Clinical Policy: Fremanezumab-vfrm (Ajovy)

Reference Number: HIM.PA.SP66
Effective Date: 10.01.20
Last Review Date: 11.25
Line of Business: HIM

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Fremanezumab-vfrm (Ajovy®) is a calcitonin gene-related peptide (CGRP) receptor antagonist.

FDA Approved Indication(s)

Ajovy is indicated for:

- The preventive treatment of migraine in adults.
- The preventive treatment of episodic migraine in pediatric patients who are 6 to 17 years of age and who weigh 45 kg or more.

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Ajovy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Migraine Prophylaxis (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Age ≥ 18 years: episodic or chronic migraine;
   b. Age 6 to 17 years: episodic migraine;
2. Provider's attestation that member experiences ≥ 4 migraine days per month for at least 3 months;
3. Age ≥ 6 years;
4. Requests for members age ≥ 18 years: Both of the following (a and b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Failure of at least 2 of the following oral migraine preventative therapies, each for 8 weeks and from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated: antiepileptic drugs (e.g., divalproex sodium, sodium valproate, topiramate), beta-blockers (e.g., metoprolol, propranolol, timolol), antidepressants (e.g., amitriptyline, venlafaxine);
   b. Failure of Aimovig®* and Emgality®*, unless clinically significant adverse effects are experienced or both are contraindicated;
      **Prior authorization may be required.*
5. Requests for members age 12 to 17 years: Failure of an 8-week trial of topiramate, unless contraindicated or clinically significant adverse effects are experienced;*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*

6. If currently receiving treatment with Botox® for migraine prophylaxis and request is for concurrent use of Botox and Ajovy (i.e., not switching from one agent to another), all of the following (a, b, and c):
   a. Sufficient evidence is provided from at least two high-quality*, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
      **Case studies or chart reviews are not considered high-quality evidence*
      i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
      ii. Adequate representation of the prescribed drug regimen;
      iii. Clinically meaningful outcomes such as a reduction in monthly migraine or headache days;
      iv. Appropriate experimental design and method to address research questions (*see Appendix E for additional information*);
   b. Member has experienced and maintained positive response to Botox monotherapy as evidenced by a ≥ 30% reduction in migraine days per month from baseline following at least 2 quarterly injection (6 months) of Botox monotherapy;
   c. Despite Botox monotherapy, member continues to experience ≥ 4 migraine days per month and/or severe migraine headaches that result in disability and functional impairment;
7. Ajovy is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig™, Emgality®, Nurtec® ODT, Qulipta™, Ubrelvy™, Vyepti™, Zavzpret™);
8. For members age 6 to 17 years, current weight is ≥ 45 kg;
9. Dose does not exceed one of the following (a or b):
   a. 225 mg (1 injection) once monthly;
   b. Age ≥ 18 years: 675 mg (3 injections) every 3 months.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Migraine Prophylaxis (must meet all)**:**

1. Member meets one of the following (a or b):

a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member has experienced and maintained positive response to therapy as evidenced by provider's attestation of a reduction in migraine days per month from baseline;
3. Ajovy is not prescribed concurrently with other CGRP inhibitors (e.g., Aimovig, Emgality, Nurtec ODT, Qulipta, Ubrelvy, Vyepti, Zavzpret);
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. 225 mg (1 injection) once monthly;
   b. Age ≥ 18 years: 675 mg (3 injections) every 3 months.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;
B. Cluster headaches.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CGRP: calcitonin gene-related peptide
FDA: Food and Drug Administration
ICHD: International Classification of Headache Disorder

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Anticonvulsants such as: divalproex (Depakote®), topiramate (Topamax®), valproate sodium	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Beta-blockers such as: propranolol (Inderal®), metoprolol (Lopressor®)*, timolol, atenolol (Tenormin®)*, nadolol (Corgard®)*	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Antidepressants/tricyclic antidepressants* such as: amitriptyline (Elavil®), venlafaxine (Effexor®)	**Migraine Prophylaxis** *Refer to prescribing information or Micromedex*	*Refer to prescribing information or Micromedex*
Aimovig® (erenumab-aaoe)	**Migraine Prophylaxis** 70 mg SC once monthly Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly	140 mg/month
Emgality® (galcanezumab-gnlm)	**Migraine Prophylaxis** Loading dose: 240 mg SC once Maintenance dose: 120 mg SC once monthly	120 mg/month

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label use*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information
- In clinical trials, a migraine day was defined as any calendar day in which the patient reported either a headache that lasted at least 2 consecutive hours and met International Classification of Headache Disorder (ICHD)-3 diagnostic criteria for migraine (with or without aura) or probable migraine (subtype in which only 1 migraine criterion is absent), or a day when a headache of any duration was treated with migraine-specific medications (triptans or ergots).
- The ENFORCE Phase III clinical trial program evaluating the efficacy of Ajovy in episodic and chronic cluster headache was discontinued after a pre-specified futility analysis revealed that the study's primary endpoints were unlikely to be met.

Appendix E: Appropriate Experimental Design Methods

- Randomized, prospective controlled trials are generally considered the gold standard; however:
  - In some clinical studies, it may be unnecessary or not feasible to use randomization, double-blind trials, placebos, or crossover.
  - Non-randomized prospective clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- Case reports and chart reviews are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Migraine prophylaxis	Adults (age ≥ 18 years): 225 mg SC once monthly or 675 mg SC every three months Pediatrics age 6 to 17 years and weight ≥ 45 kg: 225 mg SC once monthly	See dosing regimen

VI. Product Availability

Single-dose prefilled syringe, autoinjector: 225 mg/1.5 mL

VII. References

1. Ajovy Prescribing Information. North Wales, PA: Teva Pharmaceuticals USA, Inc.; August 2025. Available at: www.ajovy.com. Accessed August 18, 2025.
2. Silberstein SD, Holland S, Freitag F, et al. American Academy of Neurology: Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. Neurology 2012; 78: 1337-45.
3. Digre KB. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache 2019; 59: 1-18.
4. Ailani J, Burch RC, Robbins MS, et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. 2021; 61: 1021-1039.
5. Charles AC, Digre KB, Goadsby PJ, et al. The American Headache Society: Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache. 2024; 64: 333–341.
6. Qaseem A, Cooney TG, Etxeandia-Ikobaltzeta I, et al. Prevention of episodic migraine headache using pharmacologic treatments in outpatient settings: A clinical guideline from the American College of Physicians. Ann Intern Med. 2025 Mar; 178(3): 426-433.
7. Oskoui M, Pringsheim T, Billinghurst L, et al. Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Headache. 2019 Sep; 59(8): 1144-1157.
8. A study to test if fremanezumab is effective in preventing episodic migraine in patients 6 to 17 years of age." *ClinicalTrials.gov*, identifier: NCT04458857. Updated 22 June 2025. Available at: https://clinicaltrials.gov/study/NCT04458857. Accessed August 18, 2025.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3031	Injection, fremanezumab-vfrm, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.14.21	02.22
Clarified the following "…not prescribed concurrently with Botox or other injectable **or** oral CGRP inhibitors."	05.31.22	
4Q 2022 annual review: Added criteria for concurrent use with Botox requiring supportive evidence from published studies or clinical practice guidelines, positive response with Botox monotherapy, and continued migraine burden; revised initial approval duration from 3 to 6 months for every 3 month dosing frequency; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.19.22	11.22
4Q 2023 annual review: no significant changes, added clarification that PA may be required for alternative CGRP redirections; references reviewed and updated.	07.12.23	11.23
4Q 2024 annual review: added Zavzpret to list of CGRP inhibitors that should not be prescribed concurrently with Ajovy, removed references to "injectable or oral CGRP" as Zavzpret is a nasal product; references reviewed and updated.	07.15.24	11.24
4Q 2025 annual review: RT4: added pediatric extension for episodic migraine requiring redirection to topiramate; modified initial and continuation of therapy approval duration to 12 months; added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	07.10.25	11.25

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical

practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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