BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE:	**2/13/2020**
LAST REVIEW DATE:	**5/21/2020**
LAST CRITERIA REVISION DATE:	**5/21/2020**
ARCHIVE DATE:	

NURTEC™ ODT (rimegepant) orally disintegrating tablet
REYVOW™ (lasmiditan) oral tablet
UBRELVY™ (ubrogepant) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602)

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864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Reyvow (lasmiditan)

Criteria:

- **Criteria for initial therapy:** Reyvow (lasmiditan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is **ONE** of the following:
   - A Neurologist
   - A licensed professional **and ONE** of the following:
     - Is prescribing in consultation with a Neurologist or Pain Specialist
     - Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
     - Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual is 18 years of age or older

3. A confirmed diagnosis of moderate to severe headache pain intensity from acute migraine with or without aura

4. Individual has failure, intolerance or contraindication to **ALL** of the following preferred step therapy agents:
   - **AT LEAST TWO** triptan drugs (naratriptan, rizatriptan, sumatriptan, and zolmitriptan)
   - **AT LEAST ONE** NSAID (naproxen, ibuprofen, aspirin, or diclofenac)

5. Individual has failure, intolerance or contraindication to calcitonin gene-related peptide (CGRP) **either** Aimovig (erenumab) or Emgality (galcanezumab-gnlm) as a preventive agent and will not continue any other CGRP inhibitors

6. The patient is using and continues to use **AT LEAST ONE** non-CGRP preventative migraine agent(s):
   - Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol
   - Antidepressant: amitriptyline or venlafaxine
   - Anticonvulsant: topiramate, divalproex sodium, or sodium valproate

7. Will not be used for the preventive treatment of migraine

8. Does not have severe hepatic impairment (Child-Pugh Class C)

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Reyvow (lasmiditan) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by **ONE** of the following:
   - A Neurologist
   - A licensed professional **and ONE** of the following:
     - Is prescribing in consultation with a Neurologist or Pain Specialist
     - Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
     - Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual's condition responded while on therapy
   - Response is defined as:
     - Achieved and maintains a reduction of moderate or severe headache pain to no pain and absence of the most bothersome symptom (such as, photophobia, phonophobia, or nausea)
     - No evidence of disease progression
     - No emergency room or urgent care visits for acute migraine treatment

3. Individual is currently not on any other CGRP therapies

4. Uses **AT LEAST ONE** non-CRGP migraine prevention agent

5. Will not be used for the preventive treatment of migraine

6. Does not have severe hepatic impairment (Child-Pugh Class C)

7. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use:
   - Central nervous system depression, including dizziness and sedation
   - Serotonin syndrome

8. There are no significant interacting drugs

Renewal duration: 12 months

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Nurtec (rimegepant) and Ubrelvy (ubrogepant)

- **Criteria for initial therapy:** Nurtec (rimegepant) and Ubrelvy (ubrogepant) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is **ONE** of the following:
   - A Neurologist
   - A licensed professional **and ONE** of the following:
     - Is prescribing in consultation with a Neurologist or Pain Specialist
     - Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
     - Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual is 18 years of age or older

3. A confirmed diagnosis of moderate to severe headache pain intensity from acute migraine with or without aura

4. Individual has failure, intolerance or contraindication to **ALL** of the following preferred step therapy agents:
   - **AT LEAST TWO** triptan drugs (naratriptan, rizatriptan, sumatriptan, and zolmitriptan)
   - **AT LEAST ONE** NSAID (naproxen, ibuprofen, aspirin, or diclofenac)

5. Individual has failure, intolerance or contraindication to calcitonin gene-related peptide (CGRP) **either** Aimovig (erenumab) or Emgality (galcanezumab-gnlm) as a preventive agent and will not continue any other CGRP inhibitors

6. The patient is using non-CGRP preventative migraine agent(s):
   - Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol
   - Antidepressant: amitriptyline or venlafaxine
   - Anticonvulsant: topiramate, divalproex sodium, or sodium valproate

7. Uses **AT LEAST ONE** non-CGRP migraine prevention agent will be continued

8. Will not be used for the preventive treatment of migraine

9. Will not be used with strong CYP 3A4 inducers (i.e., rifampin, phenytoin, barbiturates, St. John's Wort) or CYP 3A4 inhibitors (i.e. ketoconazole, itraconazole, clarithromycin)

10. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)

11. For Nurtec only: Will not be used in patient with severe hepatic impairment (Child-Pugh C)

12. There are **NO** contraindications

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Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nurtec (rimegepant) and Ubrelvy (ubrogepant) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by **ONE** of the following:
   - A Neurologist
   - A licensed professional **and ONE** of the following:
     - Is prescribing in consultation with a Neurologist or Pain Specialist
     - Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
     - Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

2. Individual's condition responded while on therapy
   - Response is defined as:
     - Achieved and maintains a reduction of moderate or severe headache pain to no pain and absence of the most bothersome symptom (such as, photophobia, phonophobia, or nausea)
     - No evidence of disease progression
     - No emergency room or urgent care visits for acute migraine treatment

3. Individual has been adherent with the medication

4. Individual is currently not on any other CGRP therapies

5. Uses **AT LEAST ONE** migraine prevention agent

6. Will not be used for the preventive treatment of migraine

7. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)

8. For Nurtec only: Will not be used in patient with severe hepatic impairment (Child-Pugh C)

9. Will not be used with strong CYP 3A4 inducers (i.e., rifampin, phenytoin, barbiturates, St. John's Wort) or CYP 3A4 inhibitors (i.e. ketoconazole, itraconazole, clarithromycin)

10. Individual has not developed any contraindications

11. There are no significant interacting drugs

Renewal duration: 12 months

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Description:

Nurtec ODT (rimegepant) is a calcitonin gene-related peptide receptor antagonist indicated for the acute treatment of migraine with or without aura in adults.

Reyvow (lasmiditan) is a serotonin (5-HT) 1F receptor agonist indicated for the acute treatment of migraine with or without aura in adults. Lasmiditan binds with high affinity to the 5-HT1F receptor. Lasmiditan presumably exerts its therapeutic effects in the treatment of migraine through agonist effects at the 5-HT1F receptor; however, the precise mechanism is unknown.

Ubrelvy (ubrogepant) is a calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine with or without aura. It is not indicated for the preventive treatment of migraine.

The CGRP pathway is important in pain modulation, and CGRP has been observed to increase during a migraine. CGRP is a 37-amino acid peptide and functions as a neurotransmitter in the central and peripheral nervous system and as a vasodilator. The involvement of CGRP in migraine was suggested in the 1980s. Since then, new agents affecting the CGRP pathway have been developed and studied. Some approaches focused on small molecule CGRP receptor antagonists to be used to treat migraine attacks, or monoclonal antibodies to be used for migraine prevention.

Migraine is a common episodic disorder, the hallmark of which is a disabling headache generally associated with nausea, and/or light and sound sensitivity. Migraine with aura refers to the occurrence of transient visual, sensory, language, or motor disturbance that is followed by a migraine headache. The exact mechanisms of migraine are unknown, but currently it is believed to initiate from a primary neuronal dysfunction that leads to a sequence of intracranial and extracranial changes accounting for migraine, including the four phases of premonitory symptoms, aura, headache and post-drome. Specifically, activation of the trigeminovascular system, cortical spreading depression, and neuronal sensitization all seem to play a role.

Pharmacologic therapies for migraine can be categorized broadly into agents used for treatment once symptoms have started (“acute” or “abortive” medications) and agents used to decrease the frequency or severity of migraines (“preventive” or “prophylactic” therapies).

Selection of medication for acute treatment is directed by the severity of the attacks, presence of associated nausea and vomiting, treatment setting, and patient-specific factors. Abortive treatments are usually more effective if they are given early in the course of the headache (within in the first hour if possible). A 2015 guideline assessment published by the American Headache Society lists the following medications as Level A (established as effective) for acute migraine treatment: all triptan drugs, NSAIDs (naproxen, ibuprofen, aspirin, diclofenac), combination of sumatriptan and naproxen, acetaminophen/aspirin/caffeine, acetaminophen (for acute treatment of non-incapacitating migraine), and dihydroergotamine nasal spray.

Prophylactic headache treatment is indicated if the headaches are frequent, long lasting, or account for a significant amount of total disability. A number of drug classes are used for the prevention of migraine.

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Medications that are effective in controlled trials include: beta blockers (metoprolol, propranolol, and timolol); anticonvulsants (valproate, divalproex, and topiramate); and antidepressants (amitriptyline and venlafaxine).

Outcomes of clinical trials of acute treatment of migraine commonly include relief of symptoms including pain, nausea/vomiting, photophobia and phonophobia; pain freedom; freedom from the most bothersome symptom (MBS); pain relief; and sustained symptom response.

The Migraine Disability Assessment (MIDAS) is a brief, 7-item, self-administered questionnaire designed to quantify headache-related disability. Respondents answer five questions about activity limitations in the past 3 months due to migraine including (1) missed work or school days, (2) missed household chores days, (3) missed non-work activity days, and days at work or school (4) plus days of household chores (5) where productivity was reduced by half or more. Two additional questions about the number of headaches and average pain level associated with headaches over the past 3 months are not used in deriving the MIDAS score, but they are for use by the respondent's clinician.

The MIDAS score is the sum of the number of days reported for each of the five questions. Respondents with a MIDAS score of 0-5 are rated as having little or no disability, 6-10 as having mild disability, 11-20 as having moderate disability, and 21 or greater as having severe disability.

Definitions:

Pain freedom:
- A ***reduction in severity*** of headache from mild, moderate or severe pain ***at baseline to none*** at a given follow-up time point

Freedom from most bothersome symptoms (MBS):
- ***Total absence*** of nausea/vomiting, photophonia or phonophobia at a given follow-up time point

Pain relief:
- ***Having mild to no pain*** at a given follow-up time point

Sustained symptom response after 2-hours:
- Those with an initial response that is sustained at subsequent follow-up time points ***without*** the use of repeat dosing or rescue medications

Migraine Disability Assessment (MIDAS):

Please answer the following questions about **ALL** of the headaches you have had over the last 3 months. Select zero if you did not have the activity in the last 3 months.

1. _____ On how many days in the last 3 months did you miss work or school because of your headaches?

2. _____ How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)
3. _____ On how many days in the last 3 months did you not do household work (such as housework, home repairs and maintenance, shopping, caring for children and relatives) because of your headaches?
4. _____ How many days in the last 3 months was your productivity in household work reduced by half of more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)
5. _____ On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

6. Total number of days (from questions 1 through 5): _____

Answer the following for your provider:

1. _____ On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.)

_____ On a scale of 0 - 10, on average how painful were these headaches? (where 0 = no pain at all, and 10 = pain as bad as it can be.)

MIDAS Grade	Definition	MIDAS Score
I	Little or No disability	0-5
II	Mild disability	6-10
III	Moderate disability	11-20
IV	Severe disability	21+

Migraine Severity:

- **Mild Pain Level / Pain Score**
  - Does not interfere with most activities and is easy to manage both physically and psychologically. Individual able to adapt to these levels of pain with low doses of medication (e.g., acetaminophen), dietary changes, or bed rest.

- **Moderate Uncomfortable Pain Level / Pain Score**
  - Interferes with many activities of daily living and requires changes to daily lifestyle to manage pain symptoms. Migraine pain is more noticeable but is not incapacitating.

- **Severe Pain Level / Pain Score**
  - Individual is no longer able to engage in normal activities and seeks stronger medications to help improve ability to function independently.

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Identification of headache type: migraine, tension, or cluster			
	Migraine	**Tension**	**Cluster**
Location	Unilateral	Bilateral	Supraorbital/temporal
Pain intensity[1]	Moderate to severe	Mild to moderate	Severe
Duration	4–72 hours	30 minutes to 7 days	15–180 minutes
Characterization of pain	Pulsing	Pressure/squeezing	Boring/stabbing
Sensitivity to light/sound	One or both may be present	Both are absent or only one is present	No
Nausea/vomiting	One or both may be present	No	One or both may be present
Aggravated by routine activity	Yes	No	No
Aura	May be present	No	No
Associated symptoms	None	None	Miosis, ptosis, rhinorrhea

1 Pain intensity
- Mild—Patient is aware of a headache, but is able to continue daily routine with minimum alterations.
- Moderate—The headache inhibits daily activities, migraine pain is more noticeable but is not incapacitating.
- Severe—The headache is incapacitating such that patient is no longer able to engage in normal activities.

2013 Canadian Headache Society (CHS) – medications for acute migraine:

2013 Canadian Headache Society (CHS) Summary of Recommendations*		
Recommended For Use in Episodic Migraine (Use)**		
	Recommendation	
Drug	**Recommendation Strength**	**Quality of Evidence**
Almotriptan	Strong	High
Eletriptan	Strong	High
Frovatriptan	Strong	High
Naratriptan	Strong	High
Rizatriptan	Strong	High
Sumatriptan	Strong	High
Zolmitriptan	Strong	High
Aspirin	Strong	High
Diclofenac	Strong	High
Ibuprofen	Strong	High
Naproxen	Strong	High
Acetaminophen	Strong	High
Domeridone	Strong	Low
Metoclopramide	Strong	Moderate
Dihydroergotamine	Weak	Moderate
Ergotamine	Weak, not recommended for routine use	Moderate
Opioid containing compounds	Weak, not recommended for routine use	Low
Tramadol containing compounds	Weak, not recommended for routine use	Moderate
Not Recommended for Use in Episodic Migraine (Do not use***)**		
Butalbutal containing compounds	Strong	Low
Butorphanol	Strong	Low
*Utilizing Grading of Recommendations Assessment, Development and Evaluation (GRADE) Criteria		

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**Migraine with headache on less than 15 days a month
*** Except under exceptional circumstances

Metoclopramide strongly recommended for use when necessary

Resources:

NURTEC ODT (rimegepant). Packet Label, revised 3/2020 accessed 05-15-20.

Reyvow (lasmiditan) product information accessed 02-04-20 at DailyMed

Ubrelvy (ubrogepant) product information accessed 02-04-20 at DailyMed

UpToDate: Acute treatment of migraines in adults. Current through Apr 2018

UpToDate: Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. Current through Apr 2018

UpToDate: Preventive treatment of migraine in adults. Current through Apr 2018

Marmura MJ, Silberstein SD, Schwedt TJ. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. Headache 2015 Jan; 55:3-20

Worthington I, Pringsheim T, Gawel MJ, et al.: Targeted Review: Medications for Acute Migraine Treatment. Can J Neurol Sci 2013; 40: Suppl 3: S10-S32