
Title: CGRP Antagonists
Policy #: Rx.01.207

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **erenumab (Aimovig™), fremanezumab (Ajovy™), or galcanezumab (Emgality™)** as provided under the member's prescription drug benefit.

Description:

Migraine is a recurrent throbbing disabling headache disorder that usually affects one side of the head and is in many cases preceded by warning symptoms. Common symptoms include nausea, photophobia, and phonophobia. The head pain is usually severe and can last for hours or even days.

Calcitonin gene-related peptide (CGRP) is found in neurons of the cerebral cortex, hippocampus, cerebellum, thalamic nuclei and brainstem nuclei and some other sites. In migraines, CGRP is released from trigeminal nerves (the nerves associated with feeling of pain in the head and face), bind to specific receptors, and cause symptoms such as vasodilation, pain, and inflammation. Pain is transmitted from trigeminal ganglion to trigeminal nucleus and then higher central nervous system centers. This accounts for pain, photophobia, and phonophobia.

Therapy for migraine may be abortive, to stop the headache, or prophylactic, to reduce frequency of headaches, number of headache days, or severity of headaches. Current treatment options for prophylaxis of episodic and chronic migraine headaches include: topiramate, valproic acid, beta blockers, and some classes of antidepressants. Onabotulinumtoxin A (Botox) is also an option for prophylaxis of chronic migraines.

The CGRP antagonists are human monoclonal antibodies that selectively bind the CGRP receptors (erenumab) or antagonize calcitonin gene-related peptide (galcanezumab, fremanezumab) to reduce CGRP. The monoclonal antibodies have shown efficacy in clinical trials by acting at several sites in the trigeminal system and in the CNS which results in pain relief.

Erenumab (Aimovig™), fremanezumab (Ajovy™), and galcanezumab (Emgality™ 120mg/ml) are indicated for the preventive treatment of migraines in adults. It is unknown if these agents are safe and effective in children under the age of 18.

Galcanezumab (Emgality™ 100mg/ml) is indicated for episodic cluster headache. Galcanezumab is taken at the start of the cluster period (three doses of 100mg) and then every month until the end of the cluster period.

Policy:

INITIAL CRITERIA Erenumab (Aimovig™), fremanezumab (Ajovy™), or galcanezumab (Emgality™) 120mg/ml is approved when ALL of the following are met:

- A. Prescribed by or in consultation with a neurologist or headache specialist certified by the United Council for Neurologic Subspecialties; or a pain specialist and
- B. Member is 18 years of age or older; and
- C. ONE of the following:
 - 1. Diagnosis of episodic migraines defined as 5-14 headache days per month and inadequate response or inability to tolerate a 4 week trial of TWO of the following prophylactic medications:
 - a. Topiramate
 - b. Divalproex sodium/ valproic acid
 - c. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 - d. Tricyclic antidepressants: amitriptyline, nortriptyline
 - e. SNRI antidepressants: venlafaxine, duloxetine
 - OR
 - 2. Diagnosis of chronic migraines defined as 15 or more headache days per month and inadequate response or inability to tolerate a 4 week trial of TWO of the following prophylactic medications:
 - a. Topiramate
 - b. Divalproex sodium/ valproic acid
 - c. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 - d. Tricyclic antidepressants: amitriptyline, nortriptyline
 - e. SNRI antidepressants: venlafaxine, duloxetine
 - f. Trial of additional prophylactic medications does not apply if member has previously been treated with onabotulinumtoxin A (Botox) for migraines

Initial authorization: 6 months

REAUTHORIZATION CRITERIA Erenumab (Aimovig™), fremanezumab (Ajovy™), or galcanezumab (Emgality™) 120mg/ml is approved when ALL of the following are met:

- A. Prescribed by or in consultation with a neurologist, headache specialist certified by the United Council for Neurologic Subspecialties, or a pain specialist; and
- B. Documentation of response to therapy as defined by 50% reduction in headache days per month from baseline (defined as at least 4 hours duration and moderate intensity)

Reauthorization: 12 months

INITIAL CRITERIA Galcanezumab (Emgality™) 100mg/ml is approved when ALL of the following are met:

- A. Diagnosis of episodic cluster headache; AND
- B. Member has experienced at least 2 cluster periods lasting 7 days to 365 days, separated by pain-free periods lasting at least three months; AND
- C. Member is 18 years of age or older; and
- D. Prescribed by or in consultation with a neurologist, headache specialist certified by united council for neurologic subspecialties, or pain specialist; and
- E. Medication will not be used in combination with another CGRP inhibitor

Initial authorization: 3 months

REAUTHORIZATION CRITERIA Galcanezumab (Emgality™) 100mg/ml is approved when ALL of the following are met:

- A. Member has experienced a positive clinical response to therapy, demonstrated by a reduction in headache frequency and/or intensity; and
- B. Prescribed by or in consultation with a neurologist, headache specialist certified by united council for neurologic subspecialties, or pain specialist.

Reauthorization: 12 months

Black Box Warning as shown in the drug Prescribing Information:

None

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

1. Edvinsson, L. (2018), The CGRP Pathway in Migraine as a Viable Target for Therapies. *Headache: The Journal of Head and Face Pain*, 58: 33-47. doi:10.1111/head.13305. Accessed March 31, 2021.
2. Interictal increase of CGRP levels in peripheral blood as a biomarker for chronic migraine. Eva Cernuda-Morollón, Davinia Larrosa, César Ramón, Juan Vega, Pablo Martínez-Cambor, Julio Pascual. *Neurology* Oct 2013, 81 (14) 1191-1196; DOI: 10.1212/WNL. Available at: <http://n.neurology.org/content/81/14/1191.short>. Accessed March 31, 2021.
3. Giamberardino, M., Affaitati, G., Costantini, R., Cipollone, F., & Martelletti, P. (2017). Calcitonin gene-related peptide receptor as a novel target for the management of people with episodic migraine: Current evidence and safety profile of erenumab. *Journal of Pain Research.*, 10, 2751-2760. Accessed March 31, 2021.
4. Aimovig™ (erenumab-aooe) [package insert]. Thousand Oaks, CA. Amgen Inc. February 2021. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b998ed05-94b0-47fd-b28f-cddd1e128fd8&type=display>. Accessed March 31, 2021.
5. Silberstien, SD, Holland, S, Freitag, F, Dodick, DW, Argoff, C, Ashman, E. Evidence based guideline update: pharmacologic treatment for episodic migraine prevention in adults. *Neurology*.2012;78:1337-45. Accessed March 31, 2021.
6. Ajovy™ (fremanezumab-vfrm) [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc. October 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=98e344ea-5916-4947-b6f2-4a76ccc04b6b&type=display>. Accessed March 31, 2021.
7. Emgality™ (galcanezumab-gnlm) [package insert]. Indianapolis, IN: Eli Lilly and Co. December 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=33a147be-233a-40e8-a55e-e40936e28db0&type=display>. Accessed March 31, 2021.

Applicable Drugs:

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

Brand Name

Aimovig™

Ajovy™

Emgality™

Generic Name

Erenumab

Fremanezumab

Galcanezumab

Cross References:

Botulinum toxin agents 08.00.26s (medical policy)

Off-Label Use Rx.01.33

Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit Rx.01.76

Policy Version Number:	8.00
P&T Approval Date:	March 18, 2021
Policy Effective Date:	July 01, 2021
Next Required Review Date:	March 18, 2022

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.