Washington State Health Care Authority

Acute Migraine Treatment: Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist

Medical policy no. 67.70.10-1 Effective Date: TBD

Related medical policies:

- **Medical policy no. 67.70.20-** Migraine Products: CGRP Receptor Antagonist

Note
New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.

Background:

Migraine is one of the most disabling chronic health conditions worldwide, accounting for significant decreased quality of life and reduced productivity. Although the entire pathophysiology of migraines remains uncertain, calcitonin gene-related peptide (CGRP) is known to increase significantly during a migraine episode and decrease upon recovery. Additionally, CGRP infusion may trigger migraine attacks in migraineurs, and is thought to mediate trigeminovascular pain from intracranial vessels to the central nervous system. CGRP antagonists are an emerging therapeutic class for both the prevention and acute treatment of migraines. Ubrogepant (Ubrelvy) and rimegepant (Nurtec ODT) were approved by the Food and Drug Administration (FDA) in December, 2019 and February, 2020, respectively, and are the only CGRP antagonists currently approved for treatment of acute migraine.

Medical necessity:

Drug	Medical Necessity
Ubrogepant (Ubrelvy) Rimegepant (Nurtec ODT)	Ubrogepant (Ubrelvy) and rimegepant (Nurtec ODT) may be considered medically necessary for: • The acute treatment of migraine headaches with or without aura in adults

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
Acute treatment of migraine Ubrogepant (Ubrelvy) Rimegepant (Nurtec ODT)	Ubrogepant (Ubrelvy) or rimegepant (Nurtec ODT) may be considered medically necessary when **ALL** of the following are met: 1. Diagnosis of migraine, as defined by the International Classification of Headache Disorders 3rd edition (ICHD-3) (See table 1); **AND**

	2. At least 2 migraine episodes with moderate to severe pain per month during the last 3 months; **AND** 3. Documentation that the prescriber has ruled out medication overuse headache; **AND** 4. Documentation of inadequate treatment response to the following: a. At least 2 different 5-hydroxytryptamine (5HT) receptor agonists (triptans), unless contraindicated; **AND** b. At least one triptan must be used in combination with a non-steroidal anti-inflammatory steroid (NSAID), unless contraindicated; **AND** 5. Ubrogepant or Rimegepant are not prescribed within the same month as any other CGRP antagonist (i.e. Emgality, Aimovig, Ajovy); **AND** 6. Client is 18 years of age or older If all of the above criteria are met, the request will be **approved for 3 months**.
	Criteria (Reauthorization) Ubrogepant (Ubrelvy) and rimegepant (Nurtec ODT) may be reauthorized when the following criteria are met: 1. Documentation of therapeutic benefit defined as **ONE** of the following: a. Clinically meaningful reduction in pain, or pain freedom, after CGRP antagonist administration; **OR** b. Clinically meaningful reduction in migraine-associated symptoms (i.e. photophobia, phonophobia, and nausea) after CGRP antagonist administration If the above criteria are met, ubrogepant and remegepant may be **reauthorized for 12 months.**

Dosage and quantity limits

Indication	Dose and Quantity Limits
Acute treatment of migraine	• Nurtec ODT: 75 mg taken orally as needed, Max 75 mg per 24 hours; 16 tablets (two blister packs) per 30 days • Ubrelvy: 50 or 100 mg taken orally as needed, a second dose may be administered at least 2 hours after the initial dose. Max 2 doses per 24 hours; 16 tablets per 30 days.

Evidence Review:

Ubrelvy (ubrogepant) was evaluated in two phase 3 randomized controlled trials (Lipton, et al., Dodick et al.)**.** Participants were adults aged 18 to 75 years with two to eight moderate to severe pain migraine episodes per month for the preceding three months. Lipton, et al. evaluated ubrogepant 50 mg (n = 562) doses compared to placebo (n=563) and Dodick et al. studied doses of 50 mg (n=556) and 100 mg (n=557) compared to placebo (n=563). Approximately 90% of participants were women, 24% were taking concurrent non-CGRP antagonist preventive migraine therapy, and 97% had previously tried other abortive treatment, most commonly NSAIDs. Pain freedom and

improvement in bothersome symptoms (photophobia, phonophobia, and nausea) at 2 hours post-dose were primary outcomes. Study participants had the option to take a second dose of ubrogepant 2 to 48 hours after the first dose if needed for initial non-response. Both trials observed a significant number of participants achieving the primary outcomes compared to placebo at the 50 mg and 100 mg doses. Ubrogepant 50 mg increased pain freedom at 2 hours by 7.4% (p 0.002) and 7.5% (p <0.001) in each trial, respectively accounting for a number needed to treat (NNT) of 14. The 50 mg dose additionally increased the proportion of participants free of from bothersome symptoms at 2 hours by 10.8% and 11.5% (p <0.001) for both. Similarly, ubrogepant 100 mg increased freedom from pain and bothersome symptoms at 2 hours by 9.4% and 9.9%, respectively (p <0.001 for both).

Rimegepant was similarly evaluated in two phase 3 randomized controlled trials (Lipton, et al., Croop et al.). In Croop et al. the effectiveness of rimegepant 75 mg orally dissolving tablet (n=682) was compared to placebo(n=693). Participants were adults aged 18 and older with two to eight moderate to severe pain migraine episodes per month for the preceding three months. Approximately 85% of participants were women and no concurrent CGRP antagonist treatment for migraine prevention was allowed. Pain freedom and improvement in bothersome symptoms (photophobia, phonophobia, and nausea) at 2 hours post-dose were primary outcomes. Unlike trials for ubrogepant, study participants did not have the option to take a second dose of rimegepant for non-response. Cooper et al, observed a significant number of participants achieving the primary outcomes compared to placebo, concluding a 10.3% and 8.3% (p <0.001 for both) increase for in pain and bothersome symptoms freedom at 2 hours, respectively.

References

1. Prescribing Information: Nurtec ODT. Biohaven Pharmaceuticals Inc., New Haven, CT , March, 2020.
2. Prescribing Information: Ubrelvy. Allergan, Inc., Madison, NJ, December, 2019.
3. Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. Lancet. 2019;394(10200):737-745.
4. Lipton RB, Croop R, Stock EG, et al. Rimegepant, an Oral Calcitonin Gene-Related Peptide Receptor Antagonist, for Migraine. N Engl J Med. 2019;381(2):142-149.
5. Lipton RB, Dodick DW, Ailani J, et al. Effect of Ubrogepant vs Placebo on Pain and the Most Bothersome Associated Symptom in the Acute Treatment of Migraine: The ACHIEVE II Randomized Clinical Trial. JAMA. 2019;322(19):1887-1898.
6. Dodick DW, Lipton RB, Ailani J, et al. Ubrogepant for the Treatment of Migraine. N Engl J Med. 2019;381(23):2230-2241.
7. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211.

History

Date	Action and Summary of Changes
5/12/2020	New Policy – 1st draft

Appendix

Table 1: ICHD-3 diagnostic criteria for migraine

Migraine Type	ICHD-3 Diagnostic Criteria
Migraine	A. At least five attacks fulfilling criteria B-D

	B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated) C. Headache has at least two of the following four characteristics: 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs) D. During headache at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not better accounted for by another ICHD-3 diagnosis.
Migraine with aura	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. visual 2. Sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal C. At least three of the following six characteristics: 1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within 60 minutes, by headache A. Not better accounted for by another ICHD-3 diagnosis.

Washington State Health Care Authority

Migraine Agents: CGRP Receptor Antagonists (Acute)

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation of one of the following after CGRP antagonist administration?
   - ☐ Reduction in pain, or pain freedom
   - ☐ Reduction in migraine-associated symptoms (i.e. photophobia, phonophobia, and nausea)

2. Indicate the patient's diagnosis:
   - ☐ Migraine headache
   - ☐ Other. Specify: _____

3. Has prescriber ruled out medication overuse headache? ☐ Yes ☐ No
4. Is patient experiencing at least two migraine episodes with moderate to severe pain per month during the last 3 months? ☐ Yes ☐ No

5. Indicate if patient has had an inadequate treatment response to the following (check all that apply):
   - ☐ At least 2 different 5-hydroxytryptamine (5HT) receptor agonists (triptans)
   - ☐ At least one triptan used in combination with a non-steroidal anti-inflammatory drug (NSAID)
   - ☐ NSAIDs are contraindicated
   - ☐ Triptans are contraindicated

6. Wil this be prescribed in combination with any other CGRP antagonist (i.e. Emgality, Aimovig, Ajovy)?
   ☐ Yes ☐ No

CHART NOTES ARE REQUIRED WITH THIS REQUEST

Prescriber signature	Prescriber specialty	Date