PHARMACY COVERAGE GUIDELINE

AIMOVIG™ (erenumab-aooe) subcutaneous injection
AJOVY™ (fremanezumab-vfrm) subcutaneous injection
EMGALITY™ (galcanezumab-gnlm) subcutaneous injection

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

Section A. Migraine Headaches:
AIMOVIG (erenumab-aooe)
AJOVY (fremanezumab-yfrm)
EMGALITY (galcanezumba-gnlm)

- **Criteria for initial therapy:** Aimovig (erenumab), Emgality (galcanezumab-gnlm), or Ajovy (fremanezumab-vfrm) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is **ONE** of the following:
     a. A Neurologist

b. A licensed professional authorized by his or her license to prescribe Aimovig, Ajovy, or Emgality **and ONE** of the following:
   i. Is prescribing in consultation with a Neurologist or Pain Specialist
   ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
   iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following types of migraine:
   a. Episodic migraine, defined as an individual with migraine who has between 4-14 headache days per month of which at least 4 were migraine days

   b. Chronic migraine, defined as an individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura

4. Will not be used concurrently or alternating with Botox (onabotulinumtoxin A)

5. Will not be used concurrently with other CGRP related therapies (e.g. Nurtec ODT (rimegepant), Qulipta (atogepant) or Ubrelvy (ubrogepant)) or Reyvow (lasmiditan)

6. There is no history of cluster headache or hemiplegic migraine

7. Use is not for medication overuse headache or rebound headache or medication withdrawal headache

8. The individual has failure, contraindication per FDA label or intolerance to a previous trial of any **TWO** of the following preventative migraine agents where the dose has been stable for at least 2 months (60 days):
   a. Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol
   b. Antidepressant: amitriptyline or venlafaxine
   c. Anticonvulsant: topiramate, divalproex sodium, or sodium valproate

9. **Additional criteria for Ajovy (fremanezumab-vfm) only:** Individual has failure, contraindication per FDA label or intolerance to a trial of at least 3 months use of **BOTH** Aimovig (erenumab) **AND** Emgality (galcanezumab-gnlm)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Aimovig (erenumab), Emgality (galcanezumab-gnlm) or Ajovy (fremanezumab-vfrm) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:

a. Neurologist
b. A licensed professional authorized by his or her license to prescribe Aimovig or Emgality **and ONE** of the following:
    i. Is prescribing in consultation with a Neurologist or Pain Specialist
    ii. Is certified as a headache specialist by the UCNS
    iii. Has earned a CAQ in Headache Medicine from the National Headache Foundation

2. Individual's condition responded while on therapy with response defined as **ALL** of the following:
    a. At least a 50% reduction in the number of migraine days per month from baseline
    b. A reduction in the number of days of use of acute migraine-specific medications from baseline
    c. Significant reduction in emergency room or urgent care visits for acute migraine treatment

3. Individual has been adherent with the medication

4. Will not be used concurrently or alternating with Botox (onabotulinumtoxin A)

5. Will not be used concurrently with or alternating with other CGRP related therapies (e.g. Nurtec ODT (rimegepant), Qulipta (atogepant) or Ubrelvy(ubrogepant)) or Reyvow (lasmiditan)

6. Individual has not developed any significant adverse drug effects that may exclude continued use

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Section B. Episodic Cluster Headaches: EMGALITY (galcanezumab-gnlm)

- **Criteria for initial therapy:** Emgality (galcanezumab-gnlm) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is **ONE** of the following:
    a. A Neurologist
    b. A licensed professional authorized by his or her license to prescribe Emgality **and ONE** of the following:
        i. Is prescribing in consultation with a Neurologist or Pain Specialist
        ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)

iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual is 18 years of age or older

3. A confirmed diagnosis of episodic cluster headache according to International Headache Society (IHS) International Classification of Headache Disorders (ICHD)

4. Will not be used as an abortive treatment for an acute cluster headache episode

5. Individual uses **either** oxygen or sumatriptan (subcutaneous or intranasal) or intranasal zolmitriptan or other abortive therapy for acute episodes of cluster headache

6. Will not be used concurrently or alternating with Botox (onabotulinumtoxin A)

7. Will not be used concurrently with or alternating with other CGRP related therapies (e.g. Nurtec ODT (rimegepant), Qulipta (atogepant) or Ubrelvy(ubrogepant)) or Reyvow (lasmiditan)

8. There is no history of migraine headache or hemiplegic migraine

9. Use is not for medication overuse headache or rebound headache or medication withdrawal headache

10. The individual has failure, contraindication per FDA label or intolerance to a previous trial of any **TWO** of the following preventative cluster headache agents where the dose has been stable for at least 2 months (60 days)
    a. Verapamil
    b. Prednisone or dexamethasone
    c. Topiramate
    d. Lithium carbonate

Initial approval duration: 2 months

- **Criteria for continuation of coverage (renewal request):** Emgality (galcanezumab-gnlm) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:
    a. Neurologist
    b. A licensed professional authorized by his or her license to prescribe Emgality **and ONE** of the following:
        i. Is prescribing in consultation with a Neurologist or Pain Specialist
        ii. Is certified as a headache specialist by the UCNS
        iii. Has earned a CAQ in Headache Medicine from the National Headache Foundation

2. Individual's condition responded while on therapy with response defined as **TWO** of the following:

a. A reduction in the weekly cluster headache attack frequency from baseline
b. At least a 50% reduction in the weekly cluster headache frequency from baseline
c. Significant reduction in emergency room or urgent care visits for acute migraine treatment

3. Will not be used concurrently or alternating with Botox (onabotulinumtoxin A)

4. Will not be used concurrently with or alternating with other CGRP related therapies (e.g. Nurtec ODT (rimegepant), Qulipta (atogepant) or Ubrelvy(ubrogepant)) or Reyvow (lasmiditan)

5. Individual has not developed any significant adverse drug effects that may exclude continued use

Renewal duration:
Emgality: One carton per month with three 100 mg prefilled syringes for 6 months

➢ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Definitions:

Migraine day:
- Any calendar day in which the patient experiences a qualified migraine headache (onset, continuation, or recurrence of the migraine headache)
- A qualified migraine is defined a migraine with or without aura, lasting ≥ 30 minutes that meets at least one of the following:
  - ≥ 2 of the following pain features: unilateral, throbbing, moderate to severe, or exacerbated with exercise/physical activity
  - > 1 of the following associated non-pain features: nausea and or vomiting, or both photophobia, and phonophobia
- Any calendar day on which acute migraine-specific medication was used is counted as a migraine day

Treatment considerations:
- There are no strict definitions for the precise frequency or duration of migraine headaches that would prompt preventive therapy
- Migraine prevention therapy may be indicated for those with migraine headaches that are frequent (ex. as ≥ 4 headaches/month) or long-lasting (ex. ≥12 hours) and those that cause significant disability or diminished quality of life
- The goals of preventive therapy are to reduce the frequency, severity, and duration of headaches, to improve treatment responsiveness of therapies for acute attacks, prevent progression or transformation of episodic migraine to chronic migraine and to improve overall function or reduce the risk of neurologic impairment

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Episodic migraine:

- Individual with migraine who has between 4 to 14 headache days per month, of which at least 4 were migraine days

Chronic migraine:

- Individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura.
- The diagnostic criteria for chronic migraine require the presence of headache for 15 or more days per month for more than three months, with the features of migraine headache present on at least eight days per month
- Some patients with an episodic migraine pattern (<15 headache days a month) transition to a chronic migraine pattern (≥15 headache days a month), a transition that has been called "transformation" and "chronification"
- Features of migraine headache include:
  - Lasts 4-72 hours **AND** has at least 2 of the following 4 characteristics:
    - Unilateral, pulsating, moderate or severe pain intensity, aggravates or causes avoidance of routine physical activity
  - **AND** associated with at least one of the following during the headache:
    - Nausea and/or vomiting or photophobia and phonophobia.
- The management of chronic migraine should focus on prophylactic therapy and avoidance of acute headache medication overuse

2013 Canadian Headache Society (CHS) – medications for acute migraine:

2013 Canadian Headache Society (CHS) Summary of Recommendations*		
Recommended For Use in Episodic Migraine (Use)**		
	Recommendation	
Drug	**Recommendation Strength**	**Quality of Evidence**
Almotriptan	Strong	High
Eletriptan	Strong	High
Frovatriptan	Strong	High
Naratriptan	Strong	High
Rizatriptan	Strong	High
Sumatriptan	Strong	High
Zolmitriptan	Strong	High
Aspirin	Strong	High
Diclofenac	Strong	High
Ibuprofen	Strong	High
Naproxen	Strong	High
Acetaminophen	Strong	High
Domeridone	Strong	Low
Metoclopramide	Strong	Moderate
Dihydroergotamine	Weak	Moderate
Ergotamine	Weak, not recommended for routine use	Moderate
Opioid containing compounds	Weak, not recommended for routine use	Low
Tramadol containing compounds	Weak, not recommended for routine use	Moderate
Not Recommended for Use in Episodic Migraine (Do not use***)**		
Butalbital containing compounds	Strong	Low

Butorphanol	Strong	Low

*Utilizing Grading of Recommendations Assessment, Development and Evaluation (GRADE) Criteria
**Migraine with headache on less than 15 days a month
*** Except under exceptional circumstances

Metoclopramide strongly recommended for use when necessary

Cluster headache:

- The most common type of Trigeminal Autonomic Cephalalgias (TAC)
- Attacks of severe orbital, supraorbital, or temporal pain, accompanied by autonomic phenomena and/or restless or agitation
- Unilateral autonomic symptoms associated with cluster headache include ptosis, miosis, lacrimation, conjunctival injection, rhinorrhea, and nasal congestion, occur only during the pain attack and are ipsilateral to the pain
- The attacks may strike up to eight times a day and are relatively short-lived (usually 15-180 minutes)
- The headache is strictly unilateral; the symptoms remain on the same side of the head during a single cluster attack
- The symptoms can switch to the other side during a different cluster attack (so-called side shift) in approximately 15% of cases
- In contrast to migraine, patients with cluster are restless and prefer to pace about or sit and rock back and forth

Diagnostic criteria for cluster headache:

Cluster headache: Diagnostic criteria for cluster headache require the following:
A. At least **five attacks** fulfilling criteria B through D
B. Severe or very severe **unilateral** orbital, supraorbital, and/or temporal pain lasting 15-180 minutes when untreated; during part (but less than half) of the active time course of cluster headache, attacks may be less severe and/or of shorter or longer duration
C. **Either or both** of the following:
1. At least **one** of the following symptoms or signs ipsilateral to the headache:
a) Conjunctival injection and/or lacrimation
b) Nasal congestion and/or rhinorrhea
c) Eyelid edema
d) Forehead and facial sweating
e) Miosis and/or ptosis
2. A sense of restlessness or agitation
D. Attacks have a frequency between one every other day and eight per day; during part (but less than half) of the active time-course of cluster headache, attacks may be less frequent
E. Not better accounted for by another ICHD-3 diagnosis

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Episodic cluster headache: Diagnostic criteria for episodic cluster headache require the following:
A. Attacks fulfilling criteria for cluster headache and occurring in bouts (cluster periods)
B. At least two cluster periods lasting from seven days to one year (when untreated) and separated by pain-free remission periods of three months or more
Chronic cluster headache: Diagnostic criteria for chronic cluster headache require the following:
A. Attacks fulfilling criteria for cluster headache
B. Attacks occurring without a remission period, or with remissions lasting less than three months, for at least one year
Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38:1.

Identification of headache type: migraine, tension, or cluster			
	Migraine	**Tension**	**Cluster**
Location	Unilateral	Bilateral	Supraorbital/temporal
Pain intensity[1]	Moderate to severe	Mild to moderate	Severe
Duration	4–72 hours	30 minutes to 7 days	15–180 minutes
Characterization of pain	Pulsing	Pressure/squeezing	Boring/stabbing
Sensitivity to light/sound	One or both may be present	Both are absent or only one is present	No
Nausea/vomiting	One or both may be present	No	One or both may be present
Aggravated by routine activity	Yes	No	No
Aura	May be present	No	No
Associated symptoms	None	None	Miosis, ptosis, rhinorrhea

1 Pain intensity
- Mild—Patient is aware of a headache but is able to continue daily routine with minimum alterations.
- Moderate—The headache inhibits daily activities; migraine pain is more noticeable but is not incapacitating.
- Severe—The headache is incapacitating such that patient is no longer able to engage in normal activities.

Abortive (symptomatic) treatment of acute migraine:

- Simple analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen, triptans, antiemetics, calcitonin gene-related peptide (CGRP) antagonists (remigepant, ubrogepant), lasmiditan, and dihydroergotamine

Non-Calcitonin gene-related peptide (Non-CGRP) preventative (episodic or chronic) migraine agent(s):

- Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol
- Antidepressant: amitriptyline or venlafaxine
- Anticonvulsant: topiramate, divalproex sodium, or sodium valproate

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Botulinum toxin injection:

- Treatment of chronic migraine:
  - Botox (onabotulinumtoxinA)

CGRP related agents:

- Treatment of episodic or chronic migraine:
  - Vyepti (eptinezumab-jjmr)
  - Aimovig (erenumab)
  - Ajovy (fremanezumab-vfrm)
  - Emgality (galcanezumab)
    - Also used in cluster headache
- Treatment of episodic migraine:
  - Qulipta (atogepant)
  - Nurtec ODT (rimegepant)
- Treatment of acute migraine:
  - Nurtec ODT (rimegepant)
  - Ubrelvy (ubrogepant)

Serotonin (5-HT) 1F receptor agonist:

- Treatment of acute migraine
  - Reyvow (lasmiditan)

Resources:

Aimovig (erenumab-aooe) product information, revised by manufacturer Amgen, Inc. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 08, 2022.

Ajovy (fremanezumab-vfrm) product information, revised by manufacturer Teva Pharmaceuticals USA, Inc. 09-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 08, 2022.

Emgality (galcanezumab-gnlm) product information, revised by manufacturer Eli Lilly and Company 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 08, 2022.

Schwedt TJ, Garza I. Acute treatment of migraine in adults. In: UpToDate, Swanson JW, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated October 20,2021. Accessed April 11, 2022.

Schwedt TJ, Garza I. Preventive treatment of episodic migraine in adults. In: UpToDate, Swanson JW, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated March 11, 2022. Accessed April 11, 2022.

Garza I, Schwedt TJ. Chronic migraine. In: UpToDate, Swanson JW, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated March 22, 2022. Accessed April 11, 2022.

May A. Cluster headache: Treatment and prognosis. In: UpToDate, Swanson JW, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated February 11, 2022. Accessed April 11, 2022.