Drug Coverage Policy

Effective Date.....7/1/2025
Coverage Policy Number.....IP0506
Policy Title..... Vyepti

Migraine – Calcitonin Gene-Related Peptide Inhibitors – Vyepti

- Vyepti® (eptinezumab-jjmr intravenous infusion – Lundbeck)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
Vyepti, a calcitonin gene-related peptide (CGRP) inhibitor, is indicated for the **preventive treatment of migraine** in adults.[1]

The recommended dosage is 100 mg administered by intravenous (IV) infusion over approximately 30 minutes once every 3 months; however, some patients may benefit from a dosage of 300 mg IV once every 3 months.[1] Vyepti must be administered by a healthcare provider.

Disease Overview
Migraines have been defined as chronic or episodic. Chronic migraine is described by the International Headache Society as headache occurring on ≥ 15 days/month for > 3 months and has the features of migraine headache on ≥ 8 days/month.[2] Episodic migraine is characterized by headaches that occur < 15 days/month.[3,4] Episodic migraine is more common than chronic migraine; however, chronic migraine is associated with a markedly greater personal and societal burden.

Guidelines
An updated assessment of the **preventive and acute treatment of migraine** by the **American Headache Society** (AHS) [2018; update 2021] reaffirms previous migraine guidelines.[5,6] Patients with migraine should be considered for preventive treatment in the following situations: when attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks (≥ 4 monthly headache days); at least moderate disability (Migraine Disability Assessment [MIDAS] score ≥ 11 or six-item Headache Impact Test [HIT-6] score > 50); contraindication to, failure, overuse, or adverse events with acute treatments; or patient preference. Before developing a preventive treatment plan, the appropriate use (e.g., drug type, route and timing of administration, frequency) of acute treatments should be initiated and coupled with education and lifestyle modifications. All patients with migraine should be offered a trial of acute treatment. Based on the level of evidence for efficacy and the American Academy of Neurology scheme for classification of evidence, the following oral treatments have established efficacy and should be offered for migraine prevention: antiepileptic drugs (**divalproex sodium, valproate sodium, topiramate** [not for women of childbearing potential without a reliable method of birth control]); beta-blockers (**metoprolol, propranolol, timolol**); and **frovatriptan** (for short-term preventive treatment of menstrual migraine). The following treatments are probably effective and should be considered for migraine prevention: antidepressants (**amitriptyline, venlafaxine**); beta-blockers (**atenolol, nadolol**); and angiotensin receptor blockers (**candesartan**).

The **AHS** issued an update to their position statement (2024) specifically regarding therapies targeting CGRP for the prevention of migraine.[7] The evidence for the efficacy, tolerability, and safety of CGRP-targeting migraine preventive therapies (specifically, the monoclonal antibodies: Aimovig® [erenumab-aooe subcutaneous {SC} injection], Ajovy® [fremanezumab-vfrm SC injection], Emgality® [galcanezumab-gnlm SC injection], and Vyepti), and the gepants: Nurtec® ODT (rimegepant orally disintegrating tablets) and Qulipta® (atogepant tablets) is substantial and consistent across different individual CGRP-targeting treatments. Extensive "real-world" clinical experience corroborates clinical trials. This data indicates that the efficacy and tolerability of CGRP-targeting therapies are equal to or greater than those of previous first-line therapies. The CGRP-targeting therapies should 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. Additionally, Botox® (onabotulinumtoxinA SC injection) is considered a first-line therapy for prevention of chronic migraine.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Vyepti. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the

established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Vyepti is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Migraine Headache Prevention.** Approve Vyepti for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient has ≥ 4 migraine headache days per month (prior to initiating a migraine-preventative medication); AND

C) If the patient is currently taking Vyepti, the patient has had a significant clinical benefit from the medication as determined by the prescriber; AND
Note: Examples of significant clinical benefit include a reduction in the overall number of migraine days per month or a reduction in number of severe migraine days per month from the time that Vyepti was initiated.

D) Preferred product criteria is met for the product as listed in the below tables.

Dosing. Approve up to 300 mg administered by intravenous infusion once every 3 months.

Employer Plans:

Product	Criteria
Vyepti (eptinezumab-jjmr)	Failure, contraindication, or intolerance to **TWO** of the following: 1. **Aimovig** (erenumab-aooe) [may require prior authorization] 2. **Ajovy** (fremanezumab-vfrm) [may require prior authorization] 3. **Emgality** (galcanezumab-gnlm) [may require prior authorization]

Individual and Family Plans:

Product	Criteria
Vyepti (eptinezumab-jjmr)	Failure, contraindication, or intolerance to **Emgality** (galcanezumab-gnlm) [may require prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Vyepti for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Acute Treatment of Migraine.** Clinical data are currently lacking for the use of Vyepti in the acute treatment of migraine.

2. **Cluster Headache, Treatment or Prevention.** Clinical data are currently lacking for the use of Vyepti in patients with cluster headache. The pivotal trials of Vyepti excluded patients with this condition.[8,9]

3. **Concurrent use with another calcitonin gene-related peptide (CGRP) inhibitor being prescribed for migraine headache prevention.**
   Note: CGRP inhibitors that are indicated for migraine headache prevention include Aimovig (erenumab-aooe subcutaneous injection), Ajovy (fremanezumab-vfrm subcutaneous injection), Emgality (galcanezumab-gnlm subcutaneous injection), and Qulipta (atogepant tablets). Aimovig, Ajovy, Emgality, and Vyepti are injectable CGRP inhibitors and have not been studied for use in combination with another agent in the same class.[1,10-12] Qulipta is an oral CGRP inhibitor for the preventive treatment of migraine in adults.[13]

4. **Concurrent use with Nurtec ODT (rimegepant sulfate orally disintegrating tablet) when used as a preventive treatment of migraine.** Nurtec ODT is an oral CGRP inhibitor for the acute treatment of migraine and for the preventive treatment of episodic migraine in adults.[14]

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

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

References

1. Vyepti® injection for intravenous use [prescribing information]. Bothell, WA: Lundbeck; October 2022.
2. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition. *Cephalalgia*. 2018;38:1-211.
3. MacGregor EA. In the clinic. Migraine. *Ann Intern Med*. 2017;166(7):ITC49-ITC64.
4. Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. *Headache*. 2015;52:103-122.
5. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
6. Ailani J, Burch RC, Robbins MS, on behalf of 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;00:1–19.
7. Charles AC, Digre KB, Goadsby PJ, et al; 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 Mar 11. Epub ahead of print.
8. Ashina M, Saper J, Cady R, et al. Eptinezumab in episodic migraine: a randomized, double-blind, placebo-controlled study (PROMISE-1). *Cephalalgia*. 2020;40(3):241-254.

9. Data on file. Eptinezumab-jjmr Pre-Approval Dossier, version 1.7. Lundbeck, Inc.; Deerfield, IL; received on March 2, 2020.
10. Aimovig® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; October 2022.
11. Ajovy® injection for subcutaneous use [prescribing information]. North Wales, PA: Teva; September 2021.
12. Emgality® injection for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly; May 2022.
13. Qulipta® tablets [prescribing information]. Madison, NJ: AbbVie; April 2023.
14. Nurtec® ODT [prescribing information]. New Haven, CT: Biohaven; April 2022.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Eptinezumab" to "Migraine – Calcitonin Gene-Related Peptide Inhibitors – Vyepti." **Migraine Headache Prevention:** The criteria requiring a patient to have tried botox or at least two standard prophylactic (preventive) pharmacologic therapies, each from a different pharmacologic class, and requiring that a patient has had inadequate efficacy or adverse event(s) severe enough to warrant discontinuation of those therapies have been removed. **Updated** the requirement from "prior to initiating Vyepti" to "prior to initiating a migraine-preventive medication," regarding patients needing to have 4 or more migraine headache days per month. **Removed** Aimovig and Ajovy as a preferred product step requirement for Individual and Family Plans. **Authorization Duration: Updated** initial approval duration for Migraine Headache Prevention to 12 months from 6 months.	07/15/2024
Annual Revision	**No criteria changes**	7/1/2025

The policy effective date is in force until updated or retired.