Migraine Products – Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists

WA.PHAR.106 **Effective Date: 6/1/2025**

Related medical policies:

Policy Name	Indications
N/A	N/A

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 list of 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

Medical necessity

Drug	Medical Necessity
urogepant (Ubrelvy) rimegepant (Nurtec ODT) atogepant (Qulipta) galcanezumab-gnlm (Emgality) eptinezumab-jjmr (Vyepti) erenumab-aooe (Aimovig) fremanezumab-vfrm (Ajovy) zavegepant (Zavzpret)	**Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health. Patients new to Apple Health or new to an MCO who are requesting regimens for continuation of therapy are reviewed following the reauthorization criteria listed below.

Clinical policy:

Clinical Criteria	
Migraine Prophylaxis atogepant (Qulipta)	Galcanezumab-gnlm (Emgality), erenumab-aooe (Aimovig), or fremanezumab-vfrm (Ajovy) may be approved when all of the following criteria are met:

eptinezumab-jjmr (Vyepti) erenumab-aooe (Aimovig) fremanezumab-vfrm (Ajovy) galcanezumab-gnlm (Emgality) rimegepant (Nurtec ODT)	1. Patient is 18 years of age or older; **AND** 2. CGRP antagonists indicated for migraine prophylaxis will not be used in combination with each other [exception: rimegepant (Nurtec ODT) at a dose of less than or equal to 8 tablets per 30 days]; **AND** 3. Diagnosis of migraine, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (See table 1); **AND** 4. Documentation that the prescriber has ruled out medication overuse headache; **AND** 5. Patient is experiencing 4 or more migraines per month; **AND** 6. Patient has failed (defined as an inability to reduce migraine headaches by 2 or more days per month or inability to achieve significant improvement in quality of life) 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 there is documentation that all preferred therapy classes are contraindicated or not tolerated.)* a. Anticonvulsants; **AND** b. Antidepressants; **AND** c. Beta blockers; **AND** d. Angiotensin receptor blockers Atogepant (Qulipta), eptinezumab-jjmr (Vyepti), or rimegepant (Nurtec ODT) may be approved when all of the following criteria are met: 1. Criteria 1-6 is met above; **AND** 2. Two preferred CGRP receptor antagonists on Apple Health Preferred Drug List (PDL) indicated for migraine prophylaxis have been ineffective, contraindicated, or not tolerated If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Atogepant (Qulipta), galcanezumab-gnlm (Emgality), eptinezumab-jjmr (Vyepti), erenumab-aooe (Aimovig), fremanezumab-vfrm (Ajovy), or rimegepant (Nurtec ODT) may be approved when all of 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) If ALL criteria are met, the request will be authorized for **12 months.**
Cluster Headache galcanezumab-gnlm (Emgality)	Galcanezumab-gnlm (Emgality) may be approved when all of the following criteria are met: 1. Patient is 18 years of age or older; **AND**

	2. Diagnosis of episodic cluster headache, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (see table 1); **AND** 3. Documentation that the prescriber has ruled out medication overuse headache; **AND** 4. Documentation that 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 not tolerant or contraindicated). If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Galcanezumab-gnlm (Emgality) may be approved when all of the following criteria are met: 1. Documentation confirming the patient has experienced a reduction in total headache attacks per week compared to baseline; **AND** 2. Provider attests the patient continues to need therapy for cluster headache (i.e., the cluster period has not passed, or a trial of therapy taper has been attempted and was unsuccessful). If ALL criteria are met, the request will be authorized for **12 months.**
Migraines (Acute Treatment) ubrogepant (Ubrelvy) rimegepant (Nurtec ODT) zavegepant (Zavzpret)	Ubrogepant (Ubrelvy) may be approved when all of the following criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Diagnosis of migraine as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (see table 1); **AND** 3. CGRP antagonists indicated for the acute treatment of migraines will not be used in combination with each other; **AND** 4. Documentation that patient has experienced at least 2 migraine episodes with moderate to severe pain per month during the last 3 months; **AND** 5. Documentation that the prescriber has ruled out medication overuse headache; **AND** 6. Documentation of inadequate treatment response to the following unless all are contraindicated or not tolerated: a. At least 2 different 5-hydroxytryptamine (5HT) receptor agonists (i.e., sumatriptan, naratriptan, rizatriptan); **AND** b. At least one triptan must be used in combination with a non-steroidal anti-inflammatory drug (NSAID) Rimegepant (Nurtec ODT) or zavegepant (Zavzpret) may be approved when all of the following criteria are met:

	7. Criteria 1-6 is met above; **AND** 8. One preferred CGRP receptor antagonists on Apple Health Preferred Drug List (PDL) indicated for acute migraine treatment has been ineffective, contraindicated, or not tolerated If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Ubrogepant (Ubrelvy), rimegepant (Nurtec ODT), or zavegepant (Zavzpret) may be approved when all of the following criteria are met: 1. Documentation is submitted demonstrating disease stability or a positive clinical response defined as **ONE** of the following: a. Clinically meaningful reduction in pain, or pain freedom, after CGRP antagonist administration; **OR** b. Clinically meaningful reduction in migraine-associated symptoms (i.e. photophobia, phonophobia, and nausea) after CGRP antagonist administration If ALL criteria are met, the request will be authorized for **12 months.**

Preferred therapies:

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

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
erenumab (Aimovig)	Migraine prophylaxis	140 mg once monthly	• 70 mg/1 mL autoinjector: 1 per 28-days • 140 mg/1 mL autoinjector: 1 per 28-days
galcanezumab (Emgality)	Migraine prophylaxis	240 mg single loading dose; 120 mg once monthly	• 120 mg/1 mL autoinjector: 1 per 28-days • 120 mg/1 mL prefilled syringe: 1 per 28-days • **NOTE:** The 100mg/1mL prefilled syringe is not approvable for this indication
	Episodic cluster headache	300 mg once monthly	• 100 mg/1 mL prefilled syringe: 3 per 28-days
fremanezumab (Ajovy)	Migraine prophylaxis	225 mg once monthly or 675mg every 3 months	• 225 mg/1.5 mL prefilled syringe: 1 per 28-days • 225 mg/1.5 mL autoinjector: 1 per 28-days
eptinezumab (Vyepti)	Migraine prophylaxis	100 mg IV every 3 months or 300 mg IV every 3 months	• 300 mg administered by IV infusion every 90 days

atogepant (Qulipta)	Migraine prophylaxis	60 mg once daily	• 10 mg tablet: #1 tablet per 1day • 30 mg tablet: #1 tablet per 1day • 60 mg tablet: #1 tablet per 1day
rimegepant (Nurtec ODT)	Migraine prophylaxis	75 mg every other day	• 75 mg tablet: #18 tablets per 28-days
	Acute treatment of migraine	75 mg as needed; max 75 mg per 24 hours	• 75 mg tablet: #8 tablets per 28-days
ubrogepant (Ubrelvy)	Acute treatment of migraine	50 mg or 100 mg as a single dose; if symptoms persist or return, may repeat dose after ≥2 hours	• 50 mg tablet: #16 tablets per 28-days • 100 mg tablet: #16 tablets per 28-days
zavegepant (Zavzpret)	Acute treatment of migraine	10mg as a single spray in 1 nostril. MAX 10 mg/24 hours	• One carton (6 disposable devices) per 30 days

Coding:

HCPCS Code	Description
C9399 J3590	Injection; erenumab-aooe; up to 140 mg
C9399 J3590	Injection; galcanezumab-gnlm; up to 300 mg
J3031	Injection, fremanezumab-vfrm, 225 mg
J3032	Injection, eptinezumab-jjmr, 100 mg

Background:

Migraine Prophylaxis

Chronic migraine is defined as 15 or more headache days per month for at least three months, at least eight of which have migrainous features. Calcitonin gene-related peptide (CGRP) receptor antagonists are medications approved for the prevention of chronic migraine. In the pivotal trials for the agents listed in this policy, participants had a history of four or more monthly migraine days for at least one year. Reduction in migraine days compared to placebo ranged from 0.8 to 1.9 depending on the specific CGRP receptor antagonist and trial design. The percentage of participants who achieved at least a 50% reduction in migraine days per month ranged from 30% to greater than 50%. Migraines may have numerous causes and triggers and may be transient in nature; thus, a strong history of migraine is warranted prior to consideration of coverage for CGRP agents. Guidelines recommend select beta blockers, antidepressants, angiotensin receptor blockers, anticonvulsants, and onabotulinum toxin A as efficacious or probably efficacious (Level A and B, respectively) for the prophylactic treatment of migraine in adults. Agents not listed specifically above in the policy have lower level, conflicting, or negative evidence.

Cluster Headache

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.

Acute Treatment of Migraine

Ubrelvy (ubrogepant) was evaluated in two phase 3 randomized controlled trials (Lipton, et al., Dodick et al.). Participants were adults aged 18 to 75 years with two to eight moderate to severe pain migraine episodes per month for the preceding three months. Lipton, et al. evaluated ubrogepant 50 mg (n = 562) doses compared to placebo (n=563) and Dodick et al. studied doses of 50 mg (n=556) and 100 mg (n=557) compared to placebo (n=563). Approximately 90% of participants were women, 24% were taking concurrent non-CGRP antagonist preventive migraine therapy, and 97% had previously tried other abortive treatment, most commonly NSAIDs. Pain freedom and improvement in bothersome symptoms (photophobia, phonophobia, and nausea) at 2 hours post-dose were primary outcomes. Study participants had the option to take a second dose of ubrogepant 2 to 48 hours after the first dose if needed for initial non-response. Both trials observed a significant number of participants achieving the primary outcomes compared to placebo at the 50 mg and 100 mg doses. Ubrogepant 50 mg increased pain freedom at 2 hours by 7.4% (p 0.002) and 7.5% (p <0.001) in each trial, respectively accounting for a number needed to treat (NNT) of 14. The 50 mg dose additionally increased the proportion of participants free of from bothersome symptoms at 2 hours by 10.8% and 11.5% (p <0.001) for both. Similarly, ubrogepant 100 mg increased freedom from pain and bothersome symptoms at 2 hours by 9.4% and 9.9%, respectively (p <0.001 for both).

Rimegepant was similarly evaluated in two phase 3 randomized controlled trials (Lipton, et al., Croop et al.). In Croop et al. the effectiveness of rimegepant 75 mg orally dissolving tablet (n=682) was compared to placebo(n=693). Participants were adults aged 18 and older with two to eight moderate to severe pain migraine episodes per month for the preceding three months. Approximately 85% of participants were women and no concurrent CGRP antagonist treatment for migraine prevention was allowed. Pain freedom and improvement in bothersome symptoms (photophobia, phonophobia, and nausea) at 2 hours post-dose were primary outcomes. Unlike trials for ubrogepant, study participants did not have the option to take a second dose of rimegepant for non-response. Cooper et al, observed a significant number of participants achieving the primary outcomes compared to placebo, concluding a 10.3% and 8.3% (p <0.001 for both) increase in pain and bothersome symptom freedom at 2 hours, respectively.

Zavzpret (zavegepant), the first CGRP antagonist approved as a nasal spray, was evaluated in a phase 3 randomized controlled trial with 1269 participants. At 2 hour post treatment 24% of participants in the treatment group achieved pain freedom, compared to 15% of those in the placebo group (P=<0.0001, NNT = 12). Similarly, significantly more participants in the treatment group were free of their most bothersome symptoms (40% vs 31%, p=0.0012, NNT=12). All CGRP antagonists approved for acute migraine treatment had similar outcomes in their respective clinical trials and there is no clinical evidence to prefer one over another.

References

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3. Prescribing Information: AJOVY™ subcutaneous injection, fremanezumab-vfrm subcutaneous injection. Teva Pharmaceuticals USA Inc (per FDA), North Wales, PA, 2021
4. Prescribing Information: EMGALITY™ subcutaneous injection, galcanezumab-gnlm subcutaneous injection. Eli Lilly and Company (per FDA), Indianapolis, IN, 2022

5. Prescribing Information: QULIPTA® tablets, atogepant tablets. AbbVie Inc., North Chicago, IL, 2023
6. Prescribing Information: VYEPTI® injection, eptinezumab-jjmr. Lundbeck Seattle BioPharmaceuticals, Inc., Bothell, WA, 2024
7. Prescribing Information: ZAVZPRET™ nasal spray, zavegepant. Pfizer Inc., New York, NY, 2023
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History

Approved Date	Effective Date	Version	Action and Summary of Changes
12/12/2024	06/01/2025	67.70.10-2	Combined abortive and prophylactic CGRP policies

Appendix

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

Definitions	
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 (e.g. 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 D. 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.