Injectable CGRP Antagonists

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Injectable CGRP Antagonist drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies while steering utilization to the most cost-effective medication within the therapeutic class. For this program, Ajovy (fremanezumab) and Emgality (galcanezumab) are the preferred products. The criteria will require the use of the health plan's preferred products before the use of the targeted product, Aimovig (erenumab), unless there are clinical circumstances that exclude the use of the preferred products. Vyepti is excluded from the preferred product requirement.

Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), and Vyepti (eptinezumab) are Food and Drug Administration (FDA) approved Calcitonin Gene-Related Peptide (CGRP) Antagonists indicated for preventive treatment of migraine in adults. Emgality is also indicated for the treatment of episodic cluster headache in adults.

Ajovy (fremanezumab) is indicated for the preventive treatment of episodic migraine in pediatric patients who are 6 to 17 years of age and who weigh 45 kg or more.

Limitations of Use:

- The safety and effectiveness of multiple CGRP antagonists or inhibitors used for the preventive treatment of migraine has not been evaluated.

POLICY

Must meet BOTH the Preferred Drug Plan Design and Criteria for Initial Approval/Continuation of Therapy when both are applicable.

Preferred Drug Plan Design

A. Criteria for initial approval for Aimovig (erenumab) will only apply when the following criteria are met:
    1. The patient has had an inadequate response to treatment, intolerable adverse event, or has a contraindication to therapy with BOTH preferred products, Ajovy and Emgality
    2. The patient is currently receiving therapy with Aimovig, excluding when Aimovig is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

Initial Criteria for Approval

A. Aimovig (erenumab), Ajovy (fremanezumab), and Emgality (galcanezumab) may be considered medically necessary for the preventive treatment of **chronic migraine** in patients 18 years of age and older when ALL of the following criteria are met:
    1. The patient has a diagnosis of chronic migraine defined as a headache occurring on 15 or more days per month for more than 3 months, which, on at least 8 days per month, has features of a migraine headache
    2. The patient has had a trial of at least one of the listed medications from any of the following migraine prophylactic agent classes and or has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
        a.) Anticonvulsants (e.g., divalproex sodium, sodium valproate, topiramate)
        b.) Beta blockers (e.g., atenolol, metoprolol, nadolol, propranolol, timolol)
        c.) Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine)
    3. The patient had an adequate trial of both migraine prophylaxis agents as defined by BOTH of the following unless the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR the patient is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
        a.) The trial length was at least 8 weeks at maximum tolerated dose
        b.) The patient was adherent to the prophylaxis agent during the trial
    4. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
    5. Other conditions or aggravating factors that are contributing to the development of chronic migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
    6. If the patient is also currently receiving botulinum toxin injection for chronic migraine prophylaxis and is going to be using the requested drug and botulinum toxin together for preventative treatment of chronic migraine (i.e., not switching from one agent to another), BOTH of the following must apply:
        a.) Patient has had a reduction in the overall number of migraine days or reduction in number of severe migraine days per month with botulinum toxin use
        b.) Patient continues to experience a significant number of migraine headache days or severe migraine days per month requiring additional therapy for migraine prevention
    7. The requested medication will not be used in combination with another CGRP antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Vyepti or Qulipta)

Approval will be for **6 months**

B. Aimovig (erenumab), Ajovy (fremanezumab), and Emgality (galcanezumab) may be considered medically necessary for the preventive treatment of **episodic migraine** in patients 18 years of age and older (6 years and older for Ajovy) when ALL the following criteria are met:
   1. The patient has a diagnosis of episodic migraine defined as at least 4 and fewer than 15 migraine days per month and fewer than 15 headache days per month on average during the previous 3-month period
   2. The patient has had a trial of at least one of the listed medications from any of the following migraine prophylactic agent classes and experienced an inadequate response, has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
      a.) Anticonvulsants (e.g., divalproex, valproate, topiramate)
      b.) Beta blockers (e.g., atenolol, metoprolol, nadolol, propranolol, timolol)
      c.) Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine)
   3. The patient had an adequate trial of both migraine prophylaxis agents as defined by BOTH of the following unless the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR the patient is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
      a.) The trial length was at least 8 weeks at maximum tolerated dose
      b.) The patient was adherent to the prophylaxis agent during the trial
   4. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
   5. Other conditions or aggravating factors that are contributing to the development of episodic migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
   6. The requested medication will not be used in combination with another CGRP antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Vyepti, Nurtec ODT, or Qulipta)

Approval will be for **6 months**

C. Emgality (galcanezumab) may be considered medically necessary for the treatment of episodic cluster headache in patients 18 years of age and older when ALL of the following criteria are met:
   1. The patient has a diagnosis of episodic cluster headache defined as severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes, untreated, occurring at least every other day and up to eight times per day (see Appendix A)
   2. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
   3. The requested medication will not be used concurrently with another CGRP receptor antagonist

Approval will be for **6 months**

D. Vyepti (eptinezumab) may be considered medically necessary for the preventive treatment of **chronic migraine** in patients 18 years of age and older when ALL of the following criteria are met:
   1. The patient has a diagnosis of chronic migraine defined as a headache occurring on 15 or more days per month for more than 3 months, which, on at least 8 days per month, has features of a migraine headache

2. The patient has had a trial of at least one of the listed medications in each of the following migraine prophylactic agent classes and experienced an inadequate response, has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
   a.) Anticonvulsants (e.g., divalproex sodium, sodium valproate, topiramate)
   b.) Beta blockers (e.g., atenolol, metoprolol, nadolol, propranolol, timolol)
   c.) Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine)
3. The patient had an adequate trial for each migraine prophylaxis class as defined by BOTH of the following unless the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR the patient is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
   a.) The trial length was at least 8 weeks at maximum tolerated dose
   b.) The patient was adherent to the prophylaxis agent during the trial
4. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
5. Other conditions or aggravating factors that are contributing to the development of chronic migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
6. If the patient is also currently receiving botulinum toxin injection for chronic migraine prophylaxis and is going to be using the requested drug and botulinum toxin together for preventative treatment of chronic migraine (i.e., not switching from one agent to another), BOTH of the following must apply:
   a.) Patient has had a reduction in the overall number of migraine days or reduction in number of severe migraine days per month with botulinum toxin use
   b.) Patient continues to experience a significant number of migraine headache days or severe migraine days per month requiring additional therapy for migraine prevention
7. The requested medication will not be used in combination with another CGRP antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Aimovig , Ajovy, Emgality, or Qulipta)

Approval will be for **6 months**

E. Vyepti (eptinezumab) may be considered medically necessary for the preventive treatment of **episodic migraine** in patients 18 years of age and older when ALL of the following criteria are met:
   1. The patient has a diagnosis of episodic migraine defined as at least 4 and fewer than 15 migraine days per month and fewer than 15 headache days per month on average during the previous 3-month period
   2. The patient has had a trial of at least one of the listed medications in each of the following migraine prophylactic agent classes and experienced an inadequate response, has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the alternative migraine prophylactic agents, OR is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
      a.) Anticonvulsants (e.g., divalproex, valproate, topiramate)
      b.) Beta blockers (e.g., atenolol, metoprolol, nadolol, propranolol, timolol)
      c.) Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine)
   3. The patient had an adequate trial for each migraine prophylaxis class as defined by BOTH of the following unless the patient has a documented intolerance, FDA labeled contraindication,

or hypersensitivity to the alternative migraine prophylactic agents, OR the patient is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome:
   a.) The trial length was at least 8 weeks at maximum tolerated dose
   b.) The patient was adherent to the prophylaxis agent during the trial
4. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
5. Other conditions or aggravating factors that are contributing to the development of episodic migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
6. The requested medication will not be used in combination with another CGRP antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Aimovig, Ajovy, Emgality, Nurtec ODT, or Qulipta)

Approval will be for **6 months**

Continuation of Therapy

A. Aimovig (erenumab), Ajovy (fremanezumab) and Emgality (galcanezumab) may be considered medically necessary for the continuation of preventive treatment of chronic migraine or episodic migraine when ALL of the following criteria are met:
   1. The patient's condition has responded to therapy as defined by ONE of the following:
      a.) The patient has achieved or maintained a 50% reduction in monthly headache frequency or severity with requested medication since starting therapy with medical records that support such benefit
      OR
      b.) The patient has had a reduction in headache frequency and/or severity resulting in an improvement in productivity and attendance at school or work since starting therapy with requested medication with medical records that support such benefit
   2. The patient has had a reduction in the number of days of use of acute migraine-specific medications from baseline with medical records that support such benefit
   3. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
   4. Other conditions or aggravating factors that are contributing to the development of migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
   5. If the patient is also currently receiving botulinum toxin injection for chronic migraine prophylaxis and is going to be using the requested drug and botulinum toxin together for preventative treatment of chronic migraine (i.e., not switching from one agent to another), BOTH of the following must apply:
      a.) Patient has had a reduction in the overall number of migraine days or reduction in number of severe migraine days per month with botulinum toxin use
      b.) Patient continues to experience a significant number of migraine headache days or severe migraine days per month requiring additional therapy for migraine prevention
   6. The patient has not been receiving botulinum toxin injection for headache prophylaxis **AND** will not be initiating botulinum toxin headache prophylaxis while using the requested medication for the preventative treatment of episodic migraine
   7. The requested medication will not be used in combination with another biologic CGRP antagonist or inhibitor also being used for preventive treatment of migraine (e.g., Vyepti, Nurtec ODT, or Qulipta)

Approval will be for **12 months**

B. Emgality (galcanezumab) may be considered medically necessary for the continuation of treatment of episodic cluster headache in adults when ALL of the following criteria are met:
   1. The patient's condition has responded to therapy as defined by ONE of the following:
      a.) The patient has achieved or maintained a 50% reduction in weekly cluster headache attack frequency or severity with requested medication since starting therapy with medical records that support such benefit
      OR
      b.) The patient has had a reduction in headache frequency and/or severity resulting in an improvement in productivity and attendance at school or work since starting therapy with requested medication with medical records that support such benefit
   2. The patient has had a reduction in the number of days of use of acute medications from baseline with medical records that support such benefit
   3. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)

Approval will be for **12 months**

C. Vyepti (eptinezumab) may be considered medically necessary for the continuation of preventive treatment of chronic migraine or episodic migraine in adults when ALL of the following criteria are met:
   1. Member is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs)
   2. The patient's condition has responded to therapy as defined by ONE of the following:
      a.) The patient has achieved or maintained a 50% reduction in monthly headache frequency or severity with requested medication since starting therapy with medical records that support such benefit
      OR
      b.) The patient has had a reduction in headache frequency and/or severity resulting in an improvement in productivity and attendance at school or work since starting therapy with requested medication with medical records that support such benefit
   3. The patient has had a reduction in the number of days of use of acute migraine-specific medications from baseline with medical records that support such benefit
   4. The patient has been evaluated for and does not have medication overuse headache (see Appendix B)
   5. Other conditions or aggravating factors that are contributing to the development of migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)
   6. If the patient is also currently receiving botulinum toxin injection for chronic migraine prophylaxis and is going to be using the requested drug and botulinum toxin together for preventative treatment of chronic migraine (i.e., not switching from one agent to another), BOTH of the following must apply:
      a.) Patient has had a reduction in the overall number of migraine days or reduction in number of severe migraine days per month with botulinum toxin use
      b.) Patient continues to experience a significant number of migraine headache days or severe migraine days per month requiring additional therapy for migraine prevention
   7. The patient has not been receiving botulinum toxin injection for headache prophylaxis and will not be initiating botulinum toxin headache prophylaxis while using the requested medication for the preventative treatment of episodic migraine
   8. The requested medication will not be used in combination with another CGRP antagonist or inhibitor also being used for the preventive treatment of migraine (e.g., Aimovig, Ajovy, Emgality, Nurtec ODT, or Qulipta)

Approval will be for **12 months**

Prior approval is required. Submit a prior approval/treatment request now.

Non-Formulary Exception Criteria

Non-Formulary Exception criteria applies to formularies which do not include the requested product(s) on the formulary drug list. Meeting the criteria above may satisfy some, or all, portions of the Non-Formulary Exception Criteria. A medication that is non-formulary may be covered when the Criteria for Approval AND the following criteria are met:

1. The requested drug must be used for an FDA-approved indication, or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines). Diagnostic testing/lab results required when applicable.
2. The prescribed dose/quantity must fall within the FDA-approved labeling or dosing guidelines found in the compendia of current literature.
3. All covered formulary alternative drugs on any tier will be ineffective, have been ineffective, would not be as effective as the non-formulary drug, or would have adverse effects. Documentation is required and must include chart note(s) or other documentation indicating prior treatment failure, severity of the adverse event (if any), and dosage and duration of the prior treatment, or contraindication to formulary alternatives.

Members currently receiving the requested medication as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

- Aimovig 70 mg/mL autoinjector – 1 per 28 days
- Aimovig 140 mg/mL autoinjector – 1 per 28 days
- Ajovy (fremanezumab) 225mg/1.5mL prefilled syringe/autoinjector – 3 syringes or autoinjectors/84 days
- Emgality (galcanezumab) 120mg/mL prefilled syringe/pen - 1 prefilled syringe or pen/28 days
- Emgality (galcanezumab) 100 mg/mL prefilled syringe/pen - 3 prefilled syringes or pens/28 days

Appendix

Appendix A

International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for cluster headache

A. At least five attacks fulfilling criteria B-D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated)[1]
C. Either or both of the following:
    1. at least one of the following symptoms or signs, ipsilateral to the headache:
        - conjunctival injection and/or lacrimation
        - nasal congestion and/or rhinorrhea
        - eyelid edema
        - forehead and facial sweating
        - miosis and/or ptosis
    2. a sense of restlessness or agitation
D. Occurring with a frequency between one every other day and 8 per day[2]

E. Not better accounted for by another ICHD-3 diagnosis.

Notes

1. During part, but less than half, of the active time-course of 3.1 *Cluster headache*, attacks may be less severe and/or of shorter or longer duration.
2. During part, but less than half, of the active time-course of 3.1 *Cluster headache*, attacks may be less frequent.

Appendix B

International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for medication-overuse headache

A. Headache present on ≥15 days/month
B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache
C. One of the following:
    1. Regular intake of ergotamine on ≥10 days per month for >3 months
    2. Regular intake of one or more triptans, in any formulation, on ≥10 days per month for >3 months
    3. Regular intake of acetaminophen, acetylsalicylic acid, NSAIDs, or another non-opioid analgesic on ≥15 days per month for >3 months
    4. Regular intake of one or more opioids on ≥10 days per month for >3 months
    5. Regular intake of one or more combination analgesic medications on ≥10 days/month for >3 months
    6. Regular intake of any combination of ergotamine, triptans, non-opioid analgesics and/ or opioids on a total of ≥10 days per month for >3 months
    7. Regular intake of any combination of ergotamine, triptans, non-opioid analgesics, and/or opioids on a total of ≥10 days per month for >3 months for which the identity, quantity and/or pattern of use or overuse of these classes of drug cannot be reliably established
    8. Regular overuse, on ≥10 days per month for >3 months, of one or more medications other than those described above, taken for acute or symptomatic treatment of headache

CLINICAL RATIONALE

Migraine is a chronic neurological disease that ranks as the second most disabling neurological condition globally in terms of years lost to disability as attacks can significantly impair functional ability at work or school, at home, and in social situations. It involves recurrent attacks of moderate to severe throbbing, often unilateral, head pain and may be associated with nausea, vomiting and sensitivity to light, sound and odors. Diagnoses is based on the frequency of monthly migraine days (MMDs) and monthly headache days (MHDs). Based on the International Classification of Headache Disorders (ICHD)-3 criteria for Episodic and Chronic Migraine, patients with fewer than 15 MMDs or MHDs have episodic migraine and those with at least 15 MHDs, of which at least 8 are MMDs, have chronic migraine. See Appendix for full ICHD-3 diagnostic criteria.

The severity, frequency, and characteristics of migraine vary among persons resulting in varying treatments that may include acute treatments, preventive treatments, or both. According to the American Headache Society (AHS), a process of trial and error is often necessary before treatment can be optimized with preventive treatments being part of the overall approach for a proportion of people with migraine while avoiding the overuse of acute medications. And typically, those patients with migraine featuring severe, disabling, or frequent attacks, as well as those who cannot tolerate or are nonresponsive to acute treatment, are candidates for preventive therapy.

The use of evidence-based treatments is important to migraine prevention success per AHS. The American Academy of Neurology (AAN) has evaluated the level of evidence for efficacy for preventive migraine

medications with antiepileptic drugs (e.g., divalproex sodium, valproate sodium, topiramate) and beta-blockers (e.g., metoprolol, propranolol, timolol) having established efficacy and antidepressants (e.g., amitriptyline, venlafaxine) and beta-blockers (e.g., atenolol, nadolol) having probable efficacy. AHS also recommends to give oral preventive treatments an adequate trial of at least 8 weeks at a target or usual effective dose to optimize the possibility of a therapeutic response. If there is no response to treatment after 8 weeks trial, then switching preventive treatments is recommended. If patients have a partial response, they should be counseled that cumulative benefits may occur over 6-12 months of continued use. Any of the following can define the success of migraine prevention: 1) 50% reduction in the frequency of days with headache or migraine 2) significant decrease in attack duration as defined by the patient 3) Significant decrease in attack severity as defined by the patient 4) Improved response to acute treatment 5) Reduction in migraine-related disability and improvements in functioning in important areas of life 6) Improvements in health related quality of life and reduction in psychological distress due to migraine.

Efficacy

Aimovig, Ajovy, Emgality

In 2018, the FDA approved three parenteral therapies targeting calcitonin gene-related peptide (CGRP). Aimovig (erenumab), Ajovy (fremanezumab), and Emgality (galcanezumab) are indicated for the preventive treatment of migraines in adults. However, the approval was based on phase 2 and phase 3 randomized, placebo-controlled trials demonstrating efficacy and safety in patients with episodic and chronic migraine, not all migraine, with effects occurring over days to weeks in those who have failed prior preventive treatments as well as in those on concurrent oral preventive treatments. The below table summarizes the efficacy of the CGRP antagonists along with other prophylactic agents.

Table 1: Summary of Efficacy of Migraine Prophylactic Agents* Agent

Agent	Reduction in Migraine at 12 weeks (placebo-adjusted reduction per month)		≥ 50% Reduction in Migraine at 12 weeks (placebo-adjusted)	
	EM	CM	EM	CM
Aimovig (erenumab)	1 day to 1.9 days	2.5 days	OR 1.59 to 2.81	OR 2.2 to 2.3
Ajovy (fremanezumab)	1.3 to 1.5 days	1.7-1.8 days	OR 1.7 to 1.9	OR 1.8 to 2.3
Emgality (galcanezumab)	1.8 to 2 days	1.9 to 2.1 days	OR 2.2 to 2.4§	OR 1.6 to 1.8
Botox (onabotulinumtoxinA)	No significant reduction	2.3 attacks	No risk reduction	RR 2.21
topiramate‡	0.99 attacks to 1.20 attacks	1.7 days	RR 1.2 to 2.02	Not available
divalproex‡	1.5 attacks	Not available	RR 2.1 to 2.18	
propranolol‡	1.3 attacks		RR 2.1	
timolol‡	1.7 attacks		RR 1.9	

* All data presented in this table are of Evidence level Ib from randomized, controlled trials or Evidence level Ia from pairwise meta-analyses; doses included in the analyses are generally within the range of the approved doses for migraine prophylaxis
§ Reduction in Migraine at 6 months
‡ Data for oral prophylactic agents were available mostly in patients with fewer monthly migraines or EM
CM = chronic migraine
EM = episodic migraine
Evidence level Ia = meta-analysis
Evidence level Ib = randomized, controlled trial
OR = odds ratio
RR = risk ratio
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Vyepti

The efficacy of Vyepti (eptinezumab) was evaluated as a preventive treatment of episodic and chronic migraine in two randomized, multicenter, placebo-controlled studies, both with 6-month double-blind periods: one study in patients with episodic migraine (PROMISE-1) and one study in patients with chronic migraine (PROMISE 2). Vyepti (eptinezumab) was administered by intravenous infusion every 3 months in both studies; however, the primary endpoint was measured at 12 weeks.

The PROMISE-1 study included adults with a history of episodic migraine (4 to 14 headache days per month, of which at least 4 were migraine days). A total of 665 patients were randomized to receive placebo (N=222), 100 mg eptinezumab (N=221), or 300 mg eptinezumab (N=222) every 3 months for 12 months. Patients were allowed to use concurrent acute migraine or headache medications, including migraine-specific medications (i.e., triptans, ergotamine derivatives), during the trial. The study excluded patients with a history of cardiovascular disease (hypertension, ischemic heart disease), neurological disease, or cerebrovascular disease. The primary efficacy endpoint was the change from baseline in mean monthly migraine days over Months 1-3. Secondary endpoints included the percentages of patients with 50% or greater, and 75% or greater reductions from baseline in monthly migraine days over Months 1-3. Mean MMDs at baseline was ~8.6 across treatment groups. Eptinezumab 100 mg and 300 mg met the primary endpoint, reducing MMDs across weeks 1–12 compared with placebo (30 mg, -4.0; 100 mg, -3.9, p=0.0182; 300 mg, -4.3; placebo, -3.2, p=0.0001). Patients in all eptinezumab groups were more likely to achieve ≥50% or ≥75% migraine reduction during weeks 1–12 than were patients in the placebo group. The preventive effects of eptinezumab in patients with episodic migraine were observed as early as the first day after administration (day 1), with a >50% reduction in the percentage of patients with a migraine on day 1 compared to baseline in the 100 mg and 300 mg treatment groups.

The PROMISE-2 study included adults with a history of chronic migraine (15 to 26 headache days per month, of which at least 8 were migraine days). A total of 1072 patients were randomized and received placebo (N=366), 100 mg eptinezumab (N=356), or 300 mg eptinezumab (N=350) every 3 months for 6 months. Patients were allowed to use and to continue an established stable regimen of acute migraine or headache preventive medication (except onabotulinumtoxinA). Patients with a dual diagnosis of chronic migraine and medication overuse headache attributable to acute medication overuse (triptans, ergotamine, or combination analgesics greater than 10 days per month) were included in the study population. The primary endpoint was change from baseline in mean monthly migraine days (MMDs) over weeks 1 to 12. The secondary efficacy endpoints in the PROMISE-2 study were ≥75% migraine responder rate over weeks 1 to 4, ≥75% migraine responder rate over weeks 1 to 12, ≥50% migraine responder rate over weeks 1 to 12, percentage of patients with a migraine on the day after dosing, change from baseline in daily migraine prevalence from baseline to week 4, and acute migraine medication use during weeks 1 to 12. Among treated participants (n = 1,072), baseline mean number of MMDs was ~16.1 across groups. Treatment with eptinezumab 100 and 300 mg met the primary endpoint and was associated with significant reductions in MMDs across weeks 1 to 12 compared with placebo (placebo −5.6, 100 mg −7.7, $p < 0.0001$ vs placebo; 300mg −8.2, $p < 0.0001$ vs placebo). MMDs decreased from 16.1 to 8.5 days in the eptinezumab 100mg group, from 16.1 to 7.9 days in the eptinezumab 300 mg group, and from 16.2 to 10.5 days in the placebo group. The secondary end point of ≥75% response was achieved by a larger percentage of those in the treatment groups compared to placebo, with the 100-mg group having an odds ratio [OR] of 2.4 (95% CI, 1.7–3.5) and the 300-mg group having an OR of 3.2 (95% CI, 2.2–4.6) for the first 4 weeks of treatment. Over the full 12-week study period, the results were similar for both the 100-mg (OR, 2.0; 95% CI, 1.4–3.0) and 300-mg (OR, 2.8; 95% CI, 1.9–4.0) groups. Additionally, the odds of ≥50% response during Weeks 1 to 12 were higher for both the 100-mg (OR, 2.1; 95% CI, 1.6–2.8) and 300-mg (OR, 2.4; 95% CI, 1.8–3.3) groups compared to placebo. The migraine preventive effect of eptinezumab 100 and 300 mg was observed as early as day 1 after administration, with >50% of patients reporting a significant decrease in migraine incidence compared to baseline levels.

Safety

Aimovig, Ajovy, Emgality

CGRP antagonists were generally well tolerated during clinical trials with the most commonly reported adverse effects pertaining to injection-site pain or reactions in up to 30% of patients. Nasopharyngitis and upper respiratory tract infection were reported in less than 12% of patients.

Vyepti

The most common adverse reactions (≥2% and at least 2% or greater than placebo) in the clinical trials were nasopharyngitis and hypersensitivity. In PROMISE-1 and PROMISE-2, 1.9% of patients treated with Vyepti (eptinezumab) discontinued treatment due to adverse reactions.

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PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J3032 Injection, eptinezumab-jjmr, (Vyepti) 1 mg

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POLICY HISTORY

Policy #: 05.02.49
Reviewed: October 2025
Revised: October 2025
Current Effective Date: January 1, 2026