Vyepti™ (Eptinezumab-Jjmr)

Policy Number: PHARMACY 329.3 T2
Effective Date: September 1, 2020

➲ Instructions for Use

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Related Policy

- Review at Launch for New to Market Medications

Coverage Rationale

➲ See Benefit Considerations

Vyepti has been added to the Review at Launch program. Some members may not be eligible for coverage of this medication at this time. Refer to the Clinical Policy titled Review at Launch for New to Market Medications for additional details.

Chronic Migraine

Vyepti is proven for the preventive treatment of chronic migraines when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of chronic migraines with both of the following:
    - Greater than or equal to 15 headache days per month
    - Greater than or equal to 8 migraine days per month

    and
  - Medication will not be used in combination with another CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the United States Food and Drug Administration (FDA) approved labeling; and
  - Authorization will be issued for no more than 3 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 CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the FDA approved labeling; and
  - Authorization will be issued for no more than 12 months.

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

- For initial therapy, all of the following:

- Diagnosis of chronic migraines with both of the following:
  - Greater than or equal to 15 headache days per month
  - Greater than or equal to 8 migraine days per month

  and
- Trial and failure (after a trial of at least two months) to two of the following, or contraindication or intolerance to all of the following prophylactic therapies from the list below:[4]
  - Amitriptyline (Elavil)
  - One of the following beta-blockers: atenolol, metoprolol, nadolol, propranolol, or timolol
  - Divalproex sodium (Depakote/Depakote ER)
  - OnabotulinumtoxinA (Botox) [trial of at least 2 quarterly injections (6 months)]
  - Topiramate (Topamax)
  - Venlafaxine (Effexor/Effexor XR)

  and
- Trial and failure (after a trial of at least three months), contraindication, or intolerance to both of the following:
  - Aimovig (erenumab)
  - Emgality (galcanezumab)

  and
- Medication will not be used in combination with another CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
- Dosing is in accordance with the FDA approved labeling; and
- Authorization will be issued for no more than 3 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 CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the FDA approved labeling; and
  - Authorization will be issued for no more than 12 months.

Episodic Migraine

Vyepti is proven for the preventive treatment of episodic migraines when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of episodic migraines with both of the following:
    - Less than 15 headache days per month
    - Patient has 4 to 14 migraine days per month

    and
  - Medication will not be used in combination with another CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the FDA approved labeling; and
  - Authorization will be issued for no more than 3 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 CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the FDA approved labeling; and
  - Authorization will be issued for no more than 12 months.

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

- For initial therapy, all of the following:
  - Diagnosis of episodic migraines with both of the following:
    - Less than 15 headache days per month
    - Patient has 4 to 14 migraine days per month

and
- Trial and failure (after a trial of at least two months) to two of the following, or contraindication or intolerance to all of the following prophylactic therapies from the list below:[4]
  - Amitriptyline (Elavil)
  - One of the following beta-blockers: atenolol, metoprolol, nadolol, propranolol, or timolol
  - Divalproex sodium (Depakote/Depakote ER)
  - Topiramate (Topamax)
  - Venlafaxine (Effexor/Effexor XR)

  and
- Trial and failure (after a trial of at least three months), contraindication, or intolerance to both of the following:
  - Aimovig (erenumab)
  - Emgality (galcanezumab)

  and
- Medication will not be used in combination with another CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
- Dosing is in accordance with the FDA approved labeling; and
- Authorization will be issued for no more than 3 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 CGRP antagonist or inhibitor [e.g., Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), Nurtec ODT (rimegepant), and Ubrelvy (ubrogepant)]; and
  - Dosing is in accordance with the FDA approved labeling; and
  - Authorization will be issued for no more than 12 months.

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

Prior Authorization Requirements

Prior authorization is not required; however, it is strongly recommended for Vyepti. While no penalty will be imposed for failure to request a pre-service review, if one is not requested, a medical necessity review will be conducted post-service to determine coverage. It is the referring physician's responsibility to provide medical documentation to demonstrate clinical necessity for the medication. Refer to the Clinical Policy titled Review at Launch for New to Market Medications.

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 the member specific benefit plan document 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 may apply.

HCPCS Code	Description
C9063	Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)
J3490	Unclassified drugs
J3590	Unclassified biologics

Diagnosis Code	Description
G43.001	Migraine without aura, not intractable, with status migrainosus
G43.009	Migraine without aura, not intractable, without status migrainosus

Diagnosis Code	Description
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
G43.601	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.C0	Periodic headache syndromes in child or adult, not intractable
G43.C1	Periodic headache syndromes in child or adult, intractable
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

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.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

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 30mg), 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 300mg dose (p=0.0001) and 3.9 days for 100mg (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

American Headache Society (AHS)

In 2018, the American Headache Society (AHS) published their position statement on integrating new migraine treatments into clinical practice. In regards 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 2 traditional oral therapies (e.g., beta blockers, topiramate, venlafaxine, etc.) and/or a minimum of 2 quarterly injections (6 months) of onabotulinimtoxinA (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.

References

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealth Group National Pharmacy & Therapeutics Committee. [*2020D0090A*]

1. Vyepti [prescribing information]. Bothell, WA: Lundbeck Seattle Biopharmaceuticals, Inc.; February 2020.
2. Alder Biopharmaceuticals, Inc. Evaluation of ALD403 (Eptinezumab) in the Prevention of Chronic Migraine (PROMISE 2). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2020 Jan 24]. Available from: https://clinicaltrials.gov/show/NCT02974153 NLM Identifier: NCT02974153.
3. 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.
4. International Headache Society (IHS); Headache Classification Committee. The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38:1-211.
5. The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice. Headache: The Journal of Head and Face Pain. 2019;59: 1-18.
6. 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.
7. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016 May 10;86(19):1818-26.
8. United Council for Neurologic Subspecialties website. www.ucns.org. Accessed January 24, 2020.

Policy History/Revision Information

Date	Summary of Changes

09/01/2020	**Template Update**
	• Reformatted policy; transferred content to new template
	• Removed and replaced section titled *Conditions of Coverage* with *Prior Authorization Requirements*
	  ○ Simplified and relocated language pertaining to prior authorization guidelines
	  ○ Removed language addressing benefit type and referral requirements (refer to the member specific benefit plan document)
	• Replaced references to “precertification” with “prior authorization”
	Supporting Information
	• Archived previous policy version PHARMACY 329.2 T2

Instructions for Use

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.