

Vyepti® (eptinezumab-jjmr) (Intravenous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- Vyepti 100 mg/mL solution single-dose vial: 3 vials per 84 days

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

- 300 billable units every 84 days

III. Initial Approval Criteria ^{1,6,10}

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **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**

Universal Criteria ^{1,4-10}

- Other causes of headaches have been ruled out; **AND**
- Not used in combination with prophylactic calcitonin gene-related peptide (CGRP) inhibitors (e.g., erenumab, galcanezumab, fremanezumab, atogepant, rimegepant, etc.)
*[Note: This does not include CGRP inhibitors if they are being used for acute treatment only (e.g., ubrogepant, rimegepant, zavegepant, etc.)]; **AND***
- Patient is utilizing prophylactic intervention modalities (e.g., pharmacotherapy, behavioral therapy, physical therapy, etc.); **AND**

Preventative Treatment of Migraines † ^{1,4-6,10}

- 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 failed at least an 8-week trial of any two oral medications 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 unable to tolerate) a minimum trial of at least two doses of a botulinum toxin; **OR**
- Patient has a diagnosis of frequent episodic 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

****NOTE:** 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.

† FDA Approved Indication; ‡ Compendia Recommended Indication(s); Ⓞ Orphan Drug

± Migraine-Prophylaxis Oral Medications (list not all-inclusive) ^{5,6,10}
<ul style="list-style-type: none"> • Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine, duloxetine, etc.) • Beta blockers (e.g., propranolol, metoprolol, nadolol, timolol, atenolol, pindolol etc.) • Angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (e.g. lisinopril, candesartan, etc.) • Anti-epileptics (e.g., divalproex sodium, valproate sodium, topiramate, etc.)
§ Migraine Features ^{4,10}
<p><u>Migraine without aura</u></p> <ul style="list-style-type: none"> • At least five attacks have the following: <ul style="list-style-type: none"> ○ Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) ○ Headache has at least two of the following characteristics: <ul style="list-style-type: none"> – 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 ○ During headache at least one of the following symptoms: <ul style="list-style-type: none"> – Nausea and/or vomiting – Photophobia and phonophobia
<p><u>Migraine with aura</u></p> <ul style="list-style-type: none"> • At least two attacks have the following: <ul style="list-style-type: none"> ○ One or more of the following fully reversible aura symptoms: <ul style="list-style-type: none"> – Visual – Sensory – Speech and/or language – Motor

- Brainstem
- Retinal; **AND**
- o 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

IV. 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 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:
 - o Reduction in mean monthly headache days (MHD) of at least moderate severity of $\geq 50\%$ relative to the pretreatment baseline (diary documentation or medical professional attestation); **OR**
 - o 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 $\geq 30\%$ 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**
 - o 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 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

V. Dosage/Administration ^{1,11,12}

Indication	Dose
Preventative Treatment of Migraines	The recommended dosage is 100 mg** administered by intravenous infusion every 3 months. **Note: Some patients may benefit from a dosage of 300 mg administered by intravenous infusion every 3 months (<i>Refer to criteria in section IV</i>).

VI. Billing Code/Availability Information

HCPCS Code:

- J3032 – Injection, eptinezumab-jjmr, 1 mg: 1 billable unit = 1 mg

NDC:

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

VII. References

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11. Apelian R, Boyle L, Hirman J, Asher D. Measuring dose-related efficacy of eptinezumab for migraine prevention: post hoc analysis of PROMISE-1 and PROMISE-2. *J Headache Pain*. 2022 Apr 18;23(1):48. Doi: 10.1186/s10194-022-01418-8. PMID: 35436857; PMCID: PMC9014586.
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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 Dec;42(12):5373-5376. doi: 10.1007/s10072-021-05547-x. Epub 2021 Aug 18. PMID: 34409517.

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: <https://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