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Calcitonin Gene-Related Peptide (CGRP) Antagonist – IL Medicaid

PRODUCTS AFFECTED

Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm), Nurtec ODT (rimegepant), Qulipta (atogepant), Ubrelvy (ubrogepant), Vyepti (eptinezumab-jjmr), Zavzpret (zavegepant)

COVERAGE POLICY

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing orother practice that is inappropriate or excessive.

DIAGNOSIS:
Episodic Migraine, Chronic Migraine, Episodic Cluster Headache

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. EPISODIC MIGRAINE PREVENTION (AIMOVIG, AJOVY, EMGALITY, NURTEC ODT, QULIPTA, AND VYEPTI ONLY):
   1. Prescriber attestation of a diagnosis of episodic migraine
      [Note: Episodic migraine defined as <15 HEADACHE days per month on average across 3 months, >4 and <15 MIGRAINE days per month on average across 3 months, with headaches that are not attributable to another causative disorder].
      AND
   2. FOR QUILIPTA ONLY: Prescriber attestation that member has had a trial and ineffectiveness/failure of TWO generic preventative agents or triptans.
      OR
      FOR OTHER AGENTS: Prescriber attestation that member has had a trial and ineffectiveness/failure after 2 months or clinical intolerance or contraindication to TWO

preventative agents from the following therapeutic classes: beta blockers (propranolol, timolol, atenolol, metoprolol, nadolol), antiepileptics (divalproex sodium, topiramate), antidepressants (amitriptyline, nortriptyline, venlafaxine, duloxetine), antihypertensive (verapamil, lisinopril, candesartan)
AND

3. FOR VYEPTI: Documentation of a trial/failure, intolerance or contraindication to three (3) preferred Calcitonin Gene-Related Peptide Receptor Antagonists (CGRPs).
AND
4. Prescriber attests that requested product is not prescribed concurrently with anotherprophylactic CGRP inhibitor
AND
5. FOR VYEPTI REQUESTS FOR INCREASED DOSING:
    a. Documentation that the lower dosing has been tried for at least one treatment (30 days) and clinical response has not been optimal as defined by 50% reduction in monthly migraine days (MMD). Documentation of follow-up MMD required. [Molina Reviewer: Compare baseline MMD versus follow-up MMD]
    AND
    b. Clinical rationale and documentation supporting therapy with a higher dose, including ALL of the following: Response to therapy as defined by 50% reduction in monthly migraine days has not been attained, however positive response has been documented by at least TWO (2) of the following: reduced severity of headaches and migraines, reduction in acute pharmacological medication, or reduction in monthly acute migraine-specific medication treatment days.
    AND
    c. Member has not experienced ANY of the following: Intolerable adverse effects, unacceptable toxicity from the drug, or poor response to treatment as evidenced by physical findings and/or clinical symptoms

B. CHRONIC MIGRAINE PREVENTION (AIMOVIG, AJOVY, EMGALITY, VYEPTI AND QULIPTA ONLY):

1. Prescriber attestation that member has a diagnosis of chronic migraine.
[NOTE: Chronic migraine is defined as having at least 15 monthly headache days, of which at least 8 of those headache days are migraine days for at least 3 months. Migraine days are defined as: 1. Having a headache with least 2 of the following characteristics: i. unilateral location, ii. pulsating quality, iii. moderate/severe pain intensity and iv. aggravation by or causing avoidance of routine physical activity; AND 2. At least ONE (1) of the following being met: nausea and/or vomiting OR photophobia and phonophobia [for headache with aura] or lasting 4-72 hours [for headache with aura]; OR 3. Headache is treated and relieved by triptan(s) or ergot before the expected development of the above symptoms]
AND
2. Prescriber attestation that member has had a trial and ineffectiveness/failure after 2 months or clinical intolerance or contraindication to TWO preventative agents from the following therapeutic classes: beta blockers (propranolol, timolol, atenolol, metoprolol, nadolol), antiepileptics (divalproex sodium, topiramate), antidepressants (amitriptyline, nortriptyline, venlafaxine, duloxetine), antihypertensive (verapamil, lisinopril, candesartan)
AND
3. Prescriber attests that requested product is not prescribed concurrently with other preventative CGRP inhibitors
AND
4. FOR VYEPTI: Documentation of a trial/failure, intolerance or contraindication to Aimovig and Ajovy.
AND
5. FOR VYEPTI REQUESTS FOR INCREASED DOSING:
    a. Documentation that the lower dosing has been tried for at least one treatment (30 days) and clinical response has not been optimal as defined by 50% reduction in monthly migraine days (MMD). Documentation of follow-up MMD required. [Molina Reviewer:

Compare baseline MMD versus follow-up MMD]
AND

b. Clinical rationale and documentation supporting therapy with a higher dose, including ALL of the following: Response to therapy as defined by 50% reduction in monthly migraine days has not been attained, however positive response has been documented by at least TWO (2) of the following: reduced severity of headaches and migraines, reduction in acute pharmacological medication, or reduction in monthly acute migraine-specific medication treatment days.
AND

c. Member has not experienced ANY of the following: Intolerable adverse effects, unacceptable toxicity from the drug, or poor response to treatment as evidenced by physical findings and/or clinical symptoms

C. ACUTE TREATMENT OF MIGRAINE (UBRELVY, NURTEC ODT, ZAVZPRET ONLY):

1. Prescriber attestation that member has a diagnosis of migraine.
[NOTE: Migraine defined as: 1. Having a headache with least 2 of the following characteristics: i. unilateral location, ii. pulsating quality, iii. moderate/severe pain intensity and iv. aggravation by or causing avoidance of routine physical activity; AND 2. [for migraine without aura] At least ONE (1) of the following being met: nausea and/or vomiting OR photophobia and phonophobia or [for headache with aura] headache lasting 4- 72 hours; OR 3. Headache is treated and relieved by triptan(s) or ergot before the expected development of the above symptoms.]
AND
2. (a) Documentation of trial (30 days) and inadequate response or intolerance to TWO formulary triptan agents up to maximally tolerated doses
OR
(b) Documentation that the member has one of the following cardiovascular or non- coronary vascular contraindications to use of triptans: Ischemic coronary artery disease(CAD) including angina pectoris, history of myocardial infarction, documented silent ischemia, coronary artery vasospasm (including Prinzmetal's angina); OR history of stroke or transient ischemic attack (TIA); OR Peripheral vascular disease; OR Ischemic bowel disease; OR Uncontrolled hypertension.
AND
3. FOR UBRELVY REQUESTS FOR INCREASED QUANTITY: For approval of up to a maximum of 16 tabs per 30 days of any one strength of Ubrelvy [the safety of treating more than 8 migraines in a 30-day period has not been established] the patient must meet the following criteria:
   a. Member has had a previous trial (minimum of 60 days) and an inadequate response (i.e., no change in headache days, no change in severity or duration of migraines) to one of thefollowing formulary daily preventive therapies (AAN/AHA 2012/2015, ICSI 2013): (i) tricyclic antidepressant [such as but not limited to amitriptyline, doxepin]; OR (ii) beta blocker [such as but not limited to metoprolol tartrate, propranolol, timolol, atenolol, nadolol, nebivolol]; OR (ii) calcium channel blocker [such as but not limited to nicardipine, verapamil]; OR (iv) an ACE inhibitor [such as but not limited to lisinopril];OR an angiotensin receptor blocker (ARBs) [such as but not limited to candesartan], OR (v) an alpha-2 agonist [such as but not limited to guanfacine]; OR (vii) an antiepileptic[such as butnot limited to divalproex sodium, sodium valproate, topiramate, carbamazepine, gabapentin]; OR (viii) Other select antidepressants [such as but not limited to venlafaxine];OR (ix) Cyproheptadine (Periactin)
   AND
   b. Documentation is provided to show adherence to prophylactic therapies tried
4. FOR NURTEC ODT, ZAVZPRET ONLY: Documentation of a trial (3 months) and failure of Ubrelvy

D. TREATMENT OF EPISODIC CLUSTER HEADACHE (EMGALITY ONLY):

1. Documented diagnosis of episodic cluster headache supported by a history of ≥ 2 cluster

periods lasting from 7 days to 1 year each (when untreated) and separated by pain-free remission periods of ≥ 3 months.
NOTE: Cluster periods usually last between 2 weeks and 3 months
AND

2. Documentation of trial and failure of the following: verapamil at a dose of 240-480 mg per day, unless contraindicated or clinically significant adverse effects were experienced
AND
3. Prescriber attests that Emgality is not prescribed concurrently with other injectable CGRP inhibitors

CONTINUATION OF THERAPY:

A. FOR EPISODIC OR CHRONIC MIGRAINE PREVENTION:
1. Prescriber attests to member's positive response to treatment.
OR
2. For Vyepti Increased Dosing Requests: Member continues to meet the requirements for additional quantity limits requested (see initial criteria)

B. ACUTE TREATMENT OF MIGRAINE:
1. Prescriber attests to member's positive response to treatment
AND
2. IF HIGHER UBRELVY QUANTITIES ARE NEEDED: Member continues to meet the requirements for additional quantity limits requested (see initial criteria)

C. EPISODIC CLUSTER HEADACHES:
1. Documentation that member has experienced a reduction in cluster headache attack frequency
AND
2. Prescriber attests that the member had not experienced any intolerable adverse effects or drug toxicity
AND
3. Prescriber attests that the member's cluster period is lasting longer than 3 months and that the prescriber has reviewed for continued medical necessity OR documentation provided shows member has had pain-free remission periods of three months since member last received Emgality therapy

DURATION OF APPROVAL:

Episodic, chronic, or acute migraine: Initial authorization: 12 months, Continuation of therapy: 12 months
Episodic Cluster Headache: Initial authorization: up to 3 months or until the length of typical cluster period for member, Continuation of therapy: 3 months

PRESCRIBER REQUIREMENTS:

Vyepti Only: Prescribed by, or in consultation with, a board-certified neurologist, headache specialist, UCNS certified specialists,* or pain specialist. Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.
*The United Council for Neurologic Subspecialties (UCNS) is an organization that provides accreditation to fellowship programs and certification to individual practitioners in neurologic subspecialties, including headache medicine. "UCNS certified" headache specialists may be neurologists or other type of physicians with expertise in the treatment of headache disorders.

AGE RESTRICTIONS:

18 years of age or older

QUANTITY:

Aimovig: 70 mg subcutaneously (SC) once monthly: 1 autoinjector per 30 days
140 mg injected SC once monthly: one-140mg autoinjector/prefilled syringes per 30 days

Ajovy: 225mg (1) per 28 days OR 675mg (3) per 90 days

Emgality (migraine prevention): Loading dose: 240mg (two-120mg injections), maintenance dose 120mg (1) once monthly
Emgality (cluster headache): 300mg (three-100mg injections) once monthly at onset of cluster period then monthly until the end of the cluster period

Vyepti: 100mg IV every 3 months; some patients may benefit from a dosage of 300mg [NOTE: Criteria for higher dosing must be met]

Nurtec ODT: 8 tablets per 30 days (acute treatment) or 16 tablets per 30 days (prevention)

Qulipta:
EPISODIC MIGRAINE prophylaxis: 10mg OR 30mg OR 60mg tablets once daily – maximum of 30 tablets of any one strength per 30 days
CHRONIC MIGRAINE prophylaxis: 60 mg once daily, maximum 30 tablets per 30 days

Ubrelvy: up to 200mg within 24 hours, limit of 10 tablets of either strength per 30 days; limited to 50 tablets annually; may authorize up to 16 tablets of either strength per month only if exception criteria have been met.

Zavzpret: 1 carton (6 x 10mg single dose nasal sprays) for 30 days

PLACE OF ADMINISTRATION:
Ubrelvy (ubrogepant), Nurtec ODT (rimegepant), Qulipta (atogepant)
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), Emgality (galcanezumab-gnlm)
The recommendation is that subcutaneous injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

Vyepti (eptinezumab-jjmr)
The recommendation is that infused medications (Vyepti) in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Zavzpret (zavegepant)
The recommendation is that intranasal medications in this policy will be for pharmacy benefit coverage and patient self-administered.

Note: Site of Care Utilization Management Policy applies for Vyepti (eptinezumab-jjmr). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral, Subcutaneous, Intravenous, Intranasal

DRUG CLASS:
Calcitonin Gene-Related Peptide (CGRP) antagonist, CGRP Receptor Antagonists – Monoclonal Antibodies

FDA-APPROVED USES:

AIMOVIG is indicated for the preventive treatment of migraine in adults

AJOVY is indicated for the preventive treatment of migraine in adults

EMGALITY is indicated for preventive treatment of migraine and the treatment of episodic cluster headache

NURTEC ODT is indicated for the acute treatment of migraine with or without aura in adults and for preventive treatment of episodic migraine in adults

QULIPTA is indicated for the preventive treatment of migraine in adults

UBRELVY is indicated for the acute treatment of migraine with or without aura in adults.

VYEPTI is indicated for the preventive treatment of migraine in adults

ZAVZPRET is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of use: Zavzpret is not indicated for the preventive treatment of migraine.

COMPENDIAL APPROVED OFF-LABELED USES:
NONE

APPENDIX

1.2 Migraine with aura

Previously used terms:

Classic or classical migraine; ophthalmic, hemiparaesthetic, hemiplegic or aphasic migraine; migraine accompagnée; complicated migraine.

Description:

Recurrent attacks, lasting minutes, of unilateral fully-reversible visual, sensory or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.

Diagnostic criteria:

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[1]
4. at least one aura symptom is unilateral[2]
5. at least one aura symptom is positive[3]
6. the aura is accompanied, or followed within 60 minutes, by headache

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

Appendix 1: International Headache Society Criteria for Migraine Diagnosis (ICHD-3)

Migraine without aura	Migraine with aura
A. At least five attacks fulfilling criteria B–D B. Headache attacks lasting 4-72 hours (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.	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 D. Not better accounted for by another ICHD-3 diagnosis

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Types of Migraine

- Episodic migraine (EM) is characterized by 0 to 14 headache-days per month; represents 90% of migraineurs.
- Chronic migraine (CM) is characterized by 15 or more headache-days per month; represents 10% of migraineurs.
- Cluster headaches (CH) are recurrent, severe headaches on one side of the head, typically around the eye. The duration of a typical CH attack ranges from about 15 to 180 minutes. Most untreated attacks (about 75%) last less than 60 minutes. Attacks occur every day for weeks, or even months, then disappear for up to a year. Approximately 80% of cluster patients are male, most between the ages of 20 and 50 years. A rare form of migraine, CH affects 0.1% of adults, with 80% of CH patients in the episodic category, and only 20% in the chronic category. Nurtec is not approved for cluster headaches.

Ubrelvy is the first approved oral calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine with or without aura in adults. Unlike the large molecule injectable CGRPs approved for the prevention of migraines, Ubrelvy is a small molecule CGRP antagonist that passes through the blood brain barrier to stop a migraine in progress.

Ubrelvy also does not have the cardiovascular concerns associated with other usual acute migraine treatments such as triptans.

The efficacy of Ubrelvy for the acute treatment of migraine was demonstrated in two Phase 3 randomized, double-blind, placebo-controlled trials, Study 1 (ACHIEVE I/NCT02828020) and Study2 (ACHIEVE II/NCT02867709). Study 1 randomized patients to placebo (n=559) or Ubrelvy 50 mg (n=556) or 100 mg (n=557), and Study 2 randomized patients to placebo (n=563) or Ubrelvy 50 mg(n=562). In all studies, patients were instructed to treat a migraine with moderate to severe headache pain intensity. A second dose of study medication (Ubrelvy or placebo), or the patient's usual acute treatment for migraine, was allowed between 2 and 48 hours after the initial treatment for a non-responding or recurrent migraine headache. Up to 23% of patients were taking preventive medications for migraine at baseline. None of these patients was on concomitant preventive medication that acts on the CGRP pathway. The primary efficacy analyses were conducted in patients who treated a migraine with moderate to severe pain.
The efficacy of Ubrelvy in Studies 1 and 2 was established by measurement compared to placebo:

- Effect on pain freedom at 2 hours post-dose
- Freedom from most bothersome symptom (MBS) at 2 hours post-dose

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 (i.e., photophobia, phonophobia, or nausea). In both studies, the percentage of patients achieving headache pain freedom and MBS freedom 2 hours post-dose was significantly greater among patients receiving Ubrelvy compared to those receiving placebo. In Study 1, the results found nearly twice as many patients were pain-free in the high-dosage treatment group after 2 hours as in the placebo group: 21.2% compared with 11.8%. The low-dose 50 mg group results in both studies were lower, but not far behind the high-dose 100 mg results.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of (CGRP) Antagonists are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to **Aimovig** (erenumab-aooe) include: patients with serious hypersensitivity to erenumab-aooe or to any of the excipients. Contraindications to **Emgality** (galcanezumab-gnlm) include: patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients. Contraindications to **Ajovy** (fremanezumab-vfrm) include: patients with serious hypersensitivity to fremanezumab-vfrm or to any of the excipients. Contraindications to **Vyepti** (eptinezumab-jjmr) include patients with serious hypersensitivity to eptinezumab-jjmr or to any of the excipients. Contraindications to **Nurtec** (Rimegepant) include: Patients with a history of hypersensitivity reaction to rimegepant, Nurtec ODT, or to any of its components. Contraindications to **Ubrelvy** (ubrogepant) include: Concomitant use with strong CYP3A4 inhibitors (i.e., ketoconazole, itraconazole, clarithromycin), patients with a history of serious hypersensitivity to ubrogepant or any component of Ubrelvy. Contraindications to **Qulipta** (atogepant) include: Patients with a history of hypersensitivity to atogepant or to any of the components of Qulipta, for Chronic Migraine treatment only: avoid concomitant use of strong CYP3A4 inhibitors, avoid concomitant use of strong, moderate, or weak CYP3A4 inducers, severe renal impairment and end stage renal disease (CrCl < 30 mL/min). Contraindications to **Zavzpret** (zavegepant) nasal spray include: patients with a history of hypersensitivity reaction to zavegepant or to any of the components of Zavzpret, patients with severe hepatic impairment (Child-Pugh class C), patients with CrCl < 30 mL/min.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3032	Injection, eptinezumab-jjmr, 1 mg

AVAILABLE DOSAGE FORMS:

Aimovig SOAJ 140MG/ML
Aimovig SOAJ 70MG/ML
Aimovig (140 MG Dose) SOAJ 70MG/ML
Ajovy SOAJ 225MG/1.5ML
Ajovy SOSY 225MG/1.5ML
Emgality SOAJ 120MG/ML
Emgality SOSY 120MG/ML
Emgality (300 MG Dose) SOSY 100MG/ML
Nurtec TBDP 75MG
Qulipta TABS 10MG
Qulipta TABS 30MG
Qulipta TABS 60MG
Ubrelvy TABS 100MG
Ubrelvy TABS 50MG
Vyepti SOLN 100MG/ML
Zavzpret SPR 10mg (1 carton of 6 nasal sprays)

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SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q4/2022
Annual Review Completed – updated references	4/2023
Updates based on stipulated language changes	7/2023
Updated Qulipta indications	8/2023
Added information for Zavzpret	10/2023