# Vyepti® (eptinezumab-jjmr)
## (Intravenous)

**Effective Date: 07/01/2020**
**Dates Reviewed: 06/15/2020, 9/9/2020, 11/16/2020, 7/22/2021, 4/14/2022, 6/29/2023, 12/14/2023, 01/04/2024**

**Scope: Medicaid, Commercial , Medicare-Medicaid Plan (MMP)**

## I. Length of Authorization

Coverage will be provided for six months and may be renewed.

## II. Dosing Limits

**A. Quantity Limit (max daily dose) [NDC Unit]:**

- Vyepti 100 mg/mL solution SDV: 3 vials per 84 days

**B. Max Units (per dose and over time) [HCPCS Unit]:**

- 300 billable units every 84 days

## III. Summary of Evidence

Vyepti (eptinezumab-jjmr) is a calcitonin gene-related peptide antagonist indicated for the preventive treatment of migraine in adults. In phase 3 studies, Vyepti has shown to significantly decrease the monthly migraine days compared to placebo, leading to a reduction in migraine frequency. Patients treated with Vyepti also experienced improvements in other migraine-related parameters, including the reduction in migraine attacks, migraine-related disability, and acute migraine medication use. Adverse events commonly reported including nasopharyngitis, upper respiratory tract infection, and injection-site reactions.

## IV. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient must be 18 years or older; **AND**
- Prescriber is a neurologist or headache specialist, or the prescription is being written for the patient in consultation with a neurologist or headache specialist; **AND**

**Universal Criteria [1,4-8]**

- Other causes of headaches have been ruled out; **AND**
- Vyepti is not used in combination with other calcitonin gene-related peptide (CGRP) antagonists (e.g., erenumab, galcanezumab, fremanezumab, etc.); **AND**
- Patient will continue to utilize prophylactic intervention modalities (i.e., pharmacotherapy, behavioral therapy, physical therapy, etc.); **AND**

- Physician has assessed baseline disease severity utilizing an objective measure/tool (e.g., Headache Impact Test [HIT]; monthly headache day [MHD]; Migraine Disability Assessment [MIDAS]; Migraine Physical Function Impact Diary [MPFID]); **AND**
- Patient has failed at least a 3 month trial of two oral medications from two different classes of drugs for the prevention of migraines (see list of prophylactic medications below for examples) prior to initiation of eptinezumab; **AND**
- Patient had an inadequate response (or intolerance or contraindication) to two triptan medications (e.g., sumatriptan, naratriptan, rizatriptan) at up to maximally indicated doses; **AND**

**Preventative Treatment of Migraines [1-9]†**

- Patient has a diagnosis of chronic migraines defined as 15 or more headache (tension-type-like and/or migraine-like) days per month for at least 3 months*; **AND**
    - Patient has had at least five attacks with features consistent with migraine (with and/or without aura)§; **AND**
    - On at least 8 days per month for at least 3 months:
        - Headaches have characteristics and symptoms consistent with migraine§; **OR**
        - Patient suspected migraines are relieved by a triptan or ergot derivative medication; **AND**
    - Patient has a documented inadequate response (or is unable to tolerate) a minimum trial of at least two quarterly injections (6 months) of a botulinum toxin and documentation of clinical response as demonstrated by change in headache frequency, duration and/or severity from baseline must be provided; **AND**
    - Patient had an inadequate response (or intolerance or contraindication) a minimum trial of at least 12 weeks to two CGRP inhibitors**, (e.g., erenumab, galcanezumab, fremanezumab, etc.); **OR**
- Patient has a diagnosis of frequent episodic migraines defined as at least 4 headache attacks lasting 4-72 hours (when untreated or unsuccessfully treated)*; **AND**
    - Headaches have characteristics and symptoms consistent with migraine without aura§; **AND**
    - Medication overuse headache has been ruled out by trial and failure of titrating off acute migraine treatments in the past; **AND**
    - Patient had an inadequate response (or intolerance or contraindication) a minimum trial of at least 12 weeks to two CGRP inhibitors**, (e.g., erenumab, galcanezumab, fremanezumab, etc.)

**Patients new to therapy must initiate treatment at the lower dosing regimen of the 100 mg dose before increasing to the subsequent 200 mg dose or 300 mg dose, if required.*

***MMP members ONLY are only required to fail one formulary CGRP inhibitor*

† FDA Approved Indication; ‡ Literature Supported Indication

| **Migraine-Prophylaxis Oral Medications *(list not all-inclusive)*** [2,3,4,6] |
|---|
| • Antidepressants (e.g., amitriptyline, fluoxetine, nortriptyline, etc.)<br>• Beta blockers (e.g., propranolol, metoprolol, nadolol, timolol, atenolol, pindolol etc.) |

| |
|---|
| • Anti-epileptics (e.g., divalproex, valproate, topiramate, etc.) |
| **§Migraine Features [4,6]** |
| **Migraine without aura**<br>o At least five attacks have the following:<br>o Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)<br>o Headache has at least two of the following characteristics:<br>– Unilateral location<br>– Pulsating quality<br>– Moderate or severe pain intensity<br>– Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs); **AND**<br>o During headache at least one of the following symptoms:<br>– Nausea and/or vomiting<br>– Photophobia and phonophobia |
| **Migraine with aura**<br>o At least two attacks have the following:<br>o One or more of the following fully reversible aura symptoms:<br>– Visual<br>– Sensory<br>– Speech and/or language<br>– Motor<br>– Brainstem<br>– Retinal; **AND**<br>o At least two of the following characteristics:<br>– At least one aura symptom spreads gradually over ≥5 minutes, and/or two or more symptoms occur in succession<br>– Each individual aura symptom lasts 5 to 60 minutes<br>– At least one aura symptom is unilateral<br>– The aura is accompanied, or followed within 60 minutes, by headache |

## V. Renewal Criteria [1,4,6]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include severe hypersensitivity reactions, etc.; **AND**
- Disease response as evidenced by the following:
  - Reduction in mean monthly headache days of ≥50% relative to the pretreatment baseline; **OR**
  - A clinically meaningful improvement in ANY of the following validated migraine-specific patient-reported outcome measures:
    - Reduction of ≥5 points when baseline score is 11–20 OR Reduction of ≥30% when baseline scores >20 in the MIDAS scores; **OR**

- Reduction of ≥5 points in the MPFID score; **OR**
- Reduction of ≥5 points in the HIT-6 score; **AND**

- Dose escalation* (up to the maximum dose and frequency specified below) may occur upon clinical review on a case by case basis provided that the patient has:
  - Shown an initial improvement or response to therapy, as described above; **AND**
  - Had subsequent loss of response or no net decrease in frequency of headaches; **AND**
  - Received a minimum of two doses at the lower dose prior to the next stepped dose and interval specified below

**Note: Patient must have a trial of 200 mg prior to escalating to the maximum dose of 300 mg*

- For continuation of an escalated dose, the patient has shown a response to therapy, as described above, and has had a clinically meaningful incremental benefit from the previous lower dose

## VI. Dosage/Administration

| Indication | Dose | Approval Coverage Units |
|---|---|---|
| Migraine – Preventative Treatment | The recommended dosage is 100 mg administered by intravenous infusion every 3 months.<br>• Some patients may benefit from a dosage of up to 300 mg every 3 months.<br>  ○ When up-dosing is deemed medically necessary, the patient must have a trial of 200 mg dosing, and be re-evaluated per the above response criteria, prior to a step-wise increase up to the maximum dosing of 300 mg. | • 100 mg dose: 100 billable units every 84 days<br>• 200 mg dose: 200 billable units every 84 days<br>• 300 mg dose: 300 billable units every 84 days |

## VII. Billing Code/Availability Information

HCPCS Code:

- J3032: Injection, eptinezumab-jjmr, 1 mg

NDC:

- Vyepti 100 mg/mL solution for injection; single-dose vial: 67386-0130-xx

## VIII. References

1. Vyepti [package insert]. Bothell, WA; Lundbeck Seattle BioPharm., Inc; October 2022. Accessed November 2023.
2. Modi S, Lowder DM. Medications for migraine prophylaxis. Am Fam Physician. 2006 Jan 1; 73(1):72-8.
3. Pringheim T, Davenport W, Mackie G, et al. Canadian Headache Society guideline for migraine prophylaxis. Can Jneurol Sci. 2012 Mar; 39(2 Suppl 2):S1-S9.
4. The International Classification of Headache Disorders, 3rd edition. Headache Classification Committee of the International Headache Society (IHS) Cephalalgia. 2018 ;38(1):1-211.

5. Garza I, Schwedt TJ. Chronic Migraine. In UpToDate, JW Swanson (Ed). UpToDate, Waltham, MA. (Accessed on April 26, 2017).
6. American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019 Jan;59(1):1-18. doi: 10.1111/head.13456. Epub 2018 Dec 10.
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 19:333102420905132. doi: 10.1177/0333102420905132. [Epub ahead of print]
8. Cady R, McGill L, Hirman J, et al. Patient Global Impression of Change Related to Improvement in Most Bothersome Symptom Following Treatment With Eptinezumab (S38.009). Neurology Apr 2019, 92 (15 Supplement) S38.009;
9. Kudrow D, Lipton R, Silberstein S, et al. Eptinezumab for Prevention of Chronic Migraine: Results of 2 Infusions in the Phase 3 PROMISE-2 (Prevention of Migraine via Intravenous Eptinezumab Safety and Efficacy–2) Trial (P2.10-006). Neurology Apr 2019, 92 (15 Supplement) P2.10-006;

## Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|---|---|
| G43.001 | Migraine without aura, not intractable, with status migrainosus |
| G43.009 | Migraine without aura, not intractable, without status migrainosus |
| G43.011 | Migraine without aura, intractable, with status migrainosus |
| G43.019 | Migraine without aura, intractable, without status migrainosus |
| G43.101 | Migraine with aura, not intractable, with status migrainosus |
| G43.109 | Migraine with aura, not intractable, without status migrainosus |
| G43.111 | Migraine with aura, intractable, with status migrainosus |
| G43.119 | Migraine with aura, intractable, without status migrainosus |
| G43.401 | Hemiplegic migraine, not intractable, with status migrainosus |
| G43.409 | Hemiplegic migraine, not intractable, without status migrainosus |
| G43.411 | Hemiplegic migraine, intractable, with status migrainosus |
| G43.419 | Hemiplegic migraine, intractable, without status migrainosus |
| G43.501 | Persistent migraine aura without cerebral infarction, not intractable, with status migrainosus |
| G43.509 | Persistent migraine aura without cerebral infarction, not intractable, without status migrainosus |
| G43.511 | Persistent migraine aura without cerebral infarction, intractable, with status migrainosus |
| G43.519 | Persistent migraine aura without cerebral infarction, intractable, without status migrainosus |
| G43.701 | Chronic migraine without aura, not intractable, with status migrainosus |
| G43.709 | Chronic migraine without aura, not intractable, without status migrainosus |
| G43.711 | Chronic migraine without aura, intractable, with status migrainosus |
| G43.719 | Chronic migraine without aura, intractable, without status migrainosus |

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/Article): N/A

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|---|---|---|
| **Jurisdiction** | **Applicable State/US Territory** | **Contractor** |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |

**Policy Rationale:**

Vyepti was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Vyepti according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.