

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

**DATE REVIEWED:** 03/25/2020; selected revision 04/15/2020

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## OVERVIEW

Vyepti, a calcitonin gene-related peptide (CGRP) inhibitor, is indicated for the preventive treatment of migraine in adults.<sup>1</sup> Vyepti is a humanized monoclonal antibody produced in *Pichia pastoris* yeast cells by recombinant DNA technology. Vyepti binds to the CGRP ligand and blocks its binding to the CGRP receptor. 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. Vyepti must be administered by a healthcare provider.

## Disease Overview

Migraine is a common, chronic condition marked by paroxysmal, unilateral attacks of moderate-to-severe throbbing headache which is aggravated by routine physical activity (e.g., walking or climbing stairs) and associated with nausea, vomiting, and/or photophobia and phonophobia.<sup>2</sup> Migraine headache episodes typically last 4 to 72 hours if untreated. Migraine affects approximately 15% of US adults.<sup>3</sup> Migraines have been defined as chronic or episodic. Chronic migraine is described by the International Headache Society as headache occurring on  $\geq 15$  days/month for  $> 3$  months and has the features of migraine headache on  $\geq 8$  days/month.<sup>2</sup> Episodic migraine is characterized by headaches that occur  $< 15$  days/month.<sup>4</sup> Patients with episodic migraine may transform to chronic migraine over time at a rate of about 2.5% of episodic-migraine patients/year. Potential strategies for preventing migraine transformation include preventing and treating headaches, lifestyle modifications, or effective management of comorbidities (e.g., obesity, obstructive sleep apnea, depression, anxiety). 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** (2018) reaffirms previous migraine guidelines.<sup>5</sup> Patients with migraine should be considered for preventive treatment when attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks ( $\geq 4$  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 (AAN) 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).<sup>6</sup> 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).

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

[erenumab-aooe injection], Ajovy® [fremanezumab-vfrm injection], and Emgality® [galcanezumab-gnlm injection]).<sup>5</sup> The update notes that a CGRP inhibitor should only be initiated in patients who are diagnosed with migraine, have  $\geq 4$  migraine headache days per 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 and 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 at least 3 months, and 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). Since migraine may improve or remit over time, it is important to reevaluate therapeutic response and, if possible, taper or discontinue treatment if patients no longer meet the criteria for offering preventive treatment. However, once control is established, the decision to discontinue or taper treatment should be a shared decision between 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(s). 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.

#### **RECOMMENDED AUTHORIZATION CRITERIA**

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

#### **FDA-Approved Indications**

- 1. Migraine Headache Prevention.** Approve Vyepti for 1 year if the patient meets the following criteria (A, B, C, and D):
  - A)** Patient is  $\geq 18$  years of age; **AND**
  - B)** Patient has  $\geq 4$  migraine headache days per month (prior to initiating a migraine-preventative medication); **AND**
  - C)** Patient has tried at least two standard prophylactic pharmacologic therapies, each from a different pharmacologic class (e.g., angiotensin receptor blocker, angiotensin converting enzyme inhibitor, anticonvulsant,  $\beta$ -blocker, calcium channel blocker, tricyclic antidepressant, other antidepressant), and meets **ONE** of the following criteria (i, ii, or iii):
    - i.** The patient has had inadequate efficacy to both of those standard prophylactic pharmacologic therapies, according to the prescriber; **OR**
    - ii.** The patient has experienced adverse event(s) severe enough to warrant discontinuation of both of those standard prophylactic pharmacologic therapies, according to the prescriber; **OR**
    - iii.** The patient has had inadequate efficacy to one standard prophylactic pharmacologic therapy and has experienced adverse event(s) severe enough to warrant discontinuation to another standard prophylactic pharmacologic therapy, according to the prescriber; **AND**

- D)** Patient meets ONE of the following (i or ii):
- i.** Patient has tried at least one triptan therapy; OR
  - ii.** Patient has a contraindication to triptan(s) according to the prescriber.

**Dosing.** Approve the following dosing regimens:

- A)** Up to 300 mg administered by intravenous infusion once every 3 months.

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#### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Vyepti has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Acute Treatment of Migraine.** Clinical data is currently lacking for the use of Vyepti in the acute treatment of migraine.
- 2. Cluster Headache, Treatment or Prevention.** Vyepti has not been studied in patients with cluster headache. The pivotal trials of Vyepti excluded patients with this condition.<sup>7,8</sup>
- 3. Combination Therapy with Aimovig® (erenumab-aooe injection for subcutaneous use), Ajovy® (fremanezumab-vfrm injection for subcutaneous use) or Emgality® (galcanezumab-gnlm injection for subcutaneous use).** Aimovig, Ajovy, Emgality, and Vyepti are calcitonin gene-related peptide (CGRP) inhibitors and have not been studied for use in combination with another agent in the same class.<sup>1,9-11</sup>
- 4.** 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 Seattle BioPharmaceuticals, Inc.; February 2020.
2. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 3rd edition (beta version). *Cephalalgia*. 2013;33:629-808.
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. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012;78(17):1337-1345.
7. Ashina M, Saper J, Cady R, et al. Eptinezumab in episodic migraine: a randomized, double-blind, placebo-controlled study (PROMISE-1). *Cephalalgia*. 2020 Feb 19. [Epub ahead of print].
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 2019.
10. Ajovy® injection for subcutaneous use [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; January 2020.
11. Emgality® injection for subcutaneous use [prescribing information]. Indianapolis, IN: Eli Lilly and Company; December 2019.

**HISTORY**

<b>Type of Revision</b>	<b>Summary of Changes</b>	<b>Date Reviewed</b>
New Policy	--	03/25/2020
Selected revision	Throughout the criteria, “prescribing physician” was changed to “prescriber”. For the Condition Not Recommended for Approval of cluster headache, “treatment or prevention” was added to clarify the intent.	04/15/2020