VENTURA COUNTY
HEALTH CARE PLAN

CARE VALUE POLICY

POLICY: Calcitonin Gene-Related Peptide Inhibitors – Emgality™ (galcanezumab-gnlm injection for subcutaneous use – Lilly) Care Value Policy

TAC APPROVAL DATE: 03/20/2019; selected revision 07/03/2019 and 10/23/2019

OVERVIEW

Emgality, a calcitonin gene-related peptide (CGRP) antagonist, is indicated for the preventive treatment of migraine in adults and for the treatment of episodic cluster headache in adults.[1] Emgality is a human monoclonal antibody that binds to the CGRP ligand and blocks its binding to the receptor. The recommended dosage of Emgality for the prevention of migraine is 240 mg (two consecutive subcutaneous [SC] injections of 120 mg each) once as a loading dose, followed by monthly doses of 120 mg injected subcutaneously. For cluster headache, Emgality is dosed as 300 mg SC (administered as three consecutive injections of 100 mg each) at the onset of the cluster period, and then monthly until the end of the cluster period. Emgality is intended for patient self-administration.

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 13% 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.

Cluster headache is the most common of the group of headache disorders known as the trigeminal autonomic cephalalgias, with a lifetime prevalence exceeding 1 in 1,000.[5] 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. Patients with cluster headache are often suboptimally treated, even though treatment of cluster headache in accordance with guidelines is associated with better outcomes.

Guidelines

An updated assessment of the **preventive and acute treatment of migraine** by the **American Headache Society** (2018) reaffirms previous migraine guidelines.[6] 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).[7] 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]).[6] 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 ≥ 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.

The **American Headache Society** 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).

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Episodic Cluster Headache Treatment.** Approve Emgality for 6 months if the patient meets the following criteria (A, B, C, and D):
   - **A)** Patient is ≥ 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 pharmacologic therapy for cluster headache; AND
     Note: Examples of standard prophylactic 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 pharmacologic therapy, according to the prescriber.

2. **Migraine Headache Prevention.** Approve Emgality for 1 year if the patient meets the following criteria (A, B, C, D and E):
   - **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; AND
     Note: Examples of standard prophylactic pharmacologic therapies for migraine include angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, β-blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant.
   - **D)** Patient 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 prescriber; 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 prescriber; 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 another standard prophylactic pharmacologic therapy, according to the prescriber; AND
   - **E)** 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 prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Emgality 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.** Emgality has not been studied for the acute treatment of migraine.

2. **Combination Therapy with Aimovig™ (erenumab-aooe injection for subcutaneous use) or with Ajovy™ (fremanezumab-vfrm injection for subcutaneous use).** Ajovy, 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.

3. 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. Emgality™ injection for subcutaneous use [prescribing information]. Indianapolis, IN: Eli Lilly and Company; June 2019.
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 Int Med*. 2013;159:!TC5-1-ITC5-16.
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. 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.
8. Aimovig® injection [prescribing information]. Thousand Oaks, CA: Amgen; March 2019.
9. Ajovy® injection for subcutaneous use [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2018.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New policy	--	3/20/2019
Selected revision	Addition of criteria for episodic cluster headache treatment.	07/03/2019
Selected revision	For the FDA-approved indication of Episodic Cluster Headache Treatment, approval criteria was changed from requiring a trial of at least two standard prophylactic pharmacologic therapies to requiring a trial of at least one standard prophylactic pharmacologic therapy. The prescriber still needs to attest to the patient having had inadequate efficacy or having experienced adverse event(s) severe enough to warrant discontinuation of the standard prophylactic pharmacologic therapy.	10/23/2019

* 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.