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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	August 10, 2018
Subject:	Migraine CGRP Antagonists SC	**Page:**	1 of 10

Last Review Date: December 8, 2023

Migraine Calcitonin Gene-Related Peptide (CGRP) Antagonists SC

Description

Aimovig (erenumab-aooe), Ajovy* (fremanezumab-vfrm), Emgality (galcanezumab-gnlm)

* Prior authorization for this product applies only to formulary exceptions due to being a non-covered medication

Background
Aimovig, Ajovy, and Emgality are human immunoglobulin G2 (IgG2) monoclonal antibodies that have high affinity for binding to the calcitonin gene-related peptide (CGRP) receptor and act by antagonizing this receptor. CGRP is a neuropeptide widely distributed in the nervous system, particularly at anatomical areas thought to be involved with migraine, including the trigeminovascular nociceptive system. In studies, CGRP has been shown to be released during severe migraine attacks. CGRP triggers migraine in patients and CGRP receptor antagonists can abort migraine. Moreover, recent data demonstrate that CGRP mechanism blockade either by small molecule receptor antagonists or by monoclonal antibodies can have a preventive effect in migraine. Aimovig, Ajovy, and Emgality are indicated for the preventive treatment of migraine in adults. Emgality is also indicated for the treatment of episodic cluster headaches in adults. Other migraine prophylaxis options include antiepileptic drugs, antidepressants, and antihypertensive agents (1-5).

Regulatory Status
FDA-approved indications: Aimovig, Ajovy, and Emgality are calcitonin gene-related peptide receptor antagonists indicated for the preventive treatment of migraine in adults (1-3).

Emgality is also indicated for the treatment of episodic cluster headache in adults (3).

The American Academy of Neurology and the American Headache Society Position Statement recommends giving at least 2 conventional oral migraine preventive treatments an adequate trial of at least 6 weeks at a target or usual effective dose prior to initiating preventive therapy with a CGRP medication (6).

The safety and effectiveness of Aimovig, Ajovy, and Emgality in pediatric patients have not been established (1-3).

Related policies
5-HT1 Agonists, Butalbital analgesics, Dihydroergotamine Nasal Sprays, Elyxyb, Maxalt, Migraine CGRP Antagonists IV, Migraine CGRP Antagonists Nasal, Migraine CGRP Antagonists Oral, Migraine Powders

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

CGRP antagonists SC may be considered **medically necessary** if the conditions indicated below are met.

CGRP antagonists SC may be considered **investigational** for all other indications.

Prior-Approval Requirements

Ajovy: *Prior authorization for Ajovy applies only to approved formulary exceptions due to being a non-covered medication.*

Age 18 years of age or older

Diagnosis

Patient must have the following:

Migraine

AND ALL of the following:

1. Used for the prevention of migraines
2. Patient has **ONE** of the following:
    a. Patient has taken a preventative CGRP medication in the past or is switching from another preventative CGRP medication
    b. Patient has had an inadequate treatment response, intolerance, or contraindication to at least **TWO** of the following prophylactic agents:
        i. Divalproex sodium/valproate sodium (Depakote, Depakote ER)
        ii. Topiramate (Topamax)
        iii. Tricyclic antidepressants: amitriptyline (Elavil), nortriptyline (Pamelor)
        iv. Serotonin-norepinephrine reuptake inhibitors: venlafaxine (Effexor XR), duloxetine (Cymbalta)
        v. Beta-blockers: atenolol, metoprolol, nadolol, propranolol, timolol
3. **Aimovig only:** Prescriber agrees to monitor for severe constipation
4. Patient has **ONE** of the following:
    a. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
    b. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
        i. Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
        ii. Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Emgality 100 mg/mL ONLY

Age 18 years of age or older

Diagnosis

Patient must have the following:

Episodic cluster headaches

AND ALL of the following:

1. Patient has completed an adequate 3-month trial **OR** patient has an intolerance or contraindication to at least **ONE** of the following:
    a. Triptan agent
    b. Ergotamine tartrate
    c. Dihydroergotamine
2. **NO** dual therapy with another CGRP antagonist (see Appendix 1)

Prior–Approval *Renewal* Requirements

Ajovy: *Prior authorization for Ajovy applies only to approved formulary exceptions due to being a non-covered medication.*

Aimovig and Emgality (excluding Emgality 100 mg/mL)

Age 18 years of age or older

Diagnosis

Patient must have the following:

Migraine

AND ALL of the following:

1. Used for prevention of migraine
2. Documented decrease in migraine days from baseline **OR** improvement in daily activities due to the reduction of debilitating migraine
3. **Aimovig only:** Prescriber agrees to monitor for severe constipation
4. Patient has **ONE** of the following:
    a. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
    b. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
        i. Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)

ii. Patient has completed an adequate 3-month trial **of** a preventative CGRP antagonist in combination with a triptan agent

Emgality 100 mg/mL ONLY

Age 18 years of age or older

Diagnosis

Patient must have the following:

Episodic cluster headaches

AND ALL of the following:

1. Patient has had a decrease in frequency of cluster headache attacks
2. **NO** dual therapy with another CGRP antagonist (see Appendix 1)

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity

Drug	Quantity
Aimovig syringe	3 injections per 90 days **OR**
Emgality prefilled pen 120 mg/mL ***for migraines only**	7 injections per 180 days **OR**
Emgality prefilled syringe 120 mg/mL ***for migraines only**	7 injections per 180 days **OR**
Emgality prefilled syringe 100 mg/mL ***for cluster headaches only**	9 injections per 90 days **OR**

Drug **With Approved Formulary Exception (FE) Only**	Quantity
Ajovy	3 injections per 90 days

Duration 6 months

Prior–Approval *Renewal* Limits

Quantity

Drug	Quantity
Aimovig syringe	3 injections per 90 days **OR**
Emgality prefilled pen 120 mg/mL ***for migraines only**	3 injections per 90 days **OR**
Emgality prefilled syringe 120 mg/mL ***for migraines only**	3 injections per 90 days **OR**
Emgality prefilled syringe 100 mg/mL ***for cluster headaches only**	9 injections per 90 days **OR**

Drug **With Approved Formulary Exception (FE) Only**	Quantity
Ajovy	3 injections per 90 days

Duration 12 months

Rationale

Summary

Aimovig, Ajovy, and Emgality are human immunoglobulin G2 (IgG2) monoclonal antibodies that have high affinity for binding to the calcitonin gene-related peptide receptor and acts by antagonizing this receptor. They are indicated for the preventive treatment of migraine in adults. Emgality is also used for the treatment of episode cluster headaches in adults. The safety and effectiveness of Aimovig, Ajovy, and Emgality in pediatric patients have not been established (1-4).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of CGRP antagonists SC while maintaining optimal therapeutic outcomes.

References

1. Aimovig [package insert]. Thousand Oaks, CA. Amgen Inc., November 2021.
2. Ajovy [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2021.
3. Emgality [package insert]. Indianapolis, IN: Eli Lily and Company; March 2021.
4. Silberstein, S.D. et al. “Evidence-Based Guideline Update: Pharmacologic Treatment for Episodic Migraine Prevention in Adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society.” Neurology 78.17 (2012): 1337–1345.
5. Karsan N, Goadsby PJ. Calcitonin gene-related peptide and migraine. Curr Opin Neurol. 2015 Jun;28(3):250-4. doi: 10.1097/WCO.0000000000000191. PMID: 25887765.
6. (2019), The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache: The Journal of Head and Face Pain, 59: 1-18. https://doi.org/10.1111/head.13456

Policy History

Date	Action
August 2018	Addition to PA
September 2018	Annual review Addition of renewal requirements of one of the following: decrease of ≥ 50% in migraine frequency from baseline, decrease in use of acute migraine medications, reduction of at least 6 migraines or more per month, added intolerance or contraindication to triptans per SME Change of policy name to Calcitonin Gene-Related Peptide (CGRP) Antagonists and addition of Ajovy and Emgality to PA

November 2018	Annual review. Changed renewal requirements from 50% reduction in migraine frequency to 30% and reduction of at least 6 migraines per month to 3 migraines per SME
March 2019	Annual review. Revised Aimovig quantity limits due to new 140 mg/mL availability
May 2019	Removal of gabapentin, verapamil/nimodipine and other oral migraine prophylactic therapy considered to be appropriate by the requesting physician Removal of the requirement of baseline migraine frequency of at least 8 migraines per month Change in the preventative trial of 3 months to 6 months Ajovy was added to MFE
June 2019	Annual review and reference update. Addition of cluster headache diagnosis to Emgality
December 2019	Annual editorial review and reference update. Addition of requirement to monitor for severe constipation for Aimovig
February 2020	Revised Emgality cluster headache initiation requirement to t/f a triptan, ergotamine, or dihydroergotamine and removed t/f preventative agent per FEP
March 2020	Annual review and reference update. Addition of Vyepti to policy and renamed policy Migraine CGRP Antagonists Injectable
April 2020	Addition of requirement of no dual therapy with another CGRP antagonist per FEP
June 2020	Annual review and reference update. Removed Vyepti to separate criteria. Renamed policy Migraine CGRP Antagonists SC. Revised renewal requirement to “documented decrease in migraine days from baseline OR improvement in daily activities due to the reduction of debilitating migraines” per SME
April 2021	Listed Ajovy under initiation and continuation sections to clarify what criteria would apply after formulary exception is processed, per FEP. Reference update.
June 2021	Annual review and reference update
September 2021	Annual review and reference update
March 2022	Annual review and reference update. Per SME, removed renewal requirement of “no dual therapy with Triptan Agents at PA quantities” and removed requirement of “no dual therapy with Botox for migraine prevention”

December 2022	Annual review. Prevention of migraines indication: Removed auto step edit. Removed the failure of triptans requirement and increased the failure of oral prophylaxis from 1 to 2 agents, per SME. Added nortriptyline and duloxetine to the list of t/f options per AAN/AHS guidelines. Per FEP, added initiation option for patients to have taken a preventative CGRP in the past or switching from another preventative CGRP in order to bypass the t/f of prophylactics.
June 2023	Annual review
September 2023	Annual review
October 2023	Per FEP, revised criteria to allow dual therapy between CGRP antagonists if patient is using one preventative and one acute treatment together after an adequate trial and failure of other CGRPs and triptans either alone or in combination
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.

Appendix 1 - List of CGRP Antagonists

Generic Name	Brand Name
atogepant	Qulipta
eptinezumab-jjmr	Vyepti
erenumab-aooe	Aimovig
fremanezumab-vfrm	Ajovy
galcanezumab-gnlm	Emgality
rimegepant	Nurtec ODT
ubrogepant	Ubrelvy
zavegepant	Zavzpret