Protocol for Calcitonin Gene-Related Peptide (CGRP) Antagonists for The Treatment of Migraines

Approved January 2024

Approved April 2019
Updated October 2020
Updated October 2022

Preferred Agents:
Emgality 120mg (galcanezumab)
Ubrelvy (ubrogepant)

Non-Preferred Agents:
Aimovig (erenumab)
Ajovy (fremanezumab)
Emgality 100mg
Vyepti (eptinezumab)
Nurtec ODT® (rimegepant)
Qulipta (atogepant)
Zavzpret (zavegepant)

Requests for non-preferred agents require that the patient is unable to take Emgality 120mg or Ubrelvy where indicated for the given diagnosis, due to a trial and inadequate treatment response or intolerance, or a contraindication. Documentation is required for approval

Background:
Calcitonin gene-related peptide (CGRP) is a neuropeptide believed to be directly involved in the pathophysiologic processes underlying migraine. CGRP antagonists for prevention of episodic and chronic migraine have provided another treatment option for migraine patients. Although comparative studies between traditional prophylaxis treatments are not available, treatment with these products have been shown to be efficacious. However, the long-term effects, particularly regarding the cardiovascular risks, are still unknown as well as the exact mode of action of the antibodies.

Criteria for approval:

1. Patient is 18 years of age or older; AND

2. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence; **AND**

3. Medication-Overuse Headaches (MOH, aka: drug-induced headache, medication-misuse headache, rebound headache) have been evaluated and addressed as follows (a and b):
    a. Patient has been evaluated for MOHs, defined as having 15 or more headache days per month in a patient who regularly overuses drugs (i and/or ii):
        i. Use of non-opioid analgesic (e.g., acetaminophen, non-steroidal anti-inflammatory drug [NSAID], acetylsalicylic acid] for 15 or more days per month for more than 3 months
        ii. Use of any other drugs for acute/symptomatic treatment of headaches for 10 or more days per month for more than 3 months
    b. For patients with MOH, the patient continues to have migraines despite discontinuing the overuse of drugs taken for acute and/or symptomatic treatment of headaches

Chronic Migraine (Aimovig, Emgality 120mg, Ajovy, Vyepti, Qulipta):

- Headache occurring on 15 or more days per month with at least 8 migraine days per month for more than 3 months

Episodic Migraine (Aimovig, Emgality 120mg, Ajovy, Vyepti, Nurtec ODT, Qulipta):

- Headache occurring less than 15 days per month with at least 4 migraine days per month

- For chronic and episodic migraines, there is documented inadequate response, or intolerable side effects to at least 2 quarterly injections (6 months) of OnabotulinumtoxinA (for chronic migraines only) OR to at least two medications for migraine prophylaxis from two different classes, for at least 2 months:
    - Beta-Blockers (e.g., propranolol, metoprolol, atenolol, timolol, nadolol)
    - Anticonvulsants (e.g., valproic acid, or divalproex, topiramate)
    - Tricyclic Antidepressants (e.g., amitriptyline, nortriptyline)
    - Serotonin-norepinephrine reuptake inhibitors (venlafaxine, duloxetine)
    - Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence): Candesartan, Lisinopril, Memantine
- Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for prevention of migraines

Acute Migraine (Ubrelvy, Nurtec ODT, Zavzpret):

- Medication is for moderate or severe pain intensity
- Documented inadequate response, or intolerable side effect, with at least two triptans, or patient has a contraindication to triptan use
- Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for treatment of acute migraines

Ubrelvy:
- Patient will not be treated for more than 8 migraine days in a 30-day period
- Patient is not concomitantly taking a strong CYP3A4 inhibitor (e.g., clarithromycin, ketoconazole)

Nurtec ODT:
- Patient will not be using more than 18 doses in a 30-day period.

Zavzpret:
- Patient will not be treated for more than 8 migraine days in a 30-day period

Episodic Cluster Headaches: (Emgality 100mg):
- Headaches occurring at maximum 8 attacks per day, or minimum one attack every other day
- Trial and failure with verapamil for preventive treatment or sumatriptan (nasal or subcutaneous) for acute treatment

Continuation of therapy:

1. Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity

2. For migraine prevention: Medication will not be used in combination with another biologic CGRP antagonist or inhibitor for migraine prevention

3. For acute migraine treatment: Medication will not be used in combination with another biologic CGRP antagonist or inhibitor used for treatment of acute migraines

   Ubrelvy:
   Patient will not be treated for more than 8 migraine days in a 30-day period

   Nurtec ODT:
   Patient will not be using more than 18 doses in a 30-day period.

   Zavzpret:
   Patient will not be treated for more than 8 migraine days in a 30-day period

4. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Initial Approval Duration: Emgality 100mg for cluster headache: 1 month; all others approve for 3 months

Renewal Approval Duration: 12 months

Quantity Level Limit:

Drug	Monthly Limit
Aimovig 70mg	1mL (1 autoinjector x 1mL each) / 30 days
Aimovig 140mg	1mL (1 autoinjector x 1mL each) / 30 days
Ajovy 225mg	4.5mL (3 autoinjectors or syringes x 1.5 mL each) / 90 days
Emgality 120mg	2 mL (2 syringes or pens x 1 mL each) / 30 days (loading dose) 1mL (1 syringe or pen x 1mL each) / 30 days (maintenance dose)
Emgality 100 mg	3 mL (3 syringes x 1 mL each) / 30 days
Vyepti 100mg	3mL (3 single dose vials x 1mL each) / 90 days
Nurtec ODT	16 orally disintegrating tablets/30 days
Qulipta	30 tablets/30 days
Ubrelvy	16 tablets/30 days
Zavzpret	6 nasal spray units per 3 weeks

References:

1. Aimovig® [package insert]. Amgen Inc. Thousand Oaks, CA 91320. May 2018.
2. Ajovy® [package insert]. Teva Pharmaceuticals USA, Inc. North Wales, PA 19454. September 2018.
3. Emgality® [package insert]. Eli Lilly and Company. Indianapolis, IN 46285. September 2018.
4. Vyepti® [package insert]. Lundbeck Seattle Biopharmaceuticals, Inc. WA 98011. February 2020.
5. Ubrelvy™ [package Insert]. Allergan USA, Inc. Madison, NJ: December 2019.
6. Nurtec™ ODT [package Insert]. Biohaven Pharmaceuticals, Inc. New Haven, CT May 2021.
7. Qulipta® [package insert]. Forest Laboratories Ireland Ltd. Dublin, Ireland. September 2021
8. Zavzpret® [package insert]. Pfizer Labs. Division of Pfizer Inc. New York, NY 10001. March 2023
9. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically
10. Giamberardino MA, Affaitati G, Costantini R et al. Calcitonin gene-related peptide receptor as a novel target for the management of people with episodic migraine: current evidence and safety profile of erenumab. J Pain Res. 2017 Dec 8;10:2751-2760
11. Estemalik E, Tepper S. Preventive treatment in migraine and the new US guidelines. Neuropsychiatric Dis Treat. 2013;9:709–720.
12. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. Headache. 2019;59:1-18. Available at: https://headachejournal.onlinelibrary.wiley.com/doi/10.1111/head.13456
13. International Headache Society (IHS); Headache Classification Committee. The International Classification of Headache Disorders, 3rd edition. Available at: https://www.ichd-3.org