09-J3000-68

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Revised: 05/15/21

Subject: Eptinezumab-jjmr (Vyepti™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Migraines

The diagnostic criteria for chronic migraine requires the inclusion of all of the following:

A. Headache (migraine-like or tension-like) on ≥15 days per month for >3 months and fulfilling criteria B and C

B. Occurring in a patient who has had at least five attacks fulfilling of migraine without aura and/or migraine with aura

C. On ≥8 days per month for >3 months, fulfilling any of the following:

   1. Migraine without aura
   2. Migraine with aura
   3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative

D. Not better accounted for by another ICHD-3a diagnosis.

Migraine prevention may be of benefit in those with the following:

- Frequent or long-lasting migraine headaches (>4 headaches/month or headaches lasting >12 hours)
- Migraine attacks that cause significant disability or diminished quality of life despite appropriate acute treatment
- Contraindication to acute therapies
- Failure of acute therapies

- Serious adverse effects of acute therapies
- Risk of medication overuse headache
- Menstrual migraine (when acute abortive therapies are incomplete or unsatisfactory)

The American Headache Society (AHS) also includes patient preference as a consideration.

Preventative pharmacotherapy for chronic migraine is less well studied than for episodic migraine. However, use of recommended episodic prevention agents is also recommended in chronic migraine. Clinical trials suggest efficacy is often first noted at four weeks and can continue to increase for three months.

The American Headache Society (AHS) and the American Academy of Neurology (AAN) suggest the following agents for the prevention of migraine:

- Established as effective (Level A)
  - Antiepileptic drugs (AEDs)
    - Divalproex
    - Valproate
    - Topiramate
  - Beta blockers
    - Metoprolol
    - Propranolol
    - Timolol
  - Triptans
    - Frovatriptan for short term menstrually associated migraines (MAMs) prevention
- Probably effective (Level B)
  - Antidepressants
    - Amitriptyline
    - Venlafaxine
  - Beta blockers
    - Atenolol
    - Nadolol
  - Triptans
    - Naratriptan, zolmitriptan for short term MAMs prevention

The 2018 American Headache Society Consensus Statement recommends the following indications for initiating treatment with a Calcitonin Gene-Related Peptide (CGRP) agent:

- Prescribed by a licensed medical professional
- Patient is at least 18 years of age

- One of the following:
  - Diagnosis of migraine with or without aura (4-7 monthly headache days) and both of the following:
    - Inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
      - Topiramate
      - Divalproex sodium/valproate sodium
      - Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      - Tricyclic antidepressant: amitriptyline, nortriptyline
      - Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
      - Other Level A or B treatment according to AAN-AHS guideline
    - At least moderate disability (Migraine Disability Assessment Questionnaire [MIDAS] >11, Headache Impact Test-6 [HIT]-6 >50)
  - Diagnosis of migraine with or without aura (8-14 monthly headache days) and inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
    - Topiramate
    - Divalproex sodium/valproate sodium
    - Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
    - Tricyclic antidepressant: amitriptyline, nortriptyline
    - Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
    - Other Level A or B treatment according to AAN-AHS guideline
  - Diagnosis of chronic migraine and one of the following:
    - Inability to tolerate (due to side effects) or inadequate response to a 6-week trial of at least 2 of the following:
      - Topiramate
      - Divalproex sodium/valproate sodium
      - Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      - Tricyclic antidepressant: amitriptyline, nortriptyline
      - Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
      - Other Level A or B treatment according to AAN-AHS guideline
    - Inability to tolerate or inadequate response to a minimum of 2 quarterly injection (6 months) of onabotulinumtoxin A

American Headache Society (2015): The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies state that specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A). The evidence base for medication efficacy should be considered along with potential medication side effects, potential adverse events, patient-specific contraindications to use of a particular medication, and drug-to-drug interactions when deciding which medication to prescribe for acute therapy of a migraine attack.

The European Headache Federation and WHO consensus article (2019) states the following:

- Individuals with migraine headaches should almost always be managed in primary care. The exception being chronic migraine, which likely requires specialist management.
- Any headache not responding satisfactorily in primary care should be referred to a specialist
- In adults and children, regular high frequency use (>2 day/week) of acute medication risks the development of medication-overuse headache
- Treatment of episodic acute migraine headaches should be approached in a step wise manner and should treat three attacks at each step before moving to the next step if needed:
    - Step 1:
        - Use non-opioid analgesics, plus an antiemetic when needed.
    - Step 2 for adults:
        - Use triptan products.
        - Triptans should not be used regularly on ≥10 days/month to avoid the risk of medication overuse headaches.
        - Triptan efficacy is highly variable between individuals, so patients should try different triptans and formulations. Sumatriptan subcutaneous injection should be considered when all other triptans are ineffective.
        - When nausea is present, zolmitriptan nasal spray or sumatriptan subcutaneous injection may be preferred.
    - Step 2 for children and adolescents:
        - Failure of Step 1 in children should lead to specialist referral. No specific anti-migraine drugs have shown efficacy in children under 12 years of age
        - Failure of Step 2 in adolescents (12-17 years of age), the following have shown efficacy and are approved:
            - Sumatriptan nasal spray
            - Zolmitriptan nasal spray
- For episodic migraine prophylaxis:
    - Indication for migraine prophylaxis include:
        - Attacks cause disability on two or more days per month
        - And acute therapy has been optimized but does not prevent this, or is poorly tolerated, or there is a risk of over-frequent use of acute therapy, even when it is effective
        - And the patient is willing to take daily medication.
        - Failure of acute therapy is an indication for migraine prophylaxis.
        - For children: frequent absence from school.
    - Migraine prophylaxis agents may take 2-3 months to show efficacy.
    - Children requiring prophylactic medication should be referred to a specialist.
    - Medications which are effective in adult prophylaxis of episodic migraine include:
        - Beta blockers:
            - Atenolol, bisoprolol, metoprolol, propranolol
        - Amitriptyline

        - Topiramate
        - Candesartan
        - Sodium valproate
        - Flunarizine
        - CGRP
    - Onabotulinum toxin A is not effective in episodic migraine.
    - When prophylaxis therapy fails:
        - Failure may be due to subtherapeutic dosage or duration of therapy.
        - Failure of one therapy does not predict the failure of another therapy.
        - Review of the following are recommended:
            - Diagnosis
            - Adherence
            - Other medications, especially for medication overuse headache causes
        - The prophylaxis therapy should be discontinued if it fails to show clear benefit.
        - If all prophylaxis therapies fail, a specialist should be referred.
- Chronic migraine management:
    - Chronic migraine patients should be referred to a specialist.
    - Medications with efficacy in chronic migraine include:
        - Topiramate
        - OnabotulinumA
        - CGRP

The European Headache Federation guideline states the following on combining migraine prophylaxis therapy:

- In episodic migraine, it's suggested to stop oral prophylaxis migraine agents before starting CGRPs, unless the patient previously had chronic migraine prior to prophylaxis. In such patients, the suggestion is to add CGRP to the ongoing oral prophylaxis therapy.
- In chronic migraine, it's suggested to add CGRP to ongoing oral prophylaxis therapy.
- In chronic migraine patients on onabotulinumA therapy and are receiving inadequate treatment response, it's suggested to stop onabotulinumA therapy before starting CGRPs.
- In patients with chronic migraine who are on treatment with CGRP and may benefit from additional prevention, it's suggested to add on oral preventative agents.
- In patients with medication overuse, it's suggested to use CGRPs before or after withdrawal of acute medications

Medication overuse headache (MOH)

The European Headache Federation and WHO consensus article (2019) states the following:

- Prevention is preferred.

- The four objectives of management are:
  - Stop the overused medication.
  - Recovery from MOH.
  - Review and reassess the underlying headache disorder
  - Prevent relapse while allowing acceptable use of medications
- Comorbidities may also require management

Safety

Vyepti is contraindicated in patients with serious hypersensitivity to eptinezumab-jjmr or to any of the excipients in Vyepti.

POSITION STATEMENT:

Initiation of eptinezumab-jjmr (Vyepti) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. **ONE** of the following:
   a. The requested agent is being used for migraine prophylaxis **AND ALL** of the following:
      i. **ONE** of the following:
         1) The member has a diagnosis of chronic migraine **AND ALL** of the following:
            a) ≥15 headache days per month of migraine-like or tension-like headache for a minimum of 3 months

            AND

            b) ≥8 migraine headache days per month for a minimum of 3 months

            AND

            c) The requested agent is FDA approved for migraine prophylaxis

            AND

            d) The prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist

         OR

         2) The member has a diagnosis of episodic migraine **AND BOTH** of the following:
            a) **ONE** of the following:
               - The member has greater than 4 migraine headache days per month

               OR

               - The member's migraine headaches last >12 hours

               OR

               - The member's migraine attacks cause significant disability or diminished

quality of life despite appropriate therapy with acute agents only

OR

- The member has contraindications to acute therapies

OR

- The member has tried and received inadequate response to acute therapies

OR

- The member has serious side effects to acute therapies

OR

- The member is at risk of medication overuse headache without preventative therapy

AND

b) The requested agent is FDA approved for migraine prophylaxis

AND

ii. **ONE** of the following:

1) The member has tried and had an inadequate response to at least one migraine prophylaxis class (i.e. anticonvulsants [divalproex, valproate, topiramate], beta blockers [atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [amitriptyline, venlafaxine], candesartan) after an adequate trial as defined by **BOTH** of the following:

a) The trial length was at least 6 weeks at generally accepted doses

AND

b) The member was ≥80% adherent to the prophylaxis agent during the trial

OR

2) The member has an intolerance or hypersensitivity to at least one migraine prophylaxis class listed above

OR

3) The member has an FDA labeled contraindication to ALL migraine prophylaxis agents listed above

AND

iii. Medication overuse headache has been ruled out

AND

iv. **ONE** of the following:

1) The member has tried and had an inadequate response to **BOTH** Aimovig (erenumab) AND Emgality (galcanezumab)

OR

2) The member has an intolerance or hypersensitivity to **BOTH** Aimovig (erenumab)

AND Emgality (galcanezumab) that is not expected to occur with the requested agent

OR

3) The member has an FDA labeled contraindication to **BOTH** Aimovig (erenumab) **AND** Emgality (galcanezumab)

OR

b. **ONE** of the following:

i. The member has another FDA approved indication for the requested agent and route of administration

OR

ii. The member has another indication that is supported in compendia (AHFS, or DrugDex 1 or 2a level of evidence) for the requested agent and route of administration

AND

2. The member will **NOT** be using the requested agent in combination with another prophylactic CGRP agent

AND

3. Dose does not exceed 300 mg every three months

Length of Approval: 6 months

Continuation of eptinezumab-jjmr (Vyepti) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for migraine prophylaxis OR the member has previously met all indication-specific criteria.

AND

2. **ONE** of the following:

a. **BOTH** of the following:

i. The requested agent is being used for migraine prophylaxis **AND ALL** of the following:

1. The prescriber has provided information indicating improvement in migraine prevention (e.g. reduced migraine headache days, reduced migraine frequency, reduced use of acute abortive migraine medication) with the requested agent

AND

2. If the member has chronic migraine, the prescriber is a headache specialist (e.g. neurologist; pain management specialist; or specialist with United Council for Neurologic Subspecialties [UCNS] certification) or has consulted with a headache specialist

AND

ii. Medication overuse headache has been ruled out

OR

b. **ONE** of the following:

i. The member has another FDA approved indication for the requested agent and route of administration

OR

ii. The member has another indication that is supported in compendia (AHFS, or DrugDex 1 or 2a level of evidence) for the requested agent and route of administration

AND

3. The member will **NOT** be using the requested agent in combination with another prophylactic CGRP agent

AND

4. Dose does not exceed 300 mg every three months

Length of Approval: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 100 mg as an intravenous infusion over approximately 30 minutes every 3 months
- Some patients may benefit from a dosage of 300 mg

Dose Adjustments

- None

Drug Availability

- 100 mg/mL solution in a single-dose vial

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Hypersensitivity

Precautions/Warnings

- Hypersensitivity Reactions: Reactions have included angioedema, urticaria, facial flushing, and rash. If a hypersensitivity reaction occurs, consider discontinuing and initiate appropriate therapy

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J3032	Injection, eptinezumab-jjmr, 1 mg

ICD-10 Diagnoses Codes That Support Medical Necessity

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
G43.601	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

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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8. Marmura M, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache. 2015;55:3–20.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 05/13/20.

GUIDELINE UPDATE INFORMATION:

06/15/20	New Medical Coverage Guideline.
07/01/20	Revision: Added HCPCS code C9063.
10/01/20	Revision: Added HCPCS code J3032 and removed codes C9063 and J3590.
10/15/20	Revision to position statement
05/15/21	Revision to position statement