Medical Policy Bulletin

Title:
Eptinezumab-jjmr (VYEPTI™)
Policy #:
MA08.116e

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Eptinezumab-jjmr (VYEPTI™) is considered medically necessary and, therefore, covered for the preventive treatment of migraine in adult individuals when all of the following criteria are met:

INITIAL CRITERIA

- A neurologist, headache specialist, or pain specialist has established a diagnosis of episodic (4–14 headache days per month) or chronic (≥15 headache days per month) migraine
- The individual is 18 years of age or older
- The individual had an inadequate response or inability to tolerate a 4-week trial of two of the following prophylactic medications:
    - Topiramate
    - Divalproex sodium/valproic acid
    - Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
    - Tricyclic antidepressants: amitriptyline, nortriptyline
    - Serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants: venlafaxine, duloxetine
    - Onabotulinumtoxin-A (Botox) for chronic migraines
- Medication will not be used for the preventive treatment of acute or episodic migraine in combination with another calcitonin gene-related peptide (CGRP) inhibitor (e.g., for episodic or chronic migraines: erenumab

[Aimovig], fremanezumab [Ajovy], or galcanezumab [Emgality]; or oral CGRP antagonist for episodic migraines: rimegepant [Nurtec ODT] or atogepant [Qulipta])

CONTINUATION CRITERIA

Documentation of response to therapy as defined by a 50% reduction in migraine days per month from baseline (defined as at least 4 hours' duration and moderate intensity).

EXPERIMENTAL/INVESTIGATIONAL

All other uses for etinezumab-jjmr (VYEPTI) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

DRUG INFORMATION

In accordance with US Food and Drug Administration (FDA) prescribing information, etinezumab-jjmr (VYEPTI™) is administered by intravenous infusion 100 mg every three months. Some individuals may benefit from a dosage of 300 mg administered by intravenous infusion every three months.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, eptinezumab-jjmr (VYEPTI™) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Etinezumab-jjmr (VYEPTI™) was approved by the FDA on February 21, 2020 for the preventive treatment of migraine in adult individuals.

PEDIATRIC USE

The safety and effectiveness of etinezumab-jjmr (VYEPTI™) for the preventive treatment of migraine have not been established in the pediatric population.

Description

Migraine is a complex and incapacitating neurological disease characterized by recurrent episodes of severe headaches typically accompanied by a range of symptoms, including nausea, vomiting, and sensitivity to light or sound. It is estimated to affect approximately 39 million people in the United States and more than 1.3 billion worldwide. Migraine affects women three times more often than men. It is the second leading cause of years lived with disability (YLD) among all diseases, and is the top YLD cause among patients aged 15 to 49 years, according to the Global Burden of Disease study. Migraine affects patients' lives, their relationships, as well as their activities of

daily living. More than 157 million work days are lost each year in the United States because of migraine. Beyond the burden of a migraine attack itself, having migraine increases the risk for other physical and psychiatric conditions.

Eptinezumab-jjmr (VYEPTI™) is a humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for calcitonin gene-related peptide (CGRP) ligand. Eptinezumab-jjmr (VYEPTI) binds to CGRP ligand and blocks its binding to the receptor. Eptinezumab-jjmr (VYEPTI) is produced in *Pichia pastoris* yeast cells by recombinant DNA technology.

PEER-REVIEWED LITERATURE

SUMMARY
The efficacy and safety of eptinezumab-jjmr (VYEPT) was evaluated in two clinical trials: Prevention of Migraine via Intravenous ALD403 Safety and Efficacy 1 (PROMISE-1) in episodic migraine and PROMISE-2 in chronic migraine. The PROMISE-1 study was a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group study for adult individuals with episodic migraine. Individuals were randomly assigned to eptinezumab-jjmr (VYEPTI) 30 mg, 100 mg, 300 mg, or placebo for up to four intravenous (IV) doses administered every 12 weeks. The primary endpoint was change from baseline in monthly migraine days (MMDs) over weeks 1 through 12. A total of 665 individuals were randomly assigned to either 100 mg (n=221) or 300 mg (n=222) IV eptinezumab-jjmr (VYEPTI) or placebo (n=222) every 3 months for 1 year. Baseline migraine frequency was 8.6 migraine days per month, comparable between groups. Between months 1 through 3, the mean change in migraine days was −3.9 days (P=0.018) and −4.3 days (P<0.001) for the 100-mg and 300-mg doses, respectively, compared to −3.2 days for the placebo group. During the same period, 49.8% of individuals in the 100-mg group (P=0.009) and 56.3% of individuals in the 300-mg group (P<0.001) experienced 50% or greater reduction in migraine days compared to 37.4% of those in the placebo group. A reduction of 75% or more in migraine days in months 1 through 3 was reported by 22.2% of the 100-mg group, 29.7% of the 300-mg group (P<0.001), and 16.2% of the placebo group.

The PROMISE-2 study was a phase 3, randomized, double-blind, placebo-controlled study evaluating safety and efficacy of two infusions for the preventive treatment of chronic migraine. The primary endpoint was change from baseline in MMDs over weeks 1 through 12. A total of 1072 individuals were randomly assigned and received placebo (N=366), 100 mg eptinezumab-jjmr (VYEPTI) (N=356), or 300 mg VYEPTI (N=350) every 3 months for 6 months. Individuals were allowed to use and to continue an established stable regimen of acute migraine or headache preventive medication (except onabotulinumtoxin-A). Individuals with a dual diagnosis of chronic migraine and medication overuse headache attributable to acute medication overuse (triptans, ergotamine, or combination analgesics >10 days per month) were included in the study population. Individuals using opioids or butalbital-containing products greater than 4 days per month were not allowed.

In the group of individuals treated with 100 mg, changes from baseline in MMDs were −7.7 days (P<0.0001) and −8.1 days (P<0.0001) over first 3 months (months 1–3) and a second 3 months (months 4–6), respectively. In the more than 75%, migraine response rates (RRs) were: 30.9% (month 1; P<0.0001), 26.7% (months 1–3; P=0.0001), and 38.5% (months 4–6). In the 50% or greater, migraine RRs were 57.6% (months 1–3; P<0.0001) and 60.7% (months 4–6).

In the group of individuals treated with 300 mg, changes from baseline in MMDs were −8.2 days (P<0.0001) and −8.8 days (P<0.0001) over the first 3 months and a second 3 months, respectively. In the 75% or greater, migraine RRs were 36.9% (month 1; P<0.0001), 33.1% (months 1–3; P<0.0001), and 42.3% (months 4–6). In the 50% or greater, migraine RRs were 61.4% (months 1–3; P<0.0001) and 63.4% (months 4–6). In the group of individuals treated with placebo, changes from baseline in MMDs were −5.6 days and −6.1 days over first 3 months and a second 3 months, respectively. In the 75% or greater, migraine RRs were 15.6% (month 1), 15.0% (months 1–3), and 22.7% (months 4–6). In the 50% or greater, migraine RRs were 39.3% (months 1–3) and 44.5% (months 4–6).

The most common adverse reactions (>2% and ≥2% than placebo) in the clinical trials for the preventive treatment of migraine were nasopharyngitis and hypersensitivity.

Eptinezumab-jjmr (VYEPTI) treatment demonstrated statistically significant improvements compared to placebo for the primary efficacy endpoint in both studies.

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria

highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)

Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

HCPCS Level II Code Number(s)

THE FOLLOWING CODE(S) ARE USED TO REPORT
Eptinezumab-jjmr (VYEPTI™)

J3032 Injection, eptinezumab-jjmr, 1 mg

Revenue Code Number(s)
N/A

Policy History

Revisions From 08.00.45e:

06/18/2026	This version of the policy will become effective 06/18/2026 This policy was updated to communicate the Company's coverage criteria for Eptinezumab-jjmr (VYEPTI™). The following was updated with clarification: • Medication will not be used for the preventive treatment of acute or episodic migraine in combination with another CGRP inhibitor(e.g. for episodic or chronic migraines Erenumab [Aimovig], fremanezumab [Ajovy], or galcanezumab [Emgality] or oral CGRP Antagonist for episodic migraines Rimegepant [Nurtec ODT] or atogepant [Qulipta])

Revisions From MA08.116d:

03/28/2025	This policy has been reissued in accordance with the Company's annual review process.

05/07/2024	This policy has been reissued in accordance with the Company's annual review process.
10/01/2023	This policy has been identified for the ICD-10 CM code update, effective 10/01/2023. The following ICD-10 CM codes have been added to this policy: 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

Revisions From MA08.116c:

02/27/2023	This version of the policy will become effective 02/27/2023. This policy was updated to communicate the Company's coverage criteria for Eptinezumab-jjmr (VYEPTI™). The following was removed: • Medication will not be used in combination with onabotuliniumtoxin A (Botox) for chronic migraine The following was updated with examples of CGRPs: • Medication will not be used in combination with another CGRP inhibitor(e.g. for episodic or chronic migraines Erenumab [Aimovig], fremanezumab [Ajovy], or galcanezumab [Emgality] or oral CGRP Antagonist for episodic migraines Rimegepant [Nurtec ODT] or atogepant [Qulipta])

Revisions From MA08.116b:

04/06/2022	This policy has been reissued in accordance with the Company's annual review process.
07/28/2021	This policy has been reissued in accordance with the Company's annual review process.
10/01/2020	This policy has been identified for the HCPCS code update, effective 10/01/2020. The following HCPCS code has been **termed** from this policy: C9063 Injection, eptinezumab-jjmr, 1 mg J3590 Unclassified biologics The following HCPCS code has been **added** to this policy: J3032 Injection, eptinezumab-jjmr, 1 mg

Revisions From MA08.116a:

07/01/2020	This policy has been identified for the HCPCS code update, effective 07/01/2020. The following HCPCS code has been **termed** from this policy: C9399 Unclassified drugs or biologics The following HCPCS code has been **added** to this policy: C9063 Injection, eptinezumab-jjmr, 1 mg

Revisions From MA08.116:

05/11/2020	This version of the policy will become effective 05/11/2020. This new policy has been developed to communicate the Company's coverage criteria for Eptinezumab-jjmr (VYEPTI™).

Version Effective Date:
06/18/2026
Version Issued Date:
06/18/2026
Version Reissued Date:
N/A