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, 01/08/2025

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 is a calcitonin gene-related peptide antagonist indicated for the preventative treatment of migraines in adults. Vyepti's efficacy as a preventive treatment for both episodic and chronic migraines was evaluated in two randomized, placebo-controlled, multicenter studies. Both studies involved a 6-month double-blind treatment period, with Vyepti administered via intravenous infusion every 3 months. The primary endpoint was assessed at 12 weeks. Study 1, which focused on episodic migraine (N=665), randomize adults with 4 to 14 headache days per month, including at least 4 migraine days, to receive placebo, 100 mg Vyepti, or 300 mg Vyepti every 3 months for 12 months. The primary endpoint was the change in mean monthly migraine days (MMD) over the first 3 months, with secondary endpoints including the percentage of patients experiencing a ≥50% or ≥75% reduction in MMD. Vyepti treatment resulted in statistically significant improvements compared to placebo. The 100 mg dose reduced MMD by 3.9 days ($p=0.018$), while the 300 mg dose reduced MMD by 4.3 days ($p<0.001$). Additionally, 56.3% of patients on the 100 mg dose and 49.8% on the 300 mg dose saw a ≥50% reduction in MMD, compared to only 37.4% of placebo-treated patients. The percentage of patients achieving a ≥75% reduction was 29.7% for the 300 mg dose and 22.2% for the 100 mg dose. The treatment also showed significant improvements in the first 7 days of the treatment period, with fewer Vyepti-treated patients experiencing migraines on consecutive days. Study 2, which focused on chronic migraine (N=1072), randomized adults with 15 to 26 headache days per month, including at least 8 migraine days, to receive placebo, 100 mg Vyepti, or 300 mg Vyepti every 3 months for 6 months. The primary endpoint was also the change in MMD over the first 3 months, and secondary endpoints included the percentage of patients achieving a ≥50% or ≥75% reduction in MMD. Both Vyepti doses demonstrated statistically significant reductions in MMD compared to placebo. The 100 mg dose reduced MMD by 7.7 days, and the 300 mg dose reduced it by 8.2 days (both $p<0.001$). More patients in the Vyepti groups achieved ≥50% and ≥75% reductions in MMD compared to those on placebo. Additionally, a

larger percentage of Vyepti-treated patients had fewer migraines on consecutive days during the initial 7-day period following treatment. Common side effects include nasopharyngitis and hypersensitivity.

IV. Initial Approval Criteria [1,6,10]

Coverage is provided in the following conditions:

- Patient must be 18 years or older; **AND**
- Prescriber is a neurologist or headache specialist, or in consultation with a neurologist or headache specialist; **AND**

Universal Criteria [1,4,5,7-10,14-15]

- Other causes of headaches have been ruled out; **AND**
- Vyepti is not used in combination with other prophylactic calcitonin gene-related peptide (CGRP) antagonists (e.g., Aimovig [erenumab], Ajovy [fremanezumab], Emgality [galcanezumab], Nurtec ODT [rimegepant[, Qulipta [atogepant], 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-6]; monthly headache day [MHD]; Migraine Disability Assessment [MIDAS]; Migraine Physical Function Impact Diary [MPFID]); **AND**
- Patient has been fully equipped with abortive migraine therapy, if appropriate, and has had inadequate relief; **AND**

Preventative Treatment of Migraines [1,4,5,7-10,14,15]†

- Patient has a diagnosis of chronic migraines defined as 15 or more headache (tension-type-like and/or migraine-like) days per month for > 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 > 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 to 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); **AND**
    - Patient has a documented inadequate response to (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 has a documented inadequate response to (or is unable to tolerate) a minimum trial of at least 12 weeks to two preferred injectable CGRP inhibitors** (e.g., Aimovig [erenumab], Ajovy [fremanezumab], Emgality [galcanezumab], etc.) and documentation of clinical response as

demonstrated by change in headache frequency, duration and/or severity from baseline must be provided; **OR**

- Patient has a diagnosis of frequent <u>episodic</u> migraines defined as at least 5 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 has a documented inadequate response to 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); **AND**
    - Patient has a documented inadequate response to (or is unable to tolerate) a minimum trial of at least 12 weeks to two preferred injectable CGRP inhibitors** (e.g., Aimovig [erenumab], Ajovy [fremanezumab], Emgality [galcanezumab], etc.) and documentation of clinical response as demonstrated by change in headache frequency, duration and/or severity from baseline must be provided

**Patients new to therapy must initiate treatment at the lower dosing regimen of the 100 mg dose before increasing to the 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)* [5,10,14]
• Antidepressants (e.g., amitriptyline, venlafaxine, nortriptyline, duloxetine, etc.) • Beta blockers (e.g., propranolol, metoprolol, nadolol, timolol, atenolol, pindolol etc.) • Anti-epileptics (e.g., divalproex, valproate, topiramate, etc.)
§Migraine Features [4,10]
<u>Migraine without aura</u> o At least five attacks have the following: o Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) o Headache has at least two of the following characteristics: – Unilateral location – Pulsating quality – Moderate or severe pain intensity – Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs); **AND** o During headache at least one of the following symptoms: – Nausea and/or vomiting – Photophobia and phonophobia
<u>Migraine with aura</u> o At least two attacks have the following: o One or more of the following fully reversible aura symptoms: – Visual

- Sensory
- Speech and/or language
- Motor
- Brainstem
- Retinal; **AND**

- At least three of the following characteristics:
  - At least one aura symptom spreads gradually over ≥5 minutes
  - Two or more symptoms occur in succession
  - Each individual aura symptom lasts 5 to 60 minutes
  - At least one aura symptom is unilateral
  - At least one aura symptom is positive (e.g., scintillations and pins and needles)
  - The aura is accompanied, or followed within 60 minutes, by headache

V. Renewal Criteria [1,10]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section IV; **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 at least moderate severity of ≥50% relative to the pretreatment baseline (diary documentation or medical professional attestation); **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 score is >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:
    - Had an initial improvement or response to therapy, as described above, and then subsequent loss of response to the 100 mg dose; **OR**
    - Had an inadequate response (e.g., no net decrease in frequency of headaches) to the 100 mg dose after receiving a minimum of two doses; **AND**

VI. Dosage/Administration

Indication	Dose	Approval Coverage Units
Migraine – Preventative Treatment	The recommended dosage is 100 mg* administered by intravenous infusion every 3 months.	• 100 mg dose: 100 billable units every 84 days

Indication	Dose	Approval Coverage Units
	***Note:** Some patients may benefit from a dosage of 300 mg every 3 months *(Refer to criteria in section V)*.	• 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

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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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: http://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): 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 VA)	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.