Reyvow (lasmiditan)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Reyvow is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use
Reyvow is not indicated for the preventive treatment of migraine.

POLICY

Criteria for Initial Approval

A. Reyvow (lasmiditan) may be considered **medically necessary** for the acute treatment of moderate to severe migraines when the following criteria is met:
   1. The member is 18 years of age or older
   2. The member has a diagnosis of migraine, with or without aura, according to the International Classification of Headache Disorders (ICHD-3) [see Appendices A & B]
   3. The requested medication is prescribed by, or in consultation with, a headache specialist or neurologist
   4. The member has had at least a 30 day trial of and experienced an inadequate treatment response (i.e., little to no relief of moderate/severe migraine symptoms) or intolerance to at least TWO of the

preferred generic triptan medications, naratriptan (Amerge), sumatriptan (Imitrex), and rizatriptan (Maxalt); OR the member is currently receiving a positive therapeutic outcome on the requested medication through health insurance (excludes obtainment as samples or via manufacturer's patient assistance programs); OR the member has a contraindication that would prohibit a trial of any triptan medication
5. The member acknowledges and agrees to not drive or operate heavy machinery for 8 hours following administration of Reyvow
6. The member has been evaluated for and does not have medication overuse headache (see Appendix C)
7. Other conditions or aggravating factors that are contributing to the development of migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)

Approval will be for **6 months**

Continuation of Therapy

A. Reyvow (lasmiditan) may be considered **medically necessary** for the continuation of acute treatment of moderate to severe migraines when ALL of the following criteria are met:
   1. The member is 18 years of age or older
   2. The member has a diagnosis of migraine, with or without aura, according to the International Classification of Headache Disorders (ICHD-3) [See Appendices A & B]
   3. The requested medication is prescribed by, or in consultation with, a headache specialist or neurologist
   4. The member has experienced a positive clinical response to therapy (e.g., reduction in headache pain severity, relief from other migraine symptoms [photophobia, phonophobia or nausea], sustained headache pain relief, and improved ability to function normally).
   5. The member has been evaluated for and does not have medication overuse headache (see Appendix C)
   6. Other conditions or aggravating factors that are contributing to the development of migraine headaches are being treated when applicable (e.g., dental or jaw problems, muscle tension, depression, fibromyalgia, sleep disorders and smoking)

Approval will be for **12 months**

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Reyvow prescribing information states that the safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established. A second dose of Reyvow has not been shown to be effective for the same migraine attack.

Quantity Limits:

Drug	Standard Benefit Allowance	Post-Limit PA Quantity Limit
Reyvow 50 mg tablet	4 tablets / 30 days	N/A
Reyvow 100mg tablet	4 tablets / 30 days	8 tablets / 30 days

Post-Limit Prior Authorization Criteria

A. Additional quantities of Reyvow 100 mg may be considered **medically necessary** for members who meet the criteria for initial approval or continuation of therapy above when ALL of the following criteria are met:

1. Medication overuse headache has been considered and ruled out
2. The requested medication is prescribed by, or in consultation with, a headache specialist or neurologist
3. The member is currently using a migraine prophylactic agent and continues to experience multiple (i.e. ≥ 4) migraine headache days per month OR has a documented intolerance, FDA labeled contraindication, or hypersensitivity to all the migraine prophylactic agents
4. The member will continue using a migraine prophylactic agent or has a clinical reason to avoid all migraine prophylactic agents
5. After a reasonable trial of the Reyvow 100 mg dose, the member has not experienced a positive clinical response to therapy (e.g., reduction in headache pain severity, relief from other migraine symptoms [photophobia, phonophobia or nausea], sustained headache pain relief, and improved ability to function normally) which necessitates a dose increase to 200 mg per dose

Approval will be for **12 months** for quantities up to 8 tablets per 30 days (a dose of 200 mg per migraine attack) for Reyvow 100 mg strength only. Any request for quantities above that limit is considered **not medically necessary**.

Note: Post-Limit Prior Authorization Criteria does not apply to requests for additional quantities of Reyvow 50 mg strength.

APPENDICES

Appendix A
International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for migraine headache without aura

A. At least five attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (when 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 (e.g. 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.

Appendix B
International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for migraine headache 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 spready 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

F. Not better accounted for by another ICHD-3 diagnosis.

Appendix C

International Classification of Headache Disorders (ICHD-3 beta) diagnostic criteria for medication-overuse headache

A. Headache present on >15 days/month
B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache
C. Headache has developed or markedly worsened during medication overuse
D. One of the following:
   1. Regular intake of ergotamine on ≥10 days per month for >3 months
   2. Regular intake of one or more triptans, in any formulation, on ≥10 days per month for >3 months
   3. Regular intake of Aspirin on ≥15 days per month for >3 months
   4. Regular intake of one or more NSAIDs other than acetylsalicylic acid on ≥15 days per month for >3 months
   5. Regular intake of one or more opioids on ≥10 days per month for >3 months
   6. Regular intake of acetaminophen on ≥15 days per month for >3 months
   7. Regular intake of one or more combination analgesic medications on ≥10 days/month for >3 months
   8. Regular intake of any combination of ergotamine, triptans, simple analgesics, NSAIDs and/ or opioids on ≥10 days per month for >3 months
   9. Regular intake of any combination of ergotamine, triptans, simple analgesics, NSAIDs and/or opioids1 on a total of ≥10 days per month for >3 months without overuse of any single drug or drug class alone
   10. Regular overuse, on ≥10 days per month for >3 months, of one or more medications other than those described above, taken for acute or symptomatic treatment of headache

CLINICAL RATIONALE

Reyvow is indicated for the acute treatment of migraine with or without aura in adults. Reyvow is not indicated for the preventative treatment of migraine. Reyvow is the first approved drug in a new class of medications known as 5-HT_{1F} receptor agonists. Reyvow is a schedule V controlled substance.

Migraine is a chronic disease characterized by episodic attacks of headaches, sensitivity to light and sound (i.e., photophobia and phonophobia), and nausea or vomiting. Migraine often begins at puberty, but it most commonly affects those between 35 years and 45 years of age. Migraine is about twice as common in women than men, which is likely due to hormonal influences. Migraine headache is caused by the activation of the trigeminal sensory pathway that innervate pain-sensitive intracranial structures (e.g., eyes and cerebral blood vessels). The migraine-associated symptoms (e.g., photophobia and phonophobia) are associated with the activation of auditory, visual, and olfactory cortical areas by the trigeminal sensory input. The release of neurotransmitters (e.g., CGRP [calcitonin gene-related peptide], glutamate, nitric oxide) result in cranial vasodilation and mast-cell degranulation, which activates meningeal nociceptors and contributes to migraine headache. Sensitization of neurons by the neurotransmitters in the brain can lower the threshold that triggers a migraine. A similar physiology is seen in latent sensitization by medication-overuse headaches (i.e., after persistent exposure to triptans or opioids), which is associated with increased expression of CGRP and nitric oxide long after discontinuation of the drugs.

In general, a diagnosis of migraine is made based on International Classification of Headache Disorder, 3rd Edition (ICHD-3) criteria and by ruling out differential diagnoses, such as tension-type headache or

intracranial disease. The ICHD-3 further classifies migraine into chronic migraine (CM) and episodic migraine. A diagnosis of CM is based on the presence of ≥ 15 headache days per month, of which ≥ 8 days meet the diagnostic criteria of a migraine headache. Episodic migraine is generally regarded as < 15 headaches days per month.

The American Headache Society (AHS) consensus statement recommends the following for first-line therapy in patients with mild to moderate migraine pain: non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., aspirin, diclofenac, ibuprofen, naproxen), nonopioid analgesics, acetaminophen, or combinations consisting of aspirin, acetaminophen, and caffeine. Triptans (5-HT_1 agonists) and ergotamine derivatives are recommended as initial treatment for acute, moderate to severe migraine or those with mild to moderate migraines who have failed previous first-line agents. The AHS notes that patients should be treated early after the onset of a migraine attack; for severe nausea or vomiting, a non-oral route is appropriate for patients and adjunctive antiemetics (e.g., prochlorperazine suppositories) may be useful; self-administered rescue medications (i.e., injectable, intranasal) should be considered after failing oral treatments; and overuse of acute medications should be avoided. The American Academy of Neurology (AAN) guideline on acute treatment of migraine in adults was published in 2000 and provided similar recommendations to the AHS guidelines.

The AHS consensus statement also states that new/emerging agents for the acute treatment of migraines (i.e., CGRP receptor antagonists Ubrelvy [ubrogepant] and Nurtec ODT [rimegepant], and Reyvow [lasmiditan]) do not result in constriction of blood vessels; these agents should be available for patients who have contraindications to triptan or who have failed at least two oral triptans and continued until at least two attacks are treated to determine efficacy and tolerability.

Patients with migraine should be considered for preventive treatment in any of the following situations: attacks significantly interfere with patients' daily routines despite acute treatment; frequent attacks (≥ 4 migraine headache days); a contraindication to, failure, or overuse of acute treatments; adverse events with acute treatments; or patient preference. Based on these recommendations, patients requiring treatment for more than 4 migraine headache days per month should be evaluated further for preventive treatment.

For prevention of migraine headache, the American Academy of Neurology and the American Headache Society 2012 guideline update recommendations state that the following medications are established as effective and should be offered for migraine prevention: β-adrenergic blocking agents, metoprolol, propranolol, timolol; and antiepileptic drugs (AEDs), divalproex sodium, topiramate, sodium valproate. Additionally, the following medications are probably effective: antidepressants, amitriptyline, venlafaxine; and β-adrenergic blocking agents, atenolol, nadolol and should be considered for migraine prevention. Efficacy and safety of individual agents, even within the same class of drugs, may vary among patients therefore, if the patient fails one preventive medication, others should be tried as failure of one agent does not rule out success with another one. The Institute for Clinical Systems Improvement (ICSI) headache guidelines state that preventive therapy should be considered for all patients, and the American Academy of Neurology (AAN) guidelines recommend preventive medications when there is either an impact on life and acute therapy is not working or where headache frequency can lead to medication overuse headache.[5,6] Therefore, patients with migraine headache requesting additional quantities of Reyvow must be currently taking prophylactic therapy or are unable to take prophylactic therapy due to an inadequate response, intolerance, or contraindication.

Frequent use of acute migraine drugs (e.g. ergotamine, triptans, opioids, or combination of these drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). To decrease the risk of medication-overuse headache ("rebound headache" or "drug-induced headache") many experts limit acute therapy to two headache days per week on a regular basis. More frequent

treatment other than this may result in medication-overuse chronic daily headaches. Therefore, the prescriber must have considered and ruled out the diagnosis of medication overuse headache.

Efficacy

The efficacy of Reyvow in the acute treatment of migraine was demonstrated in two randomized, double-blind, placebo-controlled trials. These studies enrolled patients with a history of migraine with and without aura according to the International Classification of Headache Disorders (ICHD-II) diagnostic criteria. Patients were predominantly female (84%), and White (78%), with a mean age of 42 years (range 18-81). Twenty-two percent of patients were taking preventive medication for migraine at baseline. Study 1 randomized patients to REYVOW 100 mg (n=744), or 200 mg (n=745) or placebo (n=742) and Study 2 randomized patients to REYVOW 50 mg (n=750), 100 mg (n=754), or 200 mg (n=750) or placebo (n=751). Patients were allowed to take a rescue medication 2 hours after taking study drug; however, opioids, barbiturates, triptans, and ergots were not allowed within 24 hours of study drug administration.

The primary efficacy analyses were conducted in patients that treated a migraine with moderate to severe pain within 4 hours of the onset of the attack. The efficacy of Reyvow was established by an effect on pain freedom at 2 hours and Most Bothersome Symptom (MBS) freedom at 2 hours compared to placebo for Studies 1 and 2. Pain freedom was defined as a reduction of moderate or severe headache pain to no pain, and MBS freedom was defined as the absence of the self-identified MBS (photophobia, phonophobia, or nausea). Among patients who selected an MBS, the most commonly selected MBS was photophobia (54%), followed by nausea (24%), and phonophobia (22%). In both studies, the percentage of patients achieving pain freedom and MBS freedom 2 hours after treatment was significantly greater among patients receiving Reyvow at all doses compared to those receiving placebo.

Safety

In clinical trials, Reyvow was associated with central nervous system depression, driving impairment, serotonin syndrome, and medication overuse headache. The most common adverse reactions were dizziness, fatigue, paresthesia, and sedation.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

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POLICY HISTORY

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