UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Migraine – Calcitonin Gene-Related Peptide Inhibitors – Vyepti Utilization Management Medical Policy

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

REVIEW DATE: 04/16/2025

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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Vyepti. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vyepti is recommended in those who meet the following criteria:

FDA-Approved Indication

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

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vyepti is not recommended in the following situations:

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]

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vyepti® injection for intravenous use [prescribing information]. Bothell, WA: Lundbeck; March 2025.
2. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition. *Cephalalgia*. 2018;38:1-211.
3. Damen JAA, Yang B, Idema DL, et al. Comparative effectiveness of pharmacologic treatments for the prevention of episodic migraine headache: A systematic review and network meta-analysis for the American College of Physicians. *Ann Intern Med*. 2025;178(3):369-380..
4. Burch R. Chronic migraine in adults. *JAMA*. 2025;333(5):423-424.
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;64(4):333-341.
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; March 2025.
11. Ajovy® injection for subcutaneous use [prescribing information]. North Wales, PA: Teva; March 2025.
12. Emgality® injection for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly; March 2025.
13. Qulipta® tablets [prescribing information]. Madison, NJ: AbbVie; March 2025.
14. Nurtec® ODT [prescribing information]. New York, NY: Pfizer; March 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Policy Name:** The initial descriptor "Migraine" was added to the policy name. **Migraine Headache Prevention:** The note with examples of standard prophylactic (preventive) pharmacologic therapies was expanded to include the statement: Of note, "standard prophylactic (preventive) pharmacologic therapies" do **not** include oral or injectable CGRP inhibitors.	05/24/2023
Selected Revision	**Migraine Headache Prevention:** • The note with standard prophylactic (preventive) pharmacologic therapies was changed to remove "Examples of" and to remove the statement: Of note, "standard prophylactic (preventive) pharmacologic therapies" do **not** include oral or injectable CGRP inhibitors. • A new statement was added to the note: A patient who has already tried an oral or injectable calcitonin gene-related peptide (CGRP) inhibitor indicated for the prevention of migraine or Botox (onabotulinumtoxinA injection) for the prevention of migraine is not required to try two standard prophylactic pharmacologic therapies.	08/02/2023
Early Annual Revision	**Migraine Headache Prevention:** The criteria requiring a patient to have tried at least two standard prophylactic (preventive) pharmacologic therapies, each from a different pharmacologic class, and requiring that a patient have had inadequate efficacy or adverse event(s) severe enough to warrant discontinuation of those therapies have been removed.	04/10/2024
Annual Revision	No criteria changes.	04/16/2025