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

Approved April 2019
Updated October 2020
Updated October 2022

Addendum:

1. Addition of more FDA-approved products in the class:
   a. Ubrelvy® (ubrogepant) – December 2019 (Oral tablets for acute treatment)
   b. Nurtec ODT® (rimegepant) – May 2021 (Oral disintegrating tablets for preventive and acute treatment)
   c. Qulipta® (atogepant) – September 2021 (Oral tablets for preventive treatment)
   d. Addition of new FDA-approved indications

Preferred Agent:
Emgality® (galcanezumab)
Ubrelvy® (ubrogepant)

Non-Preferred Agents:
Aimovig® (erenumab)
Ajovy® (fremanezumab)
Vyepti® (eptinezumab)
Nurtec ODT® (rimegepant)
Qulipta® (atogepant)

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. The patient unable to take the preferred formulary alternative for the given diagnosis, where indicated, due to a trial and inadequate treatment response or intolerance, or a contraindication.
2. Patient is 18 years of age or older; **AND**
3. 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**
4. 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 nth 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 Prevention (Aimovig, Emgality, Ajovy, Vyepti):

- Headache occurring on 15 or more days per month with at least 8 migraine days per month for more than 3 months
- There is documented inadequate response, or intolerable side effects, 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)
    - Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine, duloxetine)
- Medication will not be used in combination with another biologic CGRP antagonist for the prevention of migraines

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

- Headache occurring less than 15 days per month with 4 to 14 migraine days per month
- there is documented inadequate response, or intolerable side effects, 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)
    - Antidepressants (e.g., amitriptyline, nortriptyline, venlafaxine, duloxetine)
- Medication will not be used in combination with another biologic CGRP antagonist for the prevention of migraines

Acute Migraine Treatment (Ubrelvy, Nurtec ODT):

- 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
- **Ubrelvy:**
    - Patient does not experience more than 8 migraine days per month
    - Patient is not concomitantly taking a strong CYP3A4 inhibitor (e.g., clarithromycin, ketoconazole)
- **Nurtec ODT:**
    - Patient does not experience more than 15 migraine days per month

Episodic Cluster Headaches Treatment: (Emgality)

- 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

Initial approval: 3 months

Quantity Level Limit:

- Nurtec ODT: 16 orally disintegrating tablets/30 days
- Qulipta 10mg, 30mg, 60mg: 30 tablets/30 days
- Ubrelvy 50mg, 100mg: 16 tablets/30 days
- 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: 1mL (1 syringe or pen x 1mL each) / 30 days
- Vyepti 100mg 3mL: (3 single dose vials x 1mL each) / 90 days

Continuation of therapy:

1. Patient has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity
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
3. For acute migraine treatment: medication will not be used in combination with another biologic CGRP antagonist for the acute treatment of migraines
4. For migraine prevention: medication will not be used in combination with another biologic CGRP antagonist for the prevention of migraines.

Renewal approval: 6 months

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- Qulipta 10mg, 30mg, 60mg: 30 tablets/30 days
- Ubrelvy 50mg, 100mg: 16 tablets/30 days
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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. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically
9. 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
10. Estemalik E, Tepper S. Preventive treatment in migraine and the new US guidelines. Neuropsychiatric Dis Treat. 2013;9:709–720.

11. 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
12. International Headache Society (IHS); Headache Classification Committee. The International Classification of Headache s, 3rd edition. Available at: https://www.ichd-3.org/