Preventive Migraine Products:
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist

WA.PHAR.64 Effective Date: March 1, 2021

Related medical policies:

- **WA.PHAR.106- Acute Migraine Treatment: CGRP Receptor Antagonist**

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit:
https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf

Background:

Migraine is a disabling chronic health condition, accounting for significant decreased quality of life and reduced productivity. Although the entire pathophysiology of migraines remains uncertain, calcitonin gene-related peptide (CGRP) is known to increase significantly during a migraine episode and decrease upon recovery. Additionally, CGRP infusion may trigger migraine attacks in migraineurs, and is thought to mediate trigeminovascular pain from intracranial vessels to the central nervous system. CGRP antagonists are an emerging therapeutic class for both the prevention and acute treatment of migraines. Galcanezumab (Emgality), erenumab (Aimovig) and fremanuzumab (Ajovy) are subcutaneously administered CGRP antagonists used for the prevention of migraine headache in adults.

Medical necessity:

Drug	Medical Necessity
atogepant (**Qulipta**) galcanezumab-gnlm (**Emgality**) eptinezumab-jjmr (**Vyepti**) erenumab-aooe (**Aimovig**) fremanezumab-vfrm (**Ajovy**)	Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists in this policy may be considered medically necessary when used for the: • Prevention of migraine headaches Galcanezumab-gnlm (**Emgality**) may also be considered medically necessary when used for the: • Treatment of episodic cluster headaches If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial or reauthorization duration.

	Clients new to Apple Health or new to an MCO, who are requesting regimens for continuation of therapy should be reviewed following the reauthorization criteria listed below.

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
Prevention of Migraine atogepant **(Qulipta)** eptinezumab-jjmr **(Vyepti)** erenumab-aooe (**Aimovig**) fremanezumab-vfrm (**Ajovy**) galcanezumab-gnlm (**Emgality)**	The CGRP antagonists in this policy may be considered medically necessary when **ALL** of the following are met: 1. Diagnosis of migraine, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (See table 1); **AND** 2. Documentation that the prescriber has ruled out medication overuse headache; **AND** 3. Patient is experiencing 4 or more migraines per month; **AND** 4. Patient has failed *(defined as an inability to reduce migraine headaches by 2 or more days per month)* a 3-month trial of at least **ONE** agent from **TWO** of the following classes of preventive medications (See **Preferred Therapies** section listed below). Documentation of adherence is required for each therapy *(unless contraindicated or intolerance to treatment):* a. Anticonvulsants; **AND** b. Antidepressants; **AND** c. Beta blockers 5. Patient has not received onabotulinum toxin in the previous 12 weeks; **AND** 6. Is not prescribed in combination with any other CGRP antagonist; **AND** 7. Patient is 18 years of age or older If all of the above criteria are met, **the request will be approved for 3 months**
	Criteria (Reauthorization)
	The CGRP antagonists in the policy may be reauthorized when the following criteria are met: 1. Migraine days reduced by at least 40% from baseline; **OR** 2. Documentation of significant improvement in Quality of Life measures (e.g. a 6-point reduction on the HIT-6 score); **AND** 3. Patient has not received onabotulinum toxin in the previous 12 weeks; **AND** 4. Is not prescribed in combination with any other CGRP antagonist If all of the above criteria are met, **the request will be approved for 12 months**
Cluster Headache galcanezumab-gnlm (Emgality)	Galcanezumab-gnlm (Emgality) may be considered medically necessary when **ALL** of the following are met: 1. Diagnosis of episodic cluster headache, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (See table 1); **AND**

	2. Documentation that the prescriber has ruled out medication overuse headache; **AND** 3. Patient has previously tried and failed an adequate trial of verapamil, defined as taking a total daily dose of at least 360 mg for at least 1 month (unless intolerant or contraindicated); **AND** 4. Patient is 18 years of age or older If all of the above criteria are met, **the request will be approved for 2 months** (Max: 2 doses; 1 dose at the beginning of the cluster headache period, and one dose 4 weeks after)
	Criteria (Reauthorization)
	Galcanezumab-gnlm (Emgality) may be reauthorized when the following criteria are met: 1. There is a continued need for cluster headache therapy (e.g. the cluster headache period is still ongoing); **AND** 2. Patient has improved, demonstrated by a meaningful reduction in total headache attacks per week compared to baseline. If all of the above criteria are met, **the request will be approved for 6 months**

Preferred therapies:

Drug Name	Preferred For:
Anticonvulsants Antidepressants Beta-blockers	**Anticonvulsants:** Topiramate, divalproex sodium, or valproate **Antidepressants:** Venlafaxine, amitriptyline **Beta-blockers:** Propranolol, metoprolol, timolol, nadolol or atenolol

Dosage and quantity limits:

Drug Name	Dose and Quantity Limits
atogepant **(Qulipta)**	10 mg tablet: #30 tablets per 30-days 30 mg tablet: #30 tablets per 30-days 60 mg tablet: #30 tablets per 30-days
eptinezumab-jjmr **(Vyepti)**	300 mg administered by IV infusion every 84-days
erenumab-aooe (**Aimovig**)	140mg per 28-days
fremanezumab-vfrm (**Ajovy**)	225mg per 28-days or 675mg per 84-days
galcanezumab-gnlm (**Emgality**)	**Migraine** Loading Dose: 240mg one time Maintenance Dose: 120mg per 28-days **Cluster Headache** 300 mg per 28-days

Definitions:

Term	Description
CGRP	Calcitonin gene-related peptide

Clinical Review

Galcanezumab (Emgality) was evaluated for the prevention of cluster headaches by Goadsby, et al. in a phase 3 randomized controlled trial. Patients were enrolled who met the ICHD-3 diagnostic criteria for cluster headache during the baseline assessment (a minimum of 4 headache attacks, including at least one headache every other day, but not exceeding 8 headaches per day). Additionally, patients were between the ages of 18 and 65 and were required to have a history of cluster headache periods lasting at least 6 weeks to control for spontaneous resolution. Forty-nine (49) were assigned to taken galcanezumab 300 mg, administered at baseline at 4 weeks, and 57 took placebo. The primary outcome evaluated the overall mean change from baseline in the weekly headache frequency across weeks 1 through 3. The galcanezumab group experienced a decrease of 8.7 attacks per week compared to baseline versus a 5.2 decrease in the placebo group (CI 0.2 to 6.7, P = 0.04). Additionally, 71% of the galcanezumab group experienced at least a 50% decrease in attacks in weeks 1 through 3 relative to baseline compared to 53% in the placebo group (p= 0.046). Notably, the significant outcomes associated with galcanezumab did not extend passed week 3, although this could be explained by the nature of cluster headaches where spontaneous resolution often occurs.

References

1. Product Information: AIMOVIG™ subcutaneous injection, erenumab-aooe subcutaneous injection. Amgen Inc (per manufacturer), Thousand Oaks, CA, 2018
2. Product Information: AJOVY™ subcutaneous injection, fremanezumab-vfrm subcutaneous injection. Teva Pharmaceuticals USA Inc (per FDA), North Wales, PA, 2018
3. Product Information: EMGALITY™ subcutaneous injection, galcanezumab-gnlm subcutaneous injection. Eli Lilly and Company (per FDA), Indianapolis, IN, 2019
4. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: 5/5/2020).
5. International Headache Society (IHS); Headache Classification Committee. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013; 33: 629-808.
6. Beran RG. Management of chronic headache. Aust Fam Physician. 2014;43(3):106-110.
7. Goadsby PJ, Dodick DW, Leone M, et al. Trial of Galcanezumab in Prevention of Episodic Cluster Headache. N Engl J Med. 2019;381(2):132-141.

History

Date	Action and Summary of Changes
05/24/2019	New Policy
7/8/2019	Changed tried and failed criteria from one drug in each class to one drug in two of the three classes.
5/5/2020	Added cluster headache indication Clarified preventive treatment options for migraine prevention Added age 18 or older to migraine prevention Added Table 1, defining ICHD-3 diagnostic criteria Formatting update Removed baseline criteria for HIT6 and MIDAS score
11/30/2020	Removed Preferred/Non-Preferred listing and added link to AHPDL publication
10/26/2022	Version 2 Updates: 1. Added case-by-case language to medical necessity section

	2. Added criteria "Is not prescribed in combination with any other CGRP antagonist" to reauthorization criteria 3. Qulipta and Vyepti added to policy

Appendix

Table 1: ICHD-3 diagnostic criteria for migraine and cluster headache

Headache Type	ICHD-3 Diagnostic Criteria
Migraine	A. At least five attacks fulfilling criteria B-D B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs) D. During headache at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not better accounted for by another ICHD-3 diagnosis.
Migraine with aura	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. visual 2. Sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal C. At least three of the following six characteristics: 1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within 60 minutes, by headache

	A. Not better accounted for by another ICHD-3 diagnosis.
Cluster Headache	A. At least five attacks fulfilling criteria B-D B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated) C. Either or both of the following: 1. at least one of the following symptoms or signs, ipsilateral to the headache: ▪ conjunctival injection and/or lacrimation ▪ nasal congestion and/or rhinorrhoea ▪ eyelid oedema ▪ forehead and facial sweating ▪ miosis and/or ptosis 2. a sense of restlessness or agitation D. Occurring with a frequency between one every other day and 8 per day E. Not better accounted for by another ICHD-3 diagnosis