# Vyepti (eptinezumab-jjmr)
## PAM – 030

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| **Iowa Medicaid Program** | Prior Authorization | **Effective Date** | 01/01/2021 |
| **Revision Number** | 5 | **Last Reviewed** | 04/18/2025 |
| **Reviewed By** | Medicaid Medical Director | **Next Review** | 01/16/2026 |
| **Approved By** | Medicaid Clinical Advisory Committee | **Approved Date** | 12/23/2020 |

## Overview

| | |
|---|---|
| Medication: [1] | eptinezumab-jjmr |
| Brand Name: | Vyepti® |
| Pharmacologic Category: | Antimigraine agent; calcitonin gene-related peptide (CGRP) antagonist |
| FDA-Approved Indication(s): | Indicated for the preventive treatment of migraine in adults |
| How Supplied: | Single-dose vial, 100 mg/mL |
| Dosage and Administration: | • Intravenous (IV) infusion<br>• Recommended dosage is 100 mg every 3 months<br>• Some patients may benefit from a dosage of 300 mg every 3 months |
| Benefit Category: | Medical |

## Descriptive Narrative

Migraine is a neurological disorder characterized by attacks of throbbing, often unilateral headaches that are exacerbated by physical activity and associated with symptoms such as nausea, vomiting, and/or light and sound sensitivity. Migraine is widespread, with a one-year period prevalence of 18 percent in women and 6 percent in men, and prevalence peaks between the ages of 25 and 55. Among neurological conditions, it ranks second worldwide in terms of years lost to disability and is associated with increased risk for a range of common health conditions, including anxiety, depression, asthma, epilepsy, and stroke. In addition to the substantial burden of illness, migraine is also associated with a considerable financial burden, with annual total costs estimated at $27 billion in the United States.[2]

Calcitonin gene-related peptide (CGRP) is a blood-brain barrier impermeant neuropeptide that is expressed throughout the nervous system, and in high concentrations in the several regions of the brain. CGRP is increased during

migraine, causing vasodilation, pro-inflammatory response, and is involved in pain signaling. Interfering with CGRP allows an opportunity to target a cause of migraine headache. There are two classes of CGRP inhibitors—monoclonal antibodies (mAbs) and small molecule antagonists (gepants).[3]

Vyepti® is a monoclonal antibody, CGRP antagonist indicated for the preventive treatment of migraine in adults. The drug is an infused agent that requires administration by a healthcare professional at 3-month intervals.

## ICHD-3 criteria for migraine and chronic migraine[4]

**Migraine**

(A) At least five attacks fulfilling criteria B-D.
(B) Headache attacks lasting 4 – 72 hours (when 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 diagnosis.

**Chronic Migraine**

(A) Migraine-like or tension-type-like headache on ≥ 15 days/month for > 3 months that fulfill criteria B and C.
(B) Occurring in a patient who has had at least five attacks fulfilling criteria B-D for migraine without aura and/or criteria B and C for migraine with aura.
(C) On ≥ 8 days/month for > 3 months, fulfilling any of the following:
    1. Criteria C and D for migraine without aura.
    2. Criteria B and C for 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 diagnosis.

**Medication-Overuse Headache**

(A) Headache occurring on ≥ 15 days/month in a patient with a preexisting headache disorder.
(B) Regular overuse for > 3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache, with medication overuse defined as:
    1. Ten or more days/month for ergot derivatives, triptans, opioids, combination analgesics‡, and a combination of drugs from different classes that are not individually overused.
    2. Fifteen or more days/month for nonopioid analgesics, acetaminophen, and NSAIDS.
(C) Not better accounted for by another diagnosis.

** ICHD-3, International Classification of Headache Disorders, 3rd edition*
*‡ Drugs of 2 or more classes, each with analgesic effect (e.g., acetaminophen + codeine) or acting as adjuvants (e.g., caffeine)*

## Guidelines

The American Headache Society published a position statement in 2024 regarding therapies targeting calcitonin gene-related peptide (CGRP) for the prevention of migraine.[5]

**AHS Position Statement:** The CGRP-targeting migraine therapies are a first-line option for migraine prevention. Initiation of these therapies should not require trial and failure of non-specific migraine preventive medication approaches.

**Updated recommendations for migraine prevention (AHS, 2024)**

A. Diagnosis of episodic migraine with or without aura (4–14 MMDs) based upon ICHD-3 with at least moderate disability (MIDAS score ≥11 or HIT-6 score >50). Treatments to consider include:
   1. Topiramate
   2. Divalproex sodium/valproate sodium
   3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
   4. Candesartan
   5. Tricyclic antidepressant: amitriptyline, nortriptyline
   6. Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
   7. Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence
   8. Monoclonal antibodies targeting CGRP or its receptor including erenumab, fremenezumab, galcanezumab, or eptinezumab
   9. Small-molecules targeting the CGRP receptor ("gepants") including atogepant and rimegepant

B. Diagnosis of chronic migraine with or without aura (≥15 MHDs) based upon ICHD-3. Treatments to consider include:
   1. Topiramate
   2. Divalproex sodium/valproate sodium
   3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
   4. Candesartan
   5. Tricyclic antidepressant: amitriptyline, nortriptyline
   6. Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
   7. Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence
   8. OnabotulinumtoxinA
   9. Monoclonal antibodies targeting CGRP or its receptor including erenumab, fremenezumab, galcanezumab, or eptinezumab
   10. Small-molecules targeting the CGRP receptor ("gepants") including atogepant

Abbreviations: **AAN**, American Academy of Neurology; **CGRP**, calcitonin gene-related peptide; **HIT-6**, six-item Headache Impact Test; **ICHD-3**, International Classification of Headache Disorders, third edition; **MMDs/MHDs**, monthly migraine/headache days; **MIDAS**, Migraine Disability Assessment.

## Migraine Disability Assessment Test

### The Migraine Disability Assessment Test

The **MIDAS** (Migraine Disability Assessment) questionnaire was put together to help you measure the impact your headaches have on your life. The information on this questionnaire is also helpful for your primary care provider to determine the level of pain and disability caused by your headaches and to find the best treatment for you.

**INSTRUCTIONS**

Please answer the following questions about ALL of the headaches you have had over the last 3 months. Select your answer in the box next to each question. Select zero if you did not have the activity in the last 3 months. Please take the completed form to your healthcare professional.

_____ 1. On how many days in the last 3 months did you miss work or school because of your headaches?

_____ 2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)

_____ 3. On how many days in the last 3 months did you not do household work (such as housework, home repairs and maintenance, shopping, caring for children and relatives) because of your headaches?

_____ 4. How many days in the last 3 months was your productivity in household work reduced by half of more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)

_____ 5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

_____ Total (Questions 1-5)

**What your Physician will need to know about your headache:**

_____ A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.)

_____ B. On a scale of 0 - 10, on average how painful were these headaches? (where 0=no pain at all, and 10= pain as bad as it can be.)

**Scoring:** After you have filled out this questionnaire, add the total number of days from questions 1-5 (ignore A and B).

| MIDAS Grade | Definition | MIDAS Score |
|---|---|---|
| I | Little or No Disability | 0-5 |
| II | Mild Disability | 6-10 |
| III | Moderate Disability | 11-20 |
| IV | Severe Disability | 21+ |

**If Your MIDAS Score is 6 or more, please discuss this with your doctor.**

## Criteria

Prior authorization is required.

Vyepti® is considered medically necessary when **ALL** of the following are met:

1. Member is 18 years of age or older; **AND**
2. Member has been diagnosed with one of the following *(see ICHD-3 criteria in Descriptive Narrative section)*:
    a. Chronic migraine – defined as a headache occurring on 15 or more days per month for more than 3 months which, on at least 8 days per month, has features of a migraine headache; **OR**
    b. Episodic migraine – defined as at least 4 and fewer than 15 migraine days per month and fewer than 15 headache days per month on average during the previous 3-month period; **AND**
3. The member has tried and failed at least two of the following oral migraine preventative therapies, each for at least 8 weeks and from different therapeutic classes *(unless clinically significant adverse effects are experienced or all are contraindicated):*
    a. Antiepileptic (e.g., divalproex sodium, sodium valproate, topiramate); **AND/OR**
    b. Beta-blocker (e.g., metoprolol, propranolol, timolol); **AND/OR**
    c. Candesartan; **AND/OR**
    d. Tricyclic antidepressant (e.g., amitriptyline, nortriptyline); **AND/OR**
    e. Serotonin-norepinephrine reuptake inhibitor (e.g., venlafaxine, duloxetine); **AND**
4. If member is receiving botulinum toxin injection* for prophylaxis of chronic migraine, treatment with botulinum toxin must be discontinued prior to starting therapy with Vyepti®; **AND**
5. Member will not initiate botulinum toxin injection* for migraine prophylaxis while treated with Vyepti®; **AND**
6. Vyepti® will not be used in combination with another calcitonin gene-related peptide (CGRP) antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Aimovig®, Ajovy®, Emgality®, Nurtec ODT®, Qulipta®, Zavzpret®, etc.); **AND**
7. Dose does not exceed 100 mg every 3 months.

** Botulinum toxin injection requires prior authorization*

Vyepti® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Vyepti® will not be used in combination with another calcitonin gene-related peptide (CGRP) antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Aimovig®, Ajovy®, Emgality®, Nurtec ODT®, Qulipta®, Zavzpret®, etc.); **AND**
3. Either A or B applies:
    A. First request for reauthorization and one of the following applies (a or b):
        a. Member has experienced a positive response to therapy as demonstrated by a reduction in migraine days per month from baseline, and as documented by the Migraine Disability Assessment Tool (coverage may be authorized for an additional 12 months); **OR**
        b. Clinical efficacy has not been demonstrated at the 100 mg dose and provider indicates dose to be increased to 300 mg every 3 months (coverage may be authorized for an additional 6 months at the 300 mg dosage); **OR**
    B. Subsequent request for reauthorization and one of the following applies (a or b):
        a. Member continues to experience a positive clinical response to therapy and dose does not exceed 300 mg every 3 months (coverage may be continued for an additional 12 months); **OR**
        b. Clinical efficacy not achieved/maintained at 100 mg dose and provider indicates dose to be increased to 300 mg every 3 months (coverage may be continued for an additional 6 months after dose increase).

## Approval Duration and Quantity Limits

| | Initial Authorization | Subsequent Authorization(s) |
|---|---|---|
| Approval Duration | 6 months | 12 months (exception: only 6 months for first authorization after a dose increase) |
| Quantity Limits | 100 mg every 3 months | Up to 300 mg every 3 months |

## Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

| HCPCS | Description |
|---|---|
| J3032 | Injection, eptinezumab-jjmr, 1 mg |

| ICD-10 | Description |
|---|---|
| G43 – G43.919 | Migraine |

| NDC (Strength) | Labeler | Dosage | Pkg Size | Pkg Qty | Units/ Pkg |
|---|---|---|---|---|---|
| 67386-0130-51 (single-dose vial, 100 mg/mL) | Lundbeck Seattle BioPharmaceuticals, Inc. (67386) | 1 mg | 1 | EA | 100 |

## Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

## References

[1] Vyepti® prescribing information (08/2024). Lundbeck Seattle BioPharmaceuticals, Inc.: Bothell, WA. Available online: www.vyeptihcp.com. Accessed November 3, 2024.

[2] Ailani, J, Burch, RC, Robbins, MS; the Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. 2021; 61: 1021– 1039. PMID 34160823.

[3] Ray JC, Kapoor M, Stark RJ, *et al.* Calcitonin gene related peptide in migraine: current therapeutics, future implications and potential off-target effects. *Journal of Neurology, Neurosurgery & Psychiatry* 2021;92:1325-1334. PMID 33495299.

[4] Headache Classification Committee of the International Headache Society (IHS): The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1-211. doi: 10.1177/0333102417738202. PMID: 29368949.

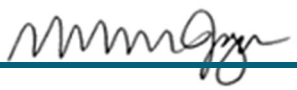
[5] Charles AC, Digre KB, Goadsby PJ, Robbins MS, Hershey A; American Headache Society. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache. 2024 Apr;64(4):333-341. Epub 2024 Mar 11. PMID: 38466028.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

## Criteria Change History

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 04/18/2025 | CAC | Annual review. Updated guidelines section with American Headache Society (AHS) position statement regarding therapies targeting calcitonin gene-related peptide (CGRP) for the prevention of migraine. Added candesartan, duloxetine, and nortriptyline to criteria as first-line treatment options.<br>Updated continuation criteria to distinguish between first and subsequent reauthorization requests.<br>Changed authorization duration after dose increase from 3- to 6-month period. | 5 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

## Criteria Change History *(continued)*

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 01/19/2024 | CAC | Annual review. Added Zavzpret® (zavagepant) to list of preventive CGRP therapies not to be used in combination with Vyepti®. | 4 |
| **Signature** William (Bill) Jagiello, DO | | | |
| **Change Date** | **Changed By** | **Description of Change** | **Version** |
| 01/20/2023 | CAC | Updated statistics and disease overview in Descriptive Narrative. Added ICHD-3 criteria for migraine. Changed initial authorization period from 3 months to 6 months. Criteria listed under "not considered medically necessary" was incorporated into main criteria section. Added summary of American Headache Society Consensus Statement to the Guidelines. | 3 |
| **Signature** William (Bill) Jagiello, DO | | | |
| **Change Date** | **Changed By** | **Description of Change** | **Version** |
| 01/21/2022 | CAC | Annual review. | 2 |
| **Signature** William (Bill) Jagiello, DO | | | |
| **Change Date** | **Changed By** | **Description of Change** | **Version** |
| 01/15/2021 | CAC | Criteria implementation. | 1 |
| **Signature** William (Bill) Jagiello, DO | | | |

CAC = Medicaid Clinical Advisory Committee