

Corporate Medical Policy: Eptinezumab-jjmr (Vyapti®) “Notification”

POLICY EFFECTIVE SEPTEMBER 1, 2026

**Restricted Product(s):**

- eptinezumab-jjmr (Vyapti®) intravenous infusion for administration by a healthcare professional

**FDA Approved Use:**

- For the preventive treatment of migraines in adults

**Criteria for Medical Necessity:**

The restricted product(s) may be considered medically necessary when the following criteria are met:

**Initial Criteria for Approval:**

1. The patient is 18 years of age or older; **AND**
2. The patient has been diagnosed with **chronic migraine** and over the last 3 months the patient has experienced BOTH of the following:
  - a. Greater than or equal to 15 headache days per month; **AND**
  - b. Greater than or equal to 8 migraine days per month; **OR**
3. The patient has been diagnosed with **episodic migraine** and over the last 3 months the patient has experienced at least ONE of the following:
  - a. Less than or equal to 14 headache days per month of which at least 4 are migraine days; **OR**
  - b. Migraine attacks that are attributed to a diminished quality of life despite the use of acute rescue medications; **OR**
  - c. The patient has contraindications to acute therapies; **OR**
  - d. The patient has tried and had an inadequate response to acute therapies; **OR**
  - e. The patient has serious side effects to acute therapies; **OR**
  - f. The patient is at risk of medication overuse headache without preventative therapy; **AND**
4. ONE of the following:
  - a. The patient has tried and had an inadequate response to ALL of the following: erenumab (Aimovig) AND galcanezumab (Emgality) AND fremanezumab (Ajovy) [**medical record documentation required**]; **OR**
  - b. The patient has a clinical contraindication or intolerance to ALL of the following: erenumab (Aimovig) AND galcanezumab (Emgality) AND fremanezumab (Ajovy) that is not expected to occur with the requested agent [**medical record documentation required**]; **AND**

5. ONE of the following:
  - a. The patient will NOT be using the requested agent in combination with a botulinum toxin agent for migraine prophylaxis; **OR**
  - b. The patient will be using the requested agent in combination with a botulinum toxin agent for the treatment of chronic migraine; **AND**
    - i. The patient is continuing to experience 4 or more migraine headache days per month after treatment with ONE of the following preventative therapies for chronic migraine **[medical record documentation required]**:
      1. At least a 3-month trial with a calcitonin gene-related peptide (CGRP) receptor antagonist **[medical record documentation required]**; **OR**
      2. At least a 6-month trial (2 injection cycles) with a botulinum toxin agent **[medical record documentation required]**; **AND**
6. The patient will initiate treatment with eptinezumab (Vyepti) 100 mg strength; **AND**
7. ONE of the following:
  - a. The requested agent will NOT be used in combination with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for migraine prophylaxis (e.g., erenumab, fremanezumab, galcanezumab, atogepant); **OR**
  - b. If using another CGRP receptor antagonist, the patient will discontinue the other CGRP prior to starting the requested agent; **AND**
8. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting**, Site of Care Criteria applies (outlined below)\*

**Initial Duration of Approval:** 180 days (6 months)

#### **Continuation Criteria for Approval:**

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy **[medical record documentation required]**; **AND**
3. The patient is using the requested agent for prevention of migraine; **AND**
4. If eptinezumab (Vyepti) 100 mg strength is being requested:
  - a. The patient has had a positive clinical response with eptinezumab treatment, demonstrated by the following:
    - i. A decrease from baseline in the number of migraine days per month or migraine frequency **[medical record documentation required]**; **AND**
    - ii. A reduction in the need for migraine rescue medications (i.e., NSAIDs, triptans, ergot derivatives); **OR**
5. If eptinezumab (Vyepti) 300 mg strength is being requested:
  - a. The patient has not been previously approved for 300 mg strength; **AND**
    - i. The patient has had an adequate trial (**at least 3 months**) and had an inadequate response to the 100 mg strength **[medical record documentation required]**; **OR**

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- b. The patient was previously approved through Blue Cross NC for the 300 mg strength; **AND**
  - i. The patient has had a positive clinical response with eptinezumab (Vyepti) 300 mg strength treatment, demonstrated by the following:
    - 1. A decrease from baseline in the number of migraine days per month or migraine frequency **[medical record documentation required]; AND**
    - 2. A reduction in the need for migraine rescue medications (i.e., NSAIDs, triptans, ergot derivatives); **AND**
- 6. ONE of the following:
  - a. The patient will NOT be using the requested agent in combination with a botulinum toxin agent for migraine prophylaxis; **OR**
  - b. The patient will be using the requested agent in combination with a botulinum toxin agent for the treatment of chronic migraine; **AND**
    - i. The patient is continuing to experience 4 or more migraine headache days per month after treatment with ONE of the following preventative therapies for chronic migraine **[medical record documentation required]**:
      - 1. At least a 3-month trial with a calcitonin gene-related peptide (CGRP) receptor antagonist **[medical record documentation required]; OR**
      - 2. At least a 6-month trial (2 injection cycles) with a botulinum toxin agent **[medical record documentation required]; AND**
- 7. The patient is NOT using the requested agent at the same time as another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for migraine prophylaxis (e.g., erenumab, fremanezumab, galcanezumab, atogepant); **AND**
- 8. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting**, Site of Care Criteria applies (outlined below)\*

**Duration of Approval:** 365 days (1 year)

FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
Eptinezumab-jjmr (Vyepti®) intravenous (IV) infusion	Preventive treatment of migraine in adults	100 mg IV every 3 months  Some patients may benefit from a dosage of <b>300 mg**</b>	J3032	<b>Initial:</b> 200**  <b>Continuation:</b> 400; 1200 if approved for 300 mg dose***

**\*Maximum units allowed for duration of approval**

\*\*300 mg strength is not eligible for approval on initial review

\*\*\*See continuation criteria for approval for requests for 300 mg strength dosing

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**\*Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
  - a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
  - b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
  - c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
  - d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
  - e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
  - f. Re-initiation of therapy, defined as ONE of the following:
    - i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
    - ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
  - g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

**References:** all information referenced is from FDA package insert unless otherwise noted below.

1. Ailani J, Burch RC, Robbins MS, 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;61:1021-39.
2. Armanious M, Khalil N, Lu Y, et al. Erenumab and onabotulinumtoxinA combination therapy for the prevention of intractable chronic migraine without aura: a retrospective analysis. *J Pain Palliat Care Pharmacother*. 2021;35(1):1-6.
3. 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.

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4. 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 Apr;64(4):333-341.
5. Cohen F, Armand C, Lipton RB, et al. Efficacy and tolerability of calcitonin gene-related peptide-targeted monoclonal antibody medications as add-on therapy to onabotulinumtoxinA in patients with chronic migraine. *Pain Med*. 2021;22(8):1857-63.
6. Evers S, Afra J, Frese A, et al. EFNS guideline on the drug treatment of migraine – revised report of an EFNS task force. *Eur J Neurol*. 2009 Sep;16(9):968-81.
7. Headache Classification Committee of the International Headache Society (HIS). The International Classification of Headache Disorders; 3rd edition. *Cephalalgia*. 2018 Jan;38(1):1-211.
8. Katsarava Z, Buse DC, Manack AN, et al. Defining the differences between episodic migraine and chronic migraine. *Curr Pain Headache Rep*. 2012;16:86-92.
9. Lipton RB, Goadsby PJ, Smith J, et al. Efficacy and safety of eptinezumab in patients with chronic migraine: PROMISE-2. *Neurology*. 2020 Mar;94(13):e1365-e1377.
10. Scuteri D, Tonin P, Nicotera P, et al. Pooled analysis of real-world evidence supports anti-CGRP mAbs and onabotulinumtoxinA combined trial in chronic migraine. *Toxins*. 2022 Aug;14(8):529.
11. 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 Apr 24;78(17):1337-45.
12. Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2000 Sep 26;55(6):754-62.
13. Toni T, Tamanaha R, Newman B, et al. Effectiveness of dual migraine therapy with CGRP inhibitors and onabotulinumtoxinA injections: case series. *Neurol Sci*. 2021;42(12):5373-76.

**Policy Implementation/Update Information:** Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q4 annually.

September 2026: Criteria change: Added within initial criteria that the patient will initiate treatment with eptinezumab (Vyepi) 100 mg strength to align with FDA label dosing table for clarity. Other minor formatting updates made throughout policy for clarity. **Policy notification given 7/2/2026 for effective date 9/1/2026.**

November 2025: Criteria change: Updated Site of Care medical necessity criteria to add additional bypass for patients with a history of severe adverse events or conditions that cause an increased risk for severe adverse event to align with the Place of Service for Medical Infusions policy for clarity of intent.

January 2025: Criteria change: Removed requirement of trial and failure of at least two categories of conventional migraine prophylaxis agents (beta blockers, antidepressants, anticonvulsants). Removed required exclusion of other specific disease-related concerns for headache/migraine frequency. Reference added.

January 2024: Criteria change: Added the option for use in combination with a botulinum toxin agent for patients continuing to experience 4 or more migraine headache days per month after treatment with either a 3-month trial of a CGRP receptor antagonist or a 6-month trial (2 injection cycles) of a botulinum toxin agent. Updated formatting to include specific examples of drugs within the distinct categories of migraine prophylaxis treatment options for clarity. References added.

November 2022: Criteria update: Added authorization termination language to clarify intent of criteria indicating no concurrent use of eptinezumab (Vyepiti) with botulinum toxin agents used for migraine prophylaxis.

February 2022: Criteria change: Added to initial criteria the requirement of trial and failure of fremanezumab (Ajovy) in addition to erenumab (Aimovig) and galcanezumab (Emgality). **Policy notification given 12/15/2021 for effective date 2/15/2022.**

October 2021: Criteria change: Added Site of Care medical necessity criteria. **Policy notification given 8/2/2021 for effective date 10/1/2021.**

June 2021: Criteria change: Added maximum units and removed review of 300 mg strength in initial criteria; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021.**

\*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.