

PHARMACY COVERAGE GUIDELINE

[NURTEC™](#) ODT (rimegepant)

[QULIPTA™](#) (atogepant)

[REYVOW™](#) (lasmiditan)

[UBRELVY™](#) (ubrogepant)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

NURTEC ODT (rimegepant)

- **Criteria for initial therapy:** Nurtec ODT (rimegepant) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:
 1. Prescriber is **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:

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- i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. 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. Individual has a confirmed diagnosis of **ONE** of the following:
 - a. Acute treatment of migraine of moderate to severe headache pain intensity
 - b. Prevention of episodic migraine with or without aura of moderate to severe headache pain intensity
4. **Additional criteria for episodic migraine only:** the individual has between 4 to 14 headache days per month, of which at least 4 were migraine days
5. Individual does **NOT** have chronic migraine
(Chronic migraine is defined as: an individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura)
6. Documented Migraine Disability Assessment (MIDAS) score of 11 or greater indicating at least moderate disability
7. Documented failure, contraindication per FDA label or intolerance to **ONE** of the following:
 - a. When request is for **acute migraine BOTH** of the following:
 - i. **At least TWO** triptan drugs (naratriptan, rizatriptan, sumatriptan, and zolmitriptan)
 - ii. **At least ONE** NSAID (naproxen, ibuprofen, aspirin, or diclofenac) **OR at least ONE** anticonvulsant (topiramate, divalproex sodium, or sodium valproate)
 - b. When request is for **episodic migraine BOTH** of the following:
 - i. **At least ONE** beta-blocker (atenolol, metoprolol, nadolol, propranolol, or timolol) **OR at least ONE** anticonvulsant (topiramate, divalproex sodium, or sodium valproate)
 - ii. **At least ONE** calcitonin gene-related peptide monoclonal antibodies (Aimovig (erenumab), Emgality (galcanezumab-gnlm), or Ajovy (fremanezumab-vfrm))
8. Documentation that the individual does **NOT** have any of the following:
 - a. History with current evidence of uncontrolled, unstable, or recently diagnosed cardiovascular disease, such as ischemic heart disease, coronary artery vasospasm, and cerebral ischemia
 - b. Myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, cardiac surgery, stroke, or transient ischemic attack within the previous 6-months
 - c. Uncontrolled hypertension
9. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)

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10. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr))
11. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)
12. Will not be used in patient with severe hepatic impairment (Child-Pugh C)
13. There are no significant interacting drugs
 - a. Strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, posaconazole, others)
 - b. Strong or moderate CYP3A4 inducers (e.g., rifampin, phenytoin, St. John's Wort, phenobarbital, primidone, others)
 - c. P-gp or BCRP inhibitors (e.g., amiodarone, clarithromycin, cyclosporine, itraconazole, verapamil, others)

Initial approval duration: 6 months, no more than 18 ODT per month

- **Criteria for continuation of coverage (renewal request):** Nurtec ODT (rimegepant) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation
2. Individual's condition responded to therapy and meets **ALL** of the following criteria:
 - a. 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)
 - b. No evidence of disease progression
 - c. Significant reduction in emergency room or urgent care visits for acute migraine treatment
3. Individual has been adherent with the medication
4. Documentation that the individual does **NOT** have any of the following:
 - a. History with current evidence of uncontrolled, unstable, or recently diagnosed cardiovascular disease, such as ischemic heart disease, coronary artery vasospasm, and cerebral ischemia
 - b. Myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, cardiac surgery, stroke, or transient ischemic attack within the previous 6-months
 - c. Uncontrolled hypertension

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5. Individual does **NOT** have chronic migraine
(Chronic migraine is defined as: an individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura)
6. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)
7. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr))
8. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)
9. Will not be used in patient with severe hepatic impairment (Child-Pugh C)
10. There are no significant interacting drugs
 - a. Strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, posaconazole, other)
 - b. Strong or moderate CYP3A4 inducers (e.g., rifampin, phenytoin, St. John's Wort, phenobarbital, primidone, other)
 - c. P-gp or BCRP inhibitors (e.g., amiodarone, clarithromycin, cyclosporine, itraconazole, verapamil, other)

Renewal duration: 12 months, no more than 18 ODT per month

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**
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QULIPTA (atogepant)

- **Criteria for initial therapy:** Qulipta (atogepant) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
1. Prescriber is **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation

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2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of prevention of episodic migraine with or without aura
4. Individual with migraine who has between 4-14 headache days per month, of which at least 4 were migraine days
5. Individual does **NOT** have **ANY** of the following:
 - a. Chronic migraine (defined as: an individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura)
 - b. Persistent daily headache
 - c. Trigeminal autonomic cephalgia (cluster headache)
 - d. Painful cranial neuropathy
6. Documented failure, contraindication per FDA label or intolerance to **BOTH** of the following:
 - a. **At least ONE** beta-blocker (atenolol, metoprolol, nadolol, propranolol, or timolol) **OR at least ONE** anticonvulsant (topiramate, divalproex sodium, or sodium valproate)
 - b. **At least ONE** calcitonin gene-related peptide monoclonal antibodies (Aimovig (erenumab), Emgality (galcanezumab-gnlm), or Ajovy (fremanezumab-vfrm))
7. Documentation that the individual does **NOT** have clinically significant cardiovascular or cerebrovascular disease such as myocardial infarction stroke or transient ischemic attack within the previous 6-months
8. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)
9. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr))
10. Will not be used in patient with severe hepatic impairment (Child-Pugh C)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Qulipta (atogepant) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)

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- iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation
2. Individual's condition responded while on therapy and meets **ALL** of the following criteria:
 - a. Achieved and maintains at least a 50% reduction in number of monthly migraine days from baseline
 - b. Achieved and maintains a reduction in number of monthly headache days
 - c. Achieved and maintains a reduction in the number of days of use of acute migraine-specific medications from baseline
 - d. Significant reduction in emergency room or urgent care visits for acute migraine treatment
3. Individual has been adherent with the medication
4. Documentation that the individual does **NOT** have clinically significant cardiovascular or cerebrovascular disease such as myocardial infarction stroke or transient ischemic attack within the previous 6-months
5. Individual does **NOT** have chronic migraine, persistent daily headache, trigeminal autonomic cephalgia (cluster headache) or painful cranial neuropathy
6. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)
7. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr))
8. Will not be used in patient with severe hepatic impairment (Child-Pugh C)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
 1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**
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REYVOW (lasmiditan)

- **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. A Neurologist

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- b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. 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. Individual has a confirmed diagnosis of moderate to severe headache pain intensity from acute migraine with or without aura
4. Documented Migraine Disability Assessment (MIDAS) score of at least 11 indicating at least moderate disability or a score of 21 indicating severe disability
5. Documented failure, contraindication per FDA label, or intolerance to the following acute migraine agents:
 - a. **At least TWO** triptan drugs (naratriptan, rizatriptan, sumatriptan, and zolmitriptan)
 - b. **At least ONE** NSAID (naproxen, ibuprofen, aspirin, or diclofenac) **OR at least ONE** anticonvulsant (topiramate, divalproex sodium, or sodium valproate)
6. Documented failure, contraindication per FDA label, or intolerance as preventive agent to **either**:
 - a. Aimovig (erenumab)
 - b. Emgality (galcanezumab-gnlm)
7. The patient is using and will continue to use **at least ONE** of the following preventative migraine agent(s):
 - a. Beta-blocker (atenolol, metoprolol, nadolol, propranolol, or timolol)
 - b. Antidepressant: amitriptyline or venlafaxine
 - c. Anticonvulsant (topiramate, divalproex sodium, or sodium valproate)
8. Documentation that the individual does **NOT** have any of the following:
 - a. Known coronary artery disease
 - b. Clinically significant arrhythmia
 - c. Uncontrolled hypertension
 - d. History or evidence of hemorrhagic stroke, epilepsy or any other condition placing the individual at increased risk of seizures
9. Will not be used for the preventive treatment of migraine
10. Will not be used in patient with severe hepatic impairment (Child-Pugh Class C)
11. Will not be used with drugs that are substrates for P-gp or BCRP substrates such as dabigatran, digoxin, fexofenadine, rosuvastatin, sulfasalazine, others

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12. Will not be used with Nurtec ODT (rimegepant) or Ubrelvy (ubrogepant)

Initial approval duration: 6 months

➤ **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 (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation
2. Individual's condition responded while on therapy and meets **ALL** of the following criteria:
 - a. 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)
 - b. No evidence of disease progression
 - c. Significant reduction in emergency room or urgent care visits for acute migraine treatment
3. Documentation that the individual does **NOT** have any of the following:
 - a. Known coronary artery disease
 - b. Clinically significant arrhythmia
 - c. Uncontrolled hypertension
 - d. History or evidence of hemorrhagic stroke, epilepsy or any other condition placing the individual at increased risk of seizures
4. Uses **at least ONE** migraine prevention agent
5. Will not be used for the preventive treatment of migraine
6. Will not be used in patient with severe hepatic impairment (Child-Pugh Class C)
7. Individual has not developed any significant adverse drug effects that may exclude continued use:
 - a. Central nervous system depression, including dizziness and sedation
 - b. Serotonin syndrome
8. Will not be used with drugs that are substrates for P-gp or BCRP substrates such as dabigatran, digoxin, fexofenadine, rosuvastatin, sulfasalazine, others

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NURTEC™ ODT QULIPTA™ REYVOW™ UBRELVY™

9. Will not be used with Nurtec ODT (rimegepant) or Ubrelyvy (ubrogepant)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**
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UBRELVY (ubrogepant)

- **Criteria for initial therapy:** Ubrelyvy (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. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. 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. Individual has a confirmed diagnosis of moderate to severe headache pain intensity from acute migraine with or without aura
 4. Documented Migraine Disability Assessment (MIDAS) score of at least 11 indicating at least moderate disability or a score of 21 indicating severe disability
 5. Documented failure, contraindication per FDA label or intolerance to the following acute migraine agents:
 - a. **At least TWO** triptan drugs (naratriptan, rizatriptan, sumatriptan, and zolmitriptan)
 - b. **At least ONE** NSAID (naproxen, ibuprofen, aspirin, or diclofenac) **OR at least ONE** anticonvulsant: topiramate, divalproex sodium, or sodium valproate
 6. Documented failure, contraindication per FDA label, or intolerance as preventive agent to **either**:
 - a. Aimovig (erenumab)
 - b. Emgality (galcanezumab-gnlm)
 7. The patient is using and will continue to use **at least ONE** of the following non-CGRP preventative migraine agent(s):

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- a. Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol
 - b. Antidepressant: amitriptyline or venlafaxine
 - c. Anticonvulsant: topiramate, divalproex sodium, or sodium valproate
8. There are **NO** FDA-label contraindications, such as concurrent use with a strong CYP3A4 inhibitor (e.g., itraconazole, ketoconazole, clarithromycin, other)
9. Documentation that the individual does **NOT** have any of the following:
- a. History with current evidence of uncontrolled, unstable or recently diagnosed cardiovascular disease, such as ischemic heart disease, coronary artery vasospasm, and cerebral ischemia
 - b. Myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, cardiac surgery, stroke or transient ischemic attack within the previous 6-months
 - c. Uncontrolled hypertension
10. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)
11. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr))
12. Will not be used for the preventive treatment of migraine
13. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)
14. Will not be used with strong CYP3A4 inducers (e.g., rifampin, phenytoin, St. John's Wort, other)

Initial approval duration: 6 months, no more than 8 tablets per month

- **Criteria for continuation of coverage (renewal request):** Ubrelvy (ubrogepant) is considered **medically necessary** and will be approved when **ALL** of the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by **ONE** of the following:
 - a. A Neurologist
 - b. A licensed professional **and ONE** of the following:
 - i. Is prescribing in consultation with a Neurologist or Pain Specialist
 - ii. Is certified as a headache specialist by the United Council for Neurologic Subspecialties (UCNS)
 - iii. Has earned a Certificate in Added Qualifications (CAQ) in Headache Medicine from the National Headache Foundation
2. Individual's condition responded while on therapy and meets **ALL** of the following criteria:
 - a. 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)
 - b. No evidence of disease progression

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- c. Significant reduction in emergency room or urgent care visits for acute migraine treatment
3. Documentation that the individual does **NOT** have any of the following:
 - a. History with current evidence of uncontrolled, unstable or recently diagnosed cardiovascular disease, such as ischemic heart disease, coronary artery vasospasm, and cerebral ischemia
 - b. Myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, cardiac surgery, stroke or transient ischemic attack within the previous 6-months
 - c. Uncontrolled hypertension
4. Uses **at least ONE** non-CGRP migraine prevention agent
5. Will not be used for the preventive treatment of migraine
6. Will not be used concurrently with or alternating with Botox (onabotulinumtoxinA)
7. Will not be used concurrently with or alternating with other calcitonin gene-related peptide (CGRP) therapies (e.g. Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm) or Vyepti (eptinezumab-jjmr)
8. Will not be used in patient with end-stage renal disease (CrCl < 15 mL/min)
9. Will not be used with strong CYP3A4 inducers (e.g., rifampin, phenytoin, St. John's Wort, other)

Renewal duration: 12 months, no more than 8 tablets per month

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**
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Description:

Nurtec ODT (rimegepant) is a calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine with or without aura in adults and for preventive treatment of episodic migraine 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-HT_{1F} receptor. Lasmiditan presumably exerts its therapeutic effects in the treatment of migraine through agonist effects at the 5-HT_{1F} receptor; however, the precise mechanism is unknown.

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Ubrovelvy (ubrogepant) is a CGRP receptor antagonist indicated for the acute treatment of migraine with or without aura. It is not indicated for the preventive treatment of migraine.

Qulipta (atogepant) is a CGRP receptor antagonist indicated for the preventive treatment of episodic migraine in adults.

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. 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

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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:

Migraine day:

- Any calendar day in which the patient experiences a qualified migraine headache (onset, continuation, or recurrence of the migraine headache)
- A qualified migraine is defined as migraine with or without aura, lasting ≥ 30 minutes that meets at least one of the following:
 - ≥ 2 of the following pain features: unilateral, throbbing, moderate to severe, or exacerbated with exercise/physical activity
 - > 1 of the following associated non-pain features: nausea and or vomiting, or both photophobia, and phonophobia
- Any calendar day on which acute migraine-specific medication was used is counted as a migraine day

Treatment considerations:

- There are no strict definitions for the precise frequency or duration of migraine headaches that would prompt preventive therapy
- Migraine prevention therapy may be indicated for those with migraine headaches that are frequent (ex. as ≥ 4 headaches/month) or long-lasting (ex. ≥ 12 hours) and those that cause significant disability or diminished quality of life
- The goals of preventive therapy are to reduce the frequency, severity, and duration of headaches, to improve treatment responsiveness of therapies for acute attacks, prevent progression or transformation of episodic migraine to chronic migraine and to improve overall function or reduce the risk of neurologic impairment

Episodic migraine:

- Individual with migraine who has between 4 to 14 headache days per month, of which at least 4 were migraine days

Chronic migraine:

- Individual with migraine who has 15 or more headache days per month for more than 3 months, of which 8 days per month meet the features of migraine with or without aura].
- The diagnostic criteria for chronic migraine require the presence of headache for 15 or more days per month for more than three months, with the features of migraine headache present on at least eight days per month

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- Some patients with an episodic migraine pattern (<15 headache days a month) transition to a chronic migraine pattern (≥15 headache days a month), a transition that has been called "transformation" and "chronification"
- Features of migraine headache include:
 - Lasts 4-72 hours **AND** has at least 2 of the following 4 characteristics:
 - Unilateral, pulsating, moderate or severe pain intensity, aggravates or causes avoidance of routine physical activity
 - **AND** associated with at least one of the following during the headache:
 - Nausea and/or vomiting or photophobia and phonophobia.
- The management of chronic migraine should focus on prophylactic therapy and avoidance of acute headache medication overuse

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, photophobia 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 or 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?

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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.)
2. _____ 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+

AHS Consensus 2018		
Identifying Patients for Preventive Treatment		
Prevention should be:	Headache days/month	Degree of MIDAS required
Offered	6 or more	None
	4 or more	Some
	3 or more	Severe
Considered	4 or 5	None
	3	Some
	2	Moderate

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.

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

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Aggravated by routine activity	Yes	No	No
Aura	May be present	No	No
Associated symptoms	None	None	Miosis, ptosis, rhinorrhea
<p>1 Pain intensity</p> <ul style="list-style-type: none"> • 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)		
Drug	Recommendation	
	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
Domperidone	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***)		
Butalbital containing compounds	Strong	Low
Butorphanol	Strong	Low
<p>*Utilizing Grading of Recommendations Assessment, Development and Evaluation (GRADE) Criteria **Migraine with headache on less than 15 days a month *** Except under exceptional circumstances</p>		

Metoclopramide strongly recommended for use when necessary

Abortive (symptomatic) treatment of acute migraine:

- Simple analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen, triptans, antiemetics, calcitonin gene-related peptide (CGRP) antagonists (remigepant, ubrogepant), lasmiditan, and dihydroergotamine

Non-Calcitonin gene-related peptide (Non-CGRP) preventative (episodic or chronic) migraine agent(s):

- Beta-blocker: atenolol, metoprolol, nadolol, propranolol, or timolol

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- Antidepressant: amitriptyline or venlafaxine
- Anticonvulsant: topiramate, divalproex sodium, or sodium valproate

Botulinum toxin injection:

- Treatment of chronic migraine:
 - Botox (onabotulinumtoxinA)

CGRP related agents:

- Treatment of episodic or chronic migraine:
 - Vyepti (eptinezumab-jjmr)
 - Aimovig (erenumab)
 - Ajovy (fremanezumab-vfrm)
 - Emgality (galcanezumab)
 - Also used in cluster headache
- Treatment of episodic migraine:
 - Qulipta (atogepant)
 - Nurtec ODT (rimegepant)
- Treatment of acute migraine:
 - Nurtec ODT (rimegepant)
 - Ubrelvy (ubrogepant)

Serotonin (5-HT) 1F receptor agonist:

- Treatment of acute migraine
 - Reyvow (lasmiditan)
-

Resources:

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