriptan nasal spray

2. **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 Emgality)
   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

Galcanezumab-gnlm (Emgality) 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 Emgality was started).

Authorization Duration

Episodic Cluster Headache Treatment (at a dose of 300 mg [3 consecutive subcutaneous injections of 100 mg each] at the onset of the cluster period, and then monthly until the end of the cluster period)
Initial approval duration: up to 3 months
Reauthorization approval duration: up to 6 months

Migraine Headache Prevention (loading dose of 240 mg [month 1], followed by monthly doses of 120 mg)
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.** 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.** 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.[8-10] Qulipta is an oral CGRP inhibitor for the preventive treatment of migraine in adults.[11]

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.[12]

Background

OVERVIEW
Emgality, a calcitonin gene-related peptide (CGRP) antagonist, is indicated in adults for the following uses:[1]

- **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 ≥ 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] 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.[2] 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.[5] 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.[6,7] 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® [fremanezumab-vfrm subcutaneous injection], Emgality, and Vyepti® [eptinezumab-jjmr intravenous infusion]).[6,7] 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.

The **AHS** has published evidence-based guidelines on the **treatment of cluster headache** (2016).[5] 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).

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.