This program applies to Medicaid.

For Medicaid, the preferred product is the MN Medicaid Preferred Drug List (PDL) preferred drug: Emgality

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

### FDA LABELED INDICATIONS\(^{1-3}\)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage and Administration</th>
<th>Limitation of Use</th>
</tr>
</thead>
</table>
| **Aimovig™**<sup>(erenumab)</sup>  
subcutaneous autoinjector, subcutaneous prefilled syringe | Preventive treatment of migraine in adults | Recommended dose is 70 mg once monthly  
Some patients may benefit from 140 mg once monthly | None |
| **Ajovy™**<sup>(fremanezumab)</sup>  
subcutaneous prefilled syringe | Preventive treatment of migraine in adults | 225 mg monthly, or 675 mg every 3 months (quarterly), which is administered as three consecutive subcutaneous injections of 225 mg each. | None |
| **Emgality™**<sup>(galcanezumab)</sup>  
subcutaneous autoinjector, subcutaneous prefilled syringe | Preventive treatment of migraine in adults | Migraine: 240 mg loading dose (administered as two consecutive injections of 120 mg each), followed by monthly doses of 120 mg.  
Cluster headache: 300 mg (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 | None |

### CLINICAL RATIONALE

**Migraines**
The diagnostic criteria for chronic migraine requires the inclusion of all of the following:\(^{10}\)

A. Headache (migraine-like or tension-like) on ≥15 days per month for >3 months and fulfilling criteria B and C
B. Occurring in a patient who has had at least five attacks fulfilling of migraine without aura and/or migraine with aura

C. On ≥8 days per month for >3 months, fulfilling any of the following:
   1. Migraine without aura
   2. Migraine with aura
   3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative

D. Not better accounted for by another ICHD-3 diagnosis.

Migraine prevention may be of benefit in those with the following:\textsuperscript{4,9,13,14}

- Frequent or long-lasting migraine headaches (>4 headaches/month or headaches lasting >12 hours)
- Migraine attacks that cause significant disability or diminished quality of life despite appropriate acute treatment
- Contraindication to acute therapies
- Failure of acute therapies
- Serious adverse effects of acute therapies
- Risk of medication overuse headache
- Menstrual migraine (when acute abortive therapies are incomplete or unsatisfactory)\textsuperscript{12}

The American Headache Society (AHS) also includes patient preference as a consideration.\textsuperscript{14}

Preventative pharmacotherapy for chronic migraine is less well studied than for episodic migraine. However, use of recommended episodic prevention agents is also recommended in chronic migraine. Clinical trials suggest efficacy is often first noted at four weeks and can continue to increase for three months.\textsuperscript{4}

The American Headache Society (AHS) and the American Academy of Neurology (AAN) suggest the following agents for the prevention of migraine:\textsuperscript{9}

- Established as effective (Level A)
  - Antiepileptic drugs (AEDs)
    - Divalproex
    - Valproate
    - Topiramate
  - Beta blockers
    - Metoprolol
    - Propranolol
    - Timolol
  - Triptans
    - Frovatriptan for short term menstrually associated migraines (MAMs) prevention

- Probably effective (Level B)
  - Antidepressants
    - Amitriptyline
    - Venlafaxine
  - Beta blockers
    - Atenolol
    - Nadolol
  - Triptans
    - Naratriptan, zolmitriptan for short term MAMs prevention

The 2018 American Headache Society Consensus Statement recommends the following indications for initiating treatment with a Calcitonin Gene-Related Peptide (CGRP) agent:\textsuperscript{14}

- Prescribed by a licensed medical professional
• Patient is at least 18 years of age
• ONE of the following:
  o Diagnosis of migraine with or without aura (4-7 monthly headache days) and both of the following:
    ▪ Inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
      • Topiramate
      • Divalproex sodium/valproate sodium
      • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      • Tricyclic antidepressant: amitriptyline, nortriptyline
      • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
      • Other Level A or B treatment according to AAN-AHS guideline
    ▪ At least moderate disability (Migraine Disability Assessment Questionnaire [MIDAS] >11, Headache Impact Test-6 [HIT]-6 >50)
  o Diagnosis of migraine with or without aura (8-14 monthly headache days) and inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
    • Topiramate
    • Divalproex sodium/valproate sodium
    • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
    • Tricyclic antidepressant: amitriptyline, nortriptyline
    • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
    • Other Level A or B treatment according to AAN-AHS guideline
  o Diagnosis of chronic migraine and one of the following:
    ▪ Inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
      • Topiramate
      • Divalproex sodium/valproate sodium
      • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      • Tricyclic antidepressant: amitriptyline, nortriptyline
      • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
      • Other Level A or B treatment according to AAN-AHS guideline
    ▪ Inability to tolerate or inadequate response to a minimum of 2 quarterly injection (6 months) of onabotulinumtoxin A

American Headache Society (2015): The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies state that specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A). The evidence base for medication efficacy should be considered along with potential medication side effects, potential adverse events, patient-specific contraindications to use of a particular medication, and drug-to-drug interactions when deciding which medication to prescribe for acute therapy of a migraine attack.15

Cluster Headaches
The International Headache Society (IHS) lists the following as diagnostic criteria for cluster headaches:16
  A. At least 5 attacks fulfilling criteria B-D
  B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes if untreated
  C. Headache is accompanied by at least one of the following:
1. ipsilateral conjunctival injection and/or lacrimation
2. ipsilateral nasal congestion and/or rhinorrhea
3. ipsilateral eyelid oedema
4. ipsilateral forehead and facial sweating
5. ipsilateral miosis and/or ptosis
6. a sense of restlessness or agitation

D. Attacks have a frequency from one every other day to 8 per day
E. Not attributed to another disorder

For episodic cluster headaches, the IHS lists the following diagnostic criteria:\(^{16}\)

A. Attacks fulfilling criteria A-E for cluster headache
B. At least two cluster periods lasting 7-365 days and separated by pain-free remission periods ≥3 month

The IHS notes that cluster periods usually last between 2 weeks and 3 months.\(^{16}\)

Guidelines suggest that prophylactic therapy should be started and continued for the duration of the cluster headache period.\(^{17-19}\) Prophylactic pharmacological therapy includes verapamil, corticosteroids, lithium, topiramate, melatonin, gabapentin, valproic acid, ergotamine and capsaicin. Verapamil is commonly considered the first option for prophylactic therapy in practice.\(^{17-19}\) Corticosteroids can be used as transitional or bridging therapy until another prophylaxis agent is established.\(^{17}\) Corticosteroids may be used by some practitioners for short periods of cluster headaches.\(^{18,19}\) The American Academy Neurology lists the following agents as option that maybe considered or should be advised as preventative treatments:

- Cimavide
- Suboccipital steroid injection
- Melatonin
- Verapamil
- Lithium

Safety
Erenumab has no FDA labeled contraindications or black box warnings.\(^{1}\)

Contraindications to fremanezumab include:\(^{2}\)

- patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients

Fremanezumab has no black box warnings.\(^{2}\)

Contraindications to galcanezumab include:\(^{3}\)

- patients with serious hypersensitivity to galcanezumab-gmlm or to any of the excipients

Galcanezumab has no black box warnings.\(^{3}\)

References:
CGRP Prior Authorization with Quantity Limit

TARGET AGENTS
For Medicaid, the preferred product is the MN Medicaid Preferred Drug List (PDL) preferred drug: Emgality

Preferred Agents
Aimovig™ (erenumab)
Emgality™ (galcanezumab)

Nonpreferred Agents
Ajovy™ (fremanezumab)

PROGRAM PRIOR AUTHORIZATION AND QUANTITY LIMIT TARGET AGENTS

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI (NDC)</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aimovig (erenumab)</td>
<td>6770202010D520</td>
<td>M, N, O, Y</td>
<td>1 autoinjector (1 mL) / 30 days^a</td>
</tr>
<tr>
<td>70 mg/mL autoinjector^a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140 mg/mL autoinjector</td>
<td>6770202010D540</td>
<td>M, N, O, Y</td>
<td>1 autoinjector (1 mL) / 30 days</td>
</tr>
<tr>
<td>Ajovy (fremanezumab)</td>
<td>6770203020E520</td>
<td>M, N, O, Y</td>
<td>3 prefilled syringes (4.5 mL) / 90 days</td>
</tr>
<tr>
<td>225 mg/1.5 mL prefilled syringe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emgality (galcanezumab)</td>
<td>6770203530E515</td>
<td>M, N, O, Y</td>
<td>9 syringes (9 mL) / 180 days</td>
</tr>
<tr>
<td>100 mg/mL syringe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>120 mg/mL autoinjector</td>
<td>6770203530D520</td>
<td>M, N, O, Y</td>
<td>1 autoinjector (1 mL) / 30 days^b</td>
</tr>
<tr>
<td>120 mg/mL syringe</td>
<td>6770203530E520</td>
<td>M, N, O, Y</td>
<td>1 syringe (1 mL) / 30 days^b</td>
</tr>
</tbody>
</table>

^a ~70 mg/mL autoinjector 2 packs are no longer available
^b – Loading dose is 2 injections (2 mL) / 30 days

PRIOR AUTHORIZATION AND QUANTITY LIMIT CRITERIA FOR APPROVAL

Initial Approval
Target Agents will be approved when ALL of the following are met:

1. ONE of the following:
   a. The requested agent is being used for migraine prophylaxis AND ALL of the following:
      i. ONE of the following:
         1. The patient has a diagnosis of chronic migraine AND ALL of the following:
             a. ≥15 headache days per month of migraine-like or tension-like headache for a minimum of 3 months AND
             b. ≥8 migraine headache days per month for a minimum of 3 months AND
             c. The requested agent is Aimovig (erenumab), Emgality (galcanezumab), OR Ajovy (fremanezumab)
      OR
      2. The patient has a diagnosis of episodic migraine AND ALL of the following:
         a. ONE of the following:
            i. The patient’s migraine headaches last >12 hours
ii. The patient’s migraine attacks cause significant disability or diminished quality of life despite appropriate therapy with acute agents only
OR

iii. The patient has contraindications to acute therapies
OR

iv. The patient has tried and received inadequate response to acute therapies
OR

v. The patient has serious side effects to acute therapies
OR

vi. The patient is at risk of medication overuse headache without preventative therapy

AND

b. ONE of the following:
   i. The patient has 4-7 migraine headache days per month AND at least moderate disability as defined by a Migraine Disability Assessment Questionnaire [MIDAS] score >11, or Headache Impact Test-6 [HIT]-6 score >50
OR

   ii. The patient has ≥8 migraine headache days per month

AND

c. The requested agent is Aimovig (erenumab), Emgality (galcanezumab), OR Ajovy (fremanezumab)

AND

ii. ONE of the following:
   1. The patient has tried and had an inadequate response to at least one migraine prophylaxis class (i.e. anticonvulsants [divalproex, valproate, topiramate], beta blockers [i.e. atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e. amitriptyline, venlafaxine]) after an adequate trial as defined by BOTH of the following:
      a. The trial length was at least 6 weeks at generally accepted doses
      AND
      b. The patient was ≥80% adherent to the prophylaxis agent during the trial
OR

   2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to an anticonvulsant, a beta blocker, AND an antidepressant listed above

AND

iii. The patient will not be using botulinum toxin headache prophylaxis after starting the requested agent

AND

iv. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist

AND

v. The patient has been evaluated for and does not have medication overuse headache
vi. ONE of the following:
   1. The requested agent is a preferred agent
      OR
   2. The requested agent is a nonpreferred agent AND ONE of the following:
      a. The patient has tried and had an inadequate response to two preferred agents
      OR
      b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to preferred agents that is not expected to occur with the requested agent

b. The requested agent is being used for the treatment of episodic cluster headache AND ALL of the following:
   i. The patient has a diagnosis of episodic cluster headache as confirmed by ALL of the following:
      1. The patient has had at least 5 cluster headache attacks
      AND
      2. The patient has at least two cluster period lasting 7-365 days
      AND
      3. The patient’s cluster periods are separated by a pain-free remission period of ≥3 month
   AND
   ii. ONE of the following:
      1. The patient has tried and had an inadequate response to verapamil, melatonin, corticosteroids, OR lithium
      OR
      2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to verapamil, melatonin, corticosteroid, OR lithium
   AND
   iii. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist
   AND
   iv. The patient has been evaluated for and does not have medication overuse headache
   AND
   v. The requested agent is FDA label indicated for episodic cluster headache treatment

OR

c. The requested agent is being used for acute migraine treatment AND ALL of the following:
   i. The patient has a diagnosis of migraine
   AND
   ii. ONE of the following:
      1. The patient has tried and had an inadequate response to two acute 5HT migraine agents with differing active ingredients OR differing route of administration
      OR
      2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to acute 5HT migraine agents
AND

iii. The patient has been evaluated for and does not have medication overuse headache
AND

iv. The requested agent is FDA label indicated for acute migraine treatment

OR
d. ONE of the following:
   i. The patient has another FDA approved indication for the requested agent and route of administration
   OR
   ii. The patient has another indication that is supported in compendia (AHFS, or DrugDex 1 or 2a level of evidence) for the requested agent and route of administration

2. ONE of the following:
a. The patient is not currently taking another CGRP agent
   OR
   b. The other CGRP agent will be discontinued prior to starting the requested agent

AND

3. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

4. ONE of the following:
a. The requested quantity (dose) is NOT greater than the program quantity limit
   OR
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is less than or equal to the maximum FDA labeled dose
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
   OR
   c. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose
      AND
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for an accepted diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval:
For migraine prophylaxis: 3 months. For agents that require a loading dose for new starts, approve the loading dose noted with the quantity limits table above AND the maintenance dose for the remainder of 3 months.
For migraine acute treatment: 12 months
For cluster headache treatment: 3 months
All other indications: 12 months

Renewal Approval
Target Agents will be approved when ALL of the following are met:
1. The patient has been approved for the requested agent previously through the Prime Therapeutics Prior Authorization process

   **AND**

2. **ONE** of the following:
   a. **BOTH** of the following:
      i. **ONE** of the following:
         1. The requested agent is being used for migraine prophylaxis **AND**
            **ALL** of the following:
            a. The prescriber has submitted documentation indicating improvement in migraine prevention (e.g. reduced migraine headache days, reduced migraine frequency, reduced use of acute abortive migraine medication) with the requested agent **AND**
            b. The patient will not be using botulinum toxin headache prophylaxis while using the requested agent **AND**
            c. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist

   OR

   2. The requested agent is being used for episodic cluster headache treatment **AND** **BOTH** of the following:
      a. The prescriber has submitted documentation indicating improvement in cluster headaches management with the requested agent **AND**
      b. The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist

   OR

   3. The requested agent is being used for acute migraine treatment **AND** the prescriber has submitted documentation indicating improvement acute migraine management with the requested agent

   ii. The patient has been evaluated for and does not have medication overuse headache

   **OR**

   b. **ONE** of the following:
      i. The patient has another FDA approved indication for the requested agent and route of administration **OR**
      ii. The patient has another indication that is supported in compendia (AHFS, or DrugDex 1 or 2a level of evidence) for the requested agent and route of administration **AND**

3. **ONE** of the following:
   a. The patient is not currently taking another CGRP agent **OR**
   b. The other CGRP agent will be discontinued prior to starting the requested agent **AND**
4. The patient does not have any FDA labeled contraindication(s) to the requested agent 
   **AND**

5. **ONE of the following:**
   a. The requested quantity (dose) is **NOT** greater than the program quantity limit  
      **OR**
   b. **ALL of the following:**
      i. The requested quantity (dose) is **NOT** greater than the program quantity limit  
         **AND**
      ii. The requested quantity (dose) is less than or equal to the maximum FDA labeled dose  
         **AND**
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of  
           a higher strength that does not exceed the limit  
      **OR**
   c. **ALL of the following:**
      i. The requested quantity (dose) is greater than the program quantity limit  
         **AND**
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose  
         **AND**
      iii. The prescriber has submitted documentation in support of therapy with a  
           higher dose for an accepted diagnosis (must be reviewed by the Clinical  
           Review pharmacist)

**Length of Approval:** 12 months
Step Therapy Supplement Program Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

2. BOTH of the following
   a. The patient’s medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
      i. Evidence of a paid claim(s) within the past 999 days
      OR
      ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days
   AND
   b. ONE of the following:
      i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
      OR
      ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria