Vyepti® (Eptinezumab-Jjmr)

Policy Number: CS2024D0090N
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➲ Instructions for Use

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Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Florida	Refer to the state's Medicaid clinical policy
Indiana	Refer to the state's Medicaid clinical policy
Kansas	Refer to the state's Medicaid clinical policy
Louisiana	Refer to the state's Medicaid clinical policy
North Carolina	None
Ohio	Vyepti® (Eptinezumab-Jjmr) (for Ohio Only)
Pennsylvania	Refer to the state's Medicaid clinical policy
Texas	Refer to the drug specific criteria found within the *Texas Medicaid Provider Procedures Manual*

Coverage Rationale

Migraine

Vyepti® is proven and medically necessary for the preventive treatment of migraines when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of migraine consistent with the International Classification of Headache Disorders, 3rd edition[4]; **and**
  - **One** of the following:
    - **Both** of the following:
      - 4 to 7 migraine days per month; **and**
      - **One** of the following:
        - Less than 15 headache days per month; **or**
        - Provider attests this is the member's predominant headache diagnosis (i.e., primary driver of headaches is not a different, non-migrainous condition)

      or
    - Greater than or equal to 8 migraine days per month
  - Trial and failure (after a trial of at least two months), contraindication, or intolerance to **two** of the following prophylactic therapies from the list below:[4]

        - One of the following tricyclic antidepressants: amitriptyline (Elavil) or nortriptyline (Pamelor)
        - One of the following beta-blockers: atenolol, metoprolol, nadolol, propranolol, or timolol
        - Candesartan (Atacand)
        - Divalproex sodium (Depakote/Depakote ER)
        - OnabotulinumtoxinA (Botox) [trial of at least two quarterly injections (6 months)]
        - Topiramate (Topamax)
        - One of the following serotonin-norepinephrine reuptake inhibitors: duloxetine (Cymbalta) or venlafaxine (Effexor/Effexor XR)

      and
    - Trial and failure (after a trial of at least three months), contraindication, or intolerance to **two** of the following therapies used for the preventive treatment of migraines:
        - Aimovig (erenumab-aooe)
        - Ajovy (fremanezumab-vfrm)
        - Emgality (galcanezumab-gnlm) (120 mg strength)
        - An oral calcitonin gene-related peptide (CGRP) receptor antagonist (e.g., Nurtec ODT, Qulipta)

      and
    - Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for the preventive treatment of migraines (e.g., Aimovig, Emgality, Nurtec ODT, Qulipta); **and**
    - Dosing is in accordance with the U.S. Food and Drug Administration (FDA) approved labeling; **and**
    - Authorization will be issued for no more than 12 months
- For **continuation of therapy, all** of the following:
    - Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity; **and**
    - Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for the preventive treatment of migraines (e.g., Aimovig, Emgality, Nurtec ODT, Qulipta); **and**
    - Dosing is in accordance with the U.S. Food and Drug Administration (FDA) approved labeling; **and**
    - Reauthorization will be issued for no more than 12 months

Vyepti is unproven and not medically necessary for:
- Acute attack of migraine
- Episodic cluster headache

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3032	Injection, eptinezumab-jjmr, 1 mg

Diagnosis Code	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

Diagnosis Code	Description
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
G43.601	Persistent migraine aura with cerebral infarction, not intractable, with status migrainosus
G43.609	Persistent migraine aura with cerebral infarction, not intractable, without status migrainosus
G43.611	Persistent migraine aura with cerebral infarction, intractable, with status migrainosus
G43.619	Persistent migraine aura with 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
G43.801	Other migraine, not intractable, with status migrainosus
G43.809	Other migraine, not intractable, without status migrainosus
G43.811	Other migraine, intractable, with status migrainosus
G43.819	Other migraine, intractable, without status migrainosus
G43.821	Menstrual migraine, not intractable, with status migrainosus
G43.829	Menstrual migraine, not intractable, without status migrainosus
G43.831	Menstrual migraine, intractable, with status migrainosus
G43.839	Menstrual migraine, intractable, without status migrainosus
G43.901	Migraine, unspecified, not intractable, with status migrainosus
G43.909	Migraine, unspecified, not intractable, without status migrainosus
G43.911	Migraine, unspecified, intractable, with status migrainosus
G43.919	Migraine, unspecified, intractable, without status migrainosus
G43.C0	Periodic headache syndromes in child or adult, not intractable
G43.C1	Periodic headache syndromes in child or adult, intractable
G43.E01	Chronic migraine with aura, not intractable, with status migrainosus
G43.E09	Chronic migraine with aura, not intractable, without status migrainosus
G43.E11	Chronic migraine with aura, intractable, with status migrainosus
G43.E19	Chronic migraine with aura, intractable, without status migrainosus

Background

Vyepti is a humanized IgG1kappa monoclonal antibody that specifically binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor.

Clinical Evidence

The PROMISE 1 (PRevention of Migraine via Intravenous eptinezumab Safety and Efficacy 1) trial was a Phase 3 randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of eptinezumab for episodic migraine prevention. In the study, 888 patients were randomized to receive eptinezumab (300 mg, 100 mg, or 30 mg), or placebo administered by infusion once every 12 weeks. Inclusion criteria included patients that had experienced ≤ 14 headache days per month, of which at least four met the criteria for migraine. The primary endpoint was the mean change from baseline in monthly migraine days over the 12-week, double-blind treatment period. Eptinezumab achieved statistically significant reductions in monthly migraine days from baseline (8.6 days average) over weeks 1 through 12, was 4.3 monthly migraine days for the 300 mg dose ($p = 0.0001$) and 3.9 days for 100 mg ($p = 0.0179$) compared to an average 3.2 days for placebo. Patients experienced day 1 clinical benefit, with ≥ 50% reduction in the proportion of patients experiencing a migraine after the first administration. The observed safety profile in the study to date was similar

to placebo. The authors concluded that eptinezumab (100 mg or 300 mg) significantly reduced migraine frequency, was well tolerated, and had an acceptable safety profile when used for the preventive treatment of migraine in adults with episodic migraine.

The PROMISE 2 trial was a Phase 3, randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of eptinezumab for chronic migraine prevention. In the study, 1,072 patients were randomized to receive eptinezumab (300 mg or 100 mg), or placebo administered by infusion once every 12 weeks. Inclusion criteria required patients have experienced at least 15 headache days per month, of which at least eight met criteria for migraine. Patients that participated in the trial had an average of 16.1 migraine days per month at baseline. The primary endpoint was the mean change from baseline in monthly migraine days over the 12-week, double-blind treatment period. Secondary study endpoints assessed through 12 weeks included reduction in migraine prevalence day 1 and days 1-28, reduction of at least 50%, 75%, and 100% from baseline in mean monthly migraine days, change from baseline in mean monthly acute migraine-specific medication days, and reductions from baseline in patient-reported impact scores on the Headache Impact Test (HIT-6). Compared to placebo, eptinezumab significantly reduced monthly migraine days by 8.2 days versus 5.6 days for placebo ($p < 0.0001$). Eptinezumab reduced migraine risk following the first administration, reducing the migraine risk by 52% compared to 27% for placebo ($p < 0.0001$). Through 12 weeks, eptinezumab demonstrated significant response rates: 61% of patients achieved at least 50% reduction in migraine days from baseline compared to 39% for placebo ($p < 0.0001$); 33% achieved 75% or greater reduction in migraine days from baseline compared to 15% with placebo ($p < 0.0001$); and 15% of patients on average for each month achieved a 100% reduction in migraine days, compared to 5% for placebo ($p < 0.0001$). Adverse event rates among eptinezumab-treated subjects were similar to placebo-treated subjects.

Professional Societies

In 2024, the American Headache Society (AHS) published a position statement update regarding therapies targeting calcitonin gene-related peptide (CGRP) for the prevention of migraine.15 In this position statement, the AHS states that the CGRP-targeting migraine therapies are a first-line option for migraine prevention. Per AHS, the basis for this focused position statement is:

- There is solid human evidence that establishes CGRP as a fundamental mechanism of migraine and therefore establishes CGRP-targeting therapies as “migraine-specific” in contrast to all the other established therapies.
- The cumulative evidence for the efficacy, safety, and tolerability of CGRP-targeting therapies is significantly greater than that for any established migraine preventive therapy. The remarkable tolerability of the CGRP-targeting therapies is a particularly positive feature.
- Nearly all CGRP-targeting therapies are FDA-approved for the preventive treatment of both episodic and chronic migraine, which simplifies decision-making in patients who may spontaneously transition back and forth between episodic and chronic migraine.
- There are multiple categories of evidence supporting the use of CGRP-targeting therapies that do not exist for other migraine preventive therapies, including: responder rates, efficacy in patients with multiple prior treatment failures, efficacy in those with acute medication overuse, and those who do and do not have aura.
- There is one head-to-head study demonstrating the superiority of a CGRP-targeting therapy (erenumab) over an established migraine preventive therapy (topiramate). In addition, multiple studies indicating the efficacy of CGRP targeting migraine preventive therapies in those who have previously failed multiple other established treatments provide indirect evidence of the superiority of CGRP-targeting therapies for some patients.
- Acknowledging CGRP-targeting therapies as first-line approaches will increase the likelihood that their efficacy and safety will be more thoroughly evaluated in understudied populations, particularly youth.
- Cost considerations regarding migraine therapies should include not only the direct cost of the treatments, but also the indirect costs of healthcare utilization and acute therapies, as well as socioeconomic costs for those who are disabled by the disease.

In 2018, the AHS published its position statement on integrating new migraine treatments into clinical practice. In regard to the preventative treatment of episodic and chronic migraines with monoclonal antibodies (mAbs) targeting CGRP or CGRP receptor, the position statement states: To achieve cost-effective care while ensuring access to those most appropriate for these treatments, it is important that the indications for initiating treatment with anti-CGRP mAbs are widely understood and followed closely. Prior to beginning an anti-CGRP product, in addition to appropriate diagnosis, age, and severity, AHS recommends a trial, inability to tolerate, or inadequate response to a 6-week trial of at least two traditional oral therapies (e.g., beta blockers, topiramate, venlafaxine, etc.) and/or a minimum of two quarterly injections (6 months) of onabotulinumtoxinA (chronic migraine only). AHS recommends continuing therapy if there has been a reduction in mean monthly headache days of ≥ 50% relative to pretreatment baseline and a clinical meaningful improvement in the scores from validated migraine-specific patient-reported outcome measures (e.g., MIDAS, MPFID, HIT-6).[4]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Vyepti is a calcitonin gene-related peptide antagonist indicated for the preventive treatment of migraine in adults. The recommended dosage is 100 mg administered by intravenous infusion every 3 months. Some patients may benefit from a dosage of 300 mg administered by intravenous infusion every 3 months. The efficacy of Vyepti was evaluated as a preventive treatment of episodic and chronic migraine in two randomized, multicenter, placebo-controlled studies.

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Policy History/Revision Information

Date	Summary of Changes
09/01/2024	**Coverage Rationale** • Updated list of examples of biologic CGRP antagonists or inhibitors the patient must not use in combination with Vyepti for the preventive treatment of migraines; added “Qulipta” • Revised coverage criteria for initial therapy: ○ Replaced criterion requiring:

Date	Summary of Changes
	▪ "Trial and failure (after a trial of at least two months), contraindication, or intolerance to amitriptyline (Elavil)" with "trial and failure (after a trial of at least two months), contraindication, or intolerance to *one of the following tricyclic antidepressants:* amitriptyline (Elavil) *or nortriptyline (Pamelor)*" ▪ "Trial and failure (after a trial of at least two months), contraindication, or intolerance to venlafaxine (Effexor/Effexor XR)" with "trial and failure (after a trial of at least two months), contraindication, or intolerance to *one of the following tricyclic serotonin-norepinephrine reuptake inhibitors: duloxetine (Cymbalta) or* venlafaxine (Effexor/Effexor XR)" ▪ "Trial and failure (after a trial of at least three months), contraindication, or intolerance to two of the following therapies used for the preventive treatment of migraines: Aimovig (erenumab- aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) (120 mg strength), and/or an oral calcitonin gene-related peptide (CGRP) receptor antagonist (e.g., Nurtec ODT)" with "trial and failure (after a trial of at least three months), contraindication, or intolerance to two of the following therapies used for the preventive treatment of migraines: Aimovig (erenumab- aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) (120 mg strength), and/or an oral calcitonin gene-related peptide (CGRP) receptor antagonist (e.g., Nurtec ODT, *Qulipta*)" **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS2024D0090M

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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