eptinezumab-jjmr (Vyepti™‡)

Medicare Advantage Medical Policy #MA-128
Original Effective Date: 10/01/2025
Current Effective Date: 10/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider Vyepti™‡ (eptinezumab-jjmr) to be **eligible for coverage**** when the patient selection criteria are met**.**

Patient Selection Criteria

Coverage eligibility for Vyepti (eptinezumab-jjmr) will be considered when the following criteria are met:

- The requested drug will be used for the prevention of migraine headaches; AND
- Patient is 18 years of age or older; AND
- Patient has greater than or equal to 4 migraine headache days per month (prior to initiating a migraine-preventive medication); AND
- The requested dose will not exceed 300 mg every 3 months.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of Vyepti (eptinezumab-jjmr) for the prevention of migraines when the patient has fewer than 4 migraine headache days per month to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of Vyepti (eptinezumab-jjmr) for indications that have not been approved by the FDA or for patients younger than 18 years of age to be **investigational.***

Background/Overview

The calcitonin gene-receptor (CGRP) antagonists are a class of drugs for the prevention and treatment of migraine headaches and can be divided into two sub-classes: gepants and monoclonal antibodies. The gepants include the oral small-molecule agents: Ubrelvy (ubrogepant), Nurtec ODT (rimegepant), Qulipta (atogepant), and Zavzpret (zavegepant). The monoclonal antibodies include

the injectable agents: Aimovig, Ajovy, Emgality, and Vyepti. All of these products work by binding either to the CGRP receptor or to the ligand to block the effects of CGRP, a protein with potent vasodilating actions that is thought to be associated with many of the phenomenon occurring with migraine attack (e.g. aura, pain, photophobia, and nausea). Aimovig, Ajovy, Emgality, and Vyepti are indicated for the prevention of migraine headaches while Ubrelvy, Nurtec ODT, and Zavzpret are indicated for the acute treatment of migraine headaches. Nurtec ODT and Qulipta are also indicated for the preventive treatment of migraine. Emgality is also approved to treat episodic cluster headaches and is the only CGRP inhibitor with this indication. The recommended dose of Vyepti is 100 mg administered by intravenous infusion every 3 months. However, some patients may benefit from a dosage of 300 mg every 3 months.

Migraine
Migraine is a common, chronic condition marked by paroxysmal, unilateral attacks of moderate to severe throbbing headache which is aggravated by routine physical activity and associated with nausea, vomiting, and/or photophobia and phonophopbia. Migraine headache episodes typically last 4 to 72 hours if untreated. Migraine affects approximately 13% of adults in the United States with three times more women affected than men. There are two major subtypes of migraine: migraine with aura and without aura. In up to 30% of patients, aura precedes migraine headache and is typically characterized by any combination of visual, hemisensory, or language abnormalities, with the most common being visual. Migraines have been defined as chronic or episodic. Chronic migraine is described by the International Headache Society as headache occurring on $\geq$ 15 days per month for more than 3 months, which has the features of migraine headache on $\geq$ 8 days per month. Episodic migraine is characterized by headaches that occur < 15 days per month. Patients with episodic migraine may transform to chronic migraine over time at a rate of about 2.5% of patients per year. Potential strategies for preventing migraine transformation include preventing and treating headaches, lifestyle modifications, or effective management of comorbidities. Episodic migraine is more common than chronic migraine; however, chronic migraine is associated with a markedly greater personal and societal burden.

The American Academy of Neurology (AAN) published an evidence-based guideline update for the prevention of episodic migraine in 2012. These guidelines recommend divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, and timolol as effective for migraine prevention and suggest that they should be offered to patients with migraine to reduce migraine attack frequency and severity. The guidelines have not been updated to address the CGRP antagonists. Guidelines also support the use of angiotensin receptor blockers, angiotensin converting enzyme inhibitors, tricyclic antidepressants, and other antidepressants as preventative therapies. Botox is indicated only for the prophylaxis of chronic migraine in adults and is administered intramuscularly once every 12 weeks.

The American Headache Society published a position statement update in 2024 regarding therapies targeting CGRP for the prevention of migraine. This update recommends that the CGRP-targeting therapies be considered as a first-line approach for migraine prevention along with previous first-

line treatments without a requirement for prior failure of other classes of migraine preventive treatment.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Vyepti was approved in February 2020 for the preventive treatment of migraine in adults.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Vyepti was evaluated as a preventive treatment of episodic and chronic migraine in two randomized, multicenter, placebo-controlled studies, both with 6-month double-blind periods: one study in patients with episodic migraine (Study 1) and one study in patients with chronic migraine (Study 2). Vyepti was administered by intravenous infusion every 3 months in both studies; however, the primary endpoint was measured at 12 weeks.

Study 1 included adults with a history of episodic migraine (4-14 headache days per month, of which at least 4 were migraine days). A total of 665 patients were randomized to receive placebo (n = 222), 100 mg Vyepti (n = 221), or 300 mg Vyepti (n = 222) every 3 months for 12 months. Patients were allowed to use concurrent acute migraine or headache medications, including migraine-specific medications during the trial. The study excluded patients with a history of cardiovascular disease, neurological disease, or cerebrovascular disease. The primary efficacy endpoint was the change from baseline in mean monthly migraine days over months 1-3. Vyepti treatment demonstrated statistically significant improvements compared to placebo with a change from baseline of -3.9 monthly migraine days in the Vyepti 100 mg group, -4.3 monthly migraine days in the Vyepti 300 mg group and -3.2 monthly migraine days in the placebo group.

Study 2 included adults with a history of chronic migraine (15-26 headache days per month, of which at least 8 were migraine days). A total of 1072 patients were randomized and received placebo (n = 366), 100 mg Vyepti (n=356), or 300 mg Vyepti (n = 350) every 3 months for 6 months. Patients were allowed to use and to continue an established stable regimen of acute migraine or headache preventive medication (except Botox). Patients with a dual diagnosis of chronic migraine and medication overuse headache attributable to acute medication overuse were included in the study population. Patients using opioids or butalbital-containing products greater than 4 days per month were not allowed. Patients with a history of cardiovascular disease, neurological disease, or cerebrovascular disease were also excluded. The primary efficacy endpoint was the change from baseline in mean monthly migraine days over months 1-3. Vyepti treatment demonstrated

statistically significant improvements compared to placebo with a change from baseline of -7.7 days in the Vyepti 100 mg group, -8.2 days in the Vyepti 300 mg group, and -5.6 days in the placebo group.

References

1. Vyepti [package insert]. Lundbeck Pharmaceuticals. Bothell, WA. Updated March 2025.
2. Charles, AC, Digre KB, Goadsby PJ, et al. 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;64(4):333-341.

Policy History

Original Effective Date: 10/01/2025
Current Effective Date: 10/01/2025
07/15/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 07/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3032
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.