WellMed Doctors helping patients for more than 25 years	**Effective Date: 01/02/2024**	**Revision Date(s):** 01/14/21, 03/07/23, 12/19/23
Department: PHARMACY	**MMC Review/ Approval Date(s):** 02/09/21, 12/27/23	**Page(s): 12**

Policy Number: 042.002

Title: Coverage Determination Policy for Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist - Vyepti (Eptinezumab-Jjmr)

Regions: ☒ **Texas** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

WellMed Coverage Determination Policies are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support WellMed coverage decision making. WellMed may modify these Policy Guidelines at any time. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the WellMed Coverage Determination Policies is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

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Coverage Policy Number: 042.002

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Step Therapy Criteria

This policy supplements Medicare NCDs, LCDs, and manuals for the purpose of determining coverage under Medicare Part B medical benefits. This policy implements a prior authorization requirement for prescriptions or administrations of medical benefit injectables only. A member cannot be required under this policy to change a current drug/product. For the purposes of this policy, a current drug/product means the member has a paid claim for the drug/product within the past 365 days. For example, a new plan member currently using a particular drug/product will not be required to switch to the preferred drug/ product upon enrollment. Similarly, an existing member currently using a particular drug/product will not be required to change drugs/products in the event this policy is updated.

Step Therapy is applicable to members who have MAPD plans only

Migraine Prophylaxis – Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist:

(Aimovig, Ajovy, Emgality, Vyepti)

Preferred Drug(s)/Product(s): Aimovig, Ajovy, Emgality

Non-Preferred Drug(s)/Product(s): Vyepti

Vyepti Non-Preferred Product Step Therapy Criteria

Vyepti may be covered when ANY of the criteria listed below are met:

A. Trial of at least 3 months of therapy each, to two of the preferred drugs (e.g. Aimovig, Emgality), resulting in minimal clinical response to therapy

   OR

B. History of contraindication, intolerance, or adverse event(s) to two of the preferred drugs (e.g. Aimovig, Emgality)

   OR

C. Continuation of prior therapy within the past 365 days.

Initial/New Requests

Vyepti (Eptinezumab-Jjmr) is proven and medically necessary for the preventive treatment of migraines in adults.

WellMed Medical Management will cover **Vyepti (Eptinezumab-Jjmr)** as medically necessary for the **preventive treatment of migraines** in adults when **ALL** of the following criteria are met:

A. Diagnosis of migraine consistent with The International Classification of Headache Disorders, 3rd edition

B. ONE of the following:

I. Both of the following:
   a. 4 to 7 migraine days per month; and
   b. One of the following:
      i. Less than 15 headache days per month; or
      ii. Provider attests this is the member's predominant headache diagnosis (i.e., primary driver of headaches is not a different, non-migrainous condition)

OR

II. Greater than or equal to 8 migraine days per month

C. Trial and failure (after a trial of at least two months), contraindication, or intolerance to TWO of the following prophylactic therapies from the list below:

I. Amitriptyline (Elavil)
II. One of the following beta-blockers: atenolol, metoprolol, nadolol, propranolol, or timolol
III. Divalproex sodium (Depakote/Depakote ER)
IV. OnabotulinumtoxinA (Botox) [trial of at least 2 quarterly injections (6 months)]
V. Topiramate (Topamax)
VI. Venlafaxine (Effexor/Effexor XR)
VII. Candesartan (Atacand)

D. Trial and failure (after a trial of at least three months), contraindication, or intolerance to TWO of the following therapies used for the preventive treatment of migraines:

I. Aimovig (erenumab-aooe)
II. Emgality (galcanezumab-gnlm) - 120 mg strength for prophylaxis
III. Nurtec ODT (rimegepant)

E. Medication will NOT be used in combination with another biologic CGRP antagonist or inhibitor used for the preventive treatment of migraines (e.g., Aimovig, Emgality, Nurtec ODT)

F. Dosing is in accordance with the FDA approved labeling

G. Vyepti will be approved for duration no more than 6 months.

Renewal/Continuation of Therapy Requests

WellMed Medical Management will cover renewal or continuation of therapy requests for Vyepti (Eptinezumab-Jjmr) if the following criteria are met:

A. Documentation of a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity

B. Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for the preventive treatment of migraines (e.g., Aimovig, Emgality, Nurtec ODT)

C. Dosing is in accordance with the FDA approved labeling.

D. Vyepti will be approved for duration no more than 12 months.

NOTE:

Vyepti is unproven and not medically necessary for:

- *Acute attack of migraine*
- *Episodic cluster headache*

FDA Approved Dose and Indication

Approved Indication	Approved Dosing
Preventive treatment of migraine	• 100 mg intravenous every 3 months • Some patients may benefit from 300 mg every 3 months

NOTE: Evaluate efficacy after a minimum of 6 months of treatment with quarterly administered medications

General Background

Eptinezumab-Jjmr (Vyepti) is a humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor. It is approved for the preventive treatment of migraine in adults.

Package insert and FDA approval label does not require treatment failure with other available migraine prophylaxis before initiation of Vyepti.

However, to achieve cost-effective care, the American Headache Society (AHS) 2018 statement highlights the importance of understanding and close monitoring of the indications for initiating treatment with anti-CGRP mAbs. The use of evidence-based treatments antiepileptic drugs (divalproex sodium, valproate sodium, topiramate); beta-blockers (metoprolol, propranolol, timolol); antidepressants (amitriptyline, venlafaxine) and OnabotulinumtoxinA are important for the success of migraine prevention.

Warnings

Eptinezumab-Jjmr has no black box warning reported. However, angioedema, urticaria, facial flushing, and rash have occurred in patients with hypersensitivity to eptinezumab or any component of the formulation. Some patients with exposure to pharmaceutical products containing polysorbate 80 may experience delayed hypersensitivity.

Clinical Evidence

The efficacy of VYEPTI was evaluated as a preventive treatment of episodic migraine. The study was a randomized, double-blinded, multicenter, placebo-controlled studies. Adults with a history of episodic migraine (4 to 14 headache days per month, of which at least 4 were migraine days) were randomize. A total of 222 patients received placebo, 221 patients received 100 mg VYEPTI and 222 patients received 300 mg VYEPTI every 3 months for 12 months.
Patients with a history of cardiovascular disease (hypertension, ischemic heart disease), neurological disease, or cerebrovascular disease were excluded from the study. The primary efficacy endpoint was the change from baseline in mean monthly migraine days over 1 to 3 months. Secondary efficacy endpoints included the percentages of patients with 50% or greater, and 75% or greater reductions from baseline in monthly migraine days over 1 to 3 months.
Subjects in VYEPTI treatment achieved statistically significant primary efficacy endpoint compared to placebo. The change from baseline (100 mg VYEPTI: -3.9, p-value 0.018), (300 mg VYEPTI: -4.3, p-value < 0.001) and placebo -3.2: p-value = 0.0001. The study concluded that eptinezumab (100 mg or 300 mg) significantly reduced migraine frequency, was well tolerated, and had an acceptable safety profile when used for the preventive treatment of migraine in adults with episodic migraine.

The second study was a randomized, double-blinded, multicenter, placebo-controlled studies. The efficacy of VYEPTI was evaluated as a preventive treatment of chronic migraine. Adults with a history of chronic migraine (15 to 26 headache days per month, of which at least 8 were migraine days) were randomized. A total of 366 patients received placebo, 356 patients received 100 mg VYEPTI and 350 patients received 300 mg VYEPTI every 3 months for 6 months.
Patients with a history of cardiovascular disease (hypertension, ischemic heart disease), neurological disease, or cerebrovascular disease were excluded from the study. The primary efficacy endpoint was the change from baseline in mean monthly migraine days over 1 to 3 months. Secondary efficacy endpoints included the percentages of patients with 50% or greater, and 75% or greater reductions from baseline in monthly migraine days over 1 to 3 months.
Subjects in VYEPTI treatment achieved statistically significant primary efficacy endpoint compared to placebo. The change from baseline (100 mg VYEPTI: -7.7, p-value < 0.001), (300 mg VYEPTI: -8.2, p-value < 0.001) and placebo -5.6. The study concluded that eptinezumab (100 mg or 300 mg) provided sustained migraine preventive benefit and demonstrated an acceptable safety profile in patients with chronic migraine.

HCPCS Code

HCPCS Code	J3032: Eptinezumab-Jjmr, 1mg
Available Dosage Form	Injection: 100 mg/1 ml in a single-dose vial
Route of Administration	Intravenous

Acronyms

CGRP = Calcitonin gene-related peptide

NCD = National Coverage Determinations

LCD = Local Coverage Determinations

CMS = Centers for Medicare and Medicaid Services

AHS = American Headache Society

mAbs = Monoclonal antibody

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