

POLICY: Calcitonin Gene-Related Peptide Inhibitors – Vyepti™ (eptinezumab-jjmr injection for intravenous use – Lundbeck)

EFFECTIVE DATE: 1/1/2021

LAST REVISION DATE: 05/24/2023; SELECTED REVISION 08/02/2023

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

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); 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**). Additionally, the following treatments are possibly effective and can be considered for migraine prevention: calcium channel blockers (e.g., **verapamil**) and angiotensin converting enzyme inhibitors (e.g., **lisinopril**).^{14,15}

Five injectable preventive therapies for migraine are mentioned in the AHS consensus statement: Botox® (onabotulinumtoxinA intramuscular injection) and four monoclonal antibodies targeting CGRP (Aimovig®

[erenumab-aooe subcutaneous injection], Ajovy® [fremanezumab-vfrm subcutaneous injection], Emgality® [galcanezumab-gnlm subcutaneous injection], and Vyepti).^{5,6} The update notes that a CGRP inhibitor should only be initiated in patients who are diagnosed with migraine, have ≥ 4 migraine headache days/month, and have intolerance or inadequate response to 6-week trials of at least two traditional oral migraine preventive medications. Additional criteria apply depending on the number and severity of monthly headache days. Clinical judgment may result in an emerging treatment being added to one or more established treatments. If initiating treatment with a CGRP inhibitor in a patient already on a preventive treatment, it is appropriate to add the CGRP inhibitor to the existing regimen. When doing so, make no other changes until the effectiveness of the CGRP inhibitor is determined since the risk of interactions between traditional oral migraine preventive medications and the CGRP inhibitors is minimal or nonexistent. Making a decision regarding continuation of therapy for a CGRP inhibitor requires a trial of the medication for ≥ 3 months for those administered monthly and ≥ 6 months for those administered quarterly. Treatment should be continued only if benefits can be documented during that time (e.g., reduction in mean monthly headache days of $\geq 50\%$ relative to the pretreatment baseline) or a meaningful improvement on a validated migraine-specific patient-reported outcome measure. Since migraine may improve or remit over time, it is important to re-evaluate the therapeutic response and, if possible, taper or discontinue treatment if patient no longer meets the criteria for offering preventive treatment. However, once control is established, the decision to discontinue or taper treatment should be a shared decision between the patient and clinician.

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 the following (A, B, C, D, and E):
 - 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)** Patient has tried at least two standard prophylactic (preventive) pharmacologic therapies, each from a different pharmacologic class; AND
Note: Standard prophylactic (preventive) pharmacologic therapies include angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant, beta-blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant. 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.
 - D)** Patient meets ONE of the following (i, ii, or iii):

- i. Patient has had inadequate efficacy to both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
 - ii. Patient has experienced adverse event(s) severe enough to warrant discontinuation of both of those standard prophylactic (preventive) pharmacologic therapies, according to the prescriber; OR
 - iii. Patient meets BOTH of the following (a and b):
 - a) Patient has had inadequate efficacy to one standard prophylactic (preventive) pharmacologic therapy; AND
 - b) Patient has experienced adverse event(s) severe enough to warrant discontinuation of another standard prophylactic (preventive) pharmacologic therapy, according to the prescriber; AND
- E) 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.^{7,8}
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.^{1,9-11} Qulipta is an oral CGRP inhibitor for the preventive treatment of migraine in adults.¹²
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.¹³
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; 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. 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.
8. Data on file. Eptinezumab-jjmr Pre-Approval Dossier, version 1.7. Lundbeck, Inc.; Deerfield, IL; received on March 2, 2020.
9. Aimovig® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; October 2022.
10. Ajovy® injection for subcutaneous use [prescribing information]. North Wales, PA: Teva; September 2021.
11. Emgality® injection for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly; May 2022.
12. Qulipta® tablets [prescribing information]. Madison, NJ: AbbVie; April 2023.
13. Nurtec® ODT [prescribing information]. New Haven, CT: Biohaven; April 2022.
14. Micromedex. Merative LP. Available at: <https://www.micromedexolutions.com/>. Accessed on August 7, 2023. Search terms: lisinopril, verapamil.
15. Clinical Pharmacology. ClinicalKey. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed on August 7, 2023. Search terms: lisinopril, verapamil.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	<p>Migraine Headache Prevention:</p> <ul style="list-style-type: none"> • The criterion requiring a trial of at least one triptan was removed. • The criterion for “Patient is NOT taking a calcitonin gene-related peptide (CGRP) inhibitor for migraine headache prevention” and “Patient is switching from a different CGRP inhibitor for migraine headache prevention to Vyepti” were removed. • The criterion “Patient is currently taking Vyepti and has had a significant clinical benefit from the medication as determined by the prescriber” was changed to “If the patient is currently taking Vyepti, the patient has had a significant clinical benefit from the medication as determined by the prescriber”. <p>Conditions Not Recommended for Approval:</p> <ul style="list-style-type: none"> • To add clarity, preventive treatment of migraine with Nurtec ODT was moved into its own criterion that cannot be used concurrently with Vyepti. • The criterion for combination use with Aimovig, Ajovy, Emgality, and Vyepti was changed to read “Concurrent use with another CGRP inhibitor indicated for migraine headache prevention”. • Qulipta was added to the Note listing CGRP inhibitors that are indicated for migraine headache prevention. 	05/18/2022
Annual Revision	<p>Policy Name: The initial descriptor “Migraine” was added to the policy name.</p> <p>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.</p>	05/24/2023
Selected Revision	<p>Migraine Headache Prevention:</p> <ul style="list-style-type: none"> • 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. 	08/02/2023

	<ul style="list-style-type: none">• 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.	
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