BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.70.077

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	January 20, 2020
Subject:	Migraine CGRP Antagonists Oral	**Page:**	1 of 12

Last Review Date: December 8, 2023

Migraine Calcitonin Gene-Related Peptide (CGRP) Antagonists Oral

Description

Nurtec ODT (rimegepant), Qulipta (atogepant), Ubrelvy* (ubrogepant)

*Prior authorization for this product applies only to formulary exceptions due to being a non-covered medication

Background
Nurtec ODT (rimegepant), Qulipta (atogepant), and Ubrelvy (ubrogepant) are calcitonin gene-related peptide receptor (CGRP) antagonists. CGRP is a neuropeptide widely distributed in the nervous system, particularly at anatomical areas thought to be involved with migraine, including the trigeminovascular nociceptive system. In studies, CGRP has been shown to be released during severe migraine attacks. CGRP mechanism blockade either by small molecule receptor antagonists or by monoclonal antibodies can have an abortive or preventive effect in migraine (1-4).

Regulatory Status
FDA-approved indications: (1-3)

- Nurtec ODT and Ubrelvy are indicated for the acute treatment of migraine with or without aura in adults.
- Nurtec ODT is also indicated for the preventative treatment of episodic migraine in adults.
- Qulipta is indicated for the preventative treatment of migraine in adults.

Limitations of Use: Ubrelvy is not indicated for the preventative treatment of migraine (1).

The recommended dose of Nurtec ODT for acute treatment is 75 mg taken orally, as needed. The maximum dose in a 24-hour period is 75 mg. The safety of using more than 18 doses in a 30-day period has not been established. The recommended dose of Nurtec ODT for preventative treatment is 75 mg taken orally every other day (3).

The recommended dosage of Qulipta for episodic migraine is 10 mg, 30 mg, or 60 mg taken orally once daily. The recommended dosage of Qulipta for chronic migraine is 60 mg taken once daily (2).

The recommended dose of Ubrelvy is 50 mg or 100 mg taken orally, as needed. If needed, a second dose may be administered at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established (1).

The American Academy of Neurology and the American Headache Society Position Statement recommends giving at least 2 conventional oral migraine preventive treatments an adequate trial of at least 6 weeks at a target or usual effective dose prior to initiating preventive therapy with a CGRP medication (5).

The safety and effectiveness of Nurtec ODT, Qulipta, and Ubrelvy in pediatric patients less than 18 years of age have not been established (1-3).

Related policies

5-HT1 Agonists, Butalbital analgesics, Dihydroergotamine Nasal Sprays, Elyxyb, Maxalt, Migraine CGRP Antagonists IV, Migraine CGRP Antagonists Nasal, Migraine CGRP Antagonists SC, Migraine Powders

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Nurtec ODT, **Qulipta**, and **Ubrelvy** may be considered **medically necessary** if the conditions indicated below are met.

Nurtec ODT, **Qulipta**, and **Ubrelvy** may be considered **investigational** for all other indications.

Prior-Approval Requirements

Nurtec ODT

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Preventive treatment of episodic migraine **AND ALL** of the following:
    a. Patient has **ONE** of the following:
        i. Patient has taken a preventative CGRP medication in the past or is switching from another preventative CGRP medication
        ii. Patient has had an inadequate treatment response, intolerance, or contraindication to at least **TWO** of the following prophylactic agents:
            a) Divalproex sodium/valproate sodium (Depakote, Depakote ER)
            b) Topiramate (Topamax)
            c) Tricyclic antidepressants: amitriptyline (Elavil), nortriptyline (Pamelor)
            d) Serotonin-norepinephrine reuptake inhibitors: venlafaxine (Effexor XR), duloxetine (Cymbalta)
            e) Beta-blockers: atenolol, metoprolol, nadolol, propranolol, timolol
    b. Patient has **ONE** of the following:
        i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
        ii. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
            a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
            b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

2. Acute treatment of migraine with or without aura **AND ALL** of the following:
    a. Patient has completed an adequate 3-month trial **OR** patient has an intolerance or contraindication to at least **TWO** Triptan Agents
    b. **NO** dual therapy with Triptan Agents at Prior Authorization quantities

c. Patient has **ONE** of the following:
   i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
   ii. Dual therapy with a preventative CGRP antagonist if **ONE** of the following applies:
      a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
      b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Qulipta

Age 18 years of age or older

Diagnosis

Patient must have the following:

Migraine

AND ALL of the following:
a. Used for the prevention of migraines
b. Patient has **ONE** of the following:
   i. Patient has taken a preventative CGRP medication in the past or is switching from another preventative CGRP medication
   ii. Patient has had an inadequate treatment response, intolerance, or contraindication to at least **TWO** of the following prophylactic agents:
      a) Divalproex sodium/valproate sodium (Depakote, Depakote ER)
      b) Topiramate (Topamax)
      c) Tricyclic antidepressants: amitriptyline (Elavil), nortriptyline (Pamelor)
      d) Serotonin-norepinephrine reuptake inhibitors: venlafaxine (Effexor XR), duloxetine (Cymbalta)
      e) Beta-blockers: atenolol, metoprolol, nadolol, propranolol, timolol

c. Patient has **ONE** of the following:
    i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
    ii. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
        a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
        b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Ubrelvy *Prior authorization for Ubrelvy applies only to formulary exceptions due to being a non-covered medication*

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Acute treatment of migraine with or without aura **AND ALL** of the following:
    a. **NOT** used for the prevention of migraines
    b. Patient has completed an adequate 3-month trial **OR** patient has an intolerance or contraindication to at least **TWO** Triptan Agents
    c. **NO** dual therapy with Triptan Agents at Prior Authorization quantities
    d. Patient has **ONE** of the following:
        i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
        ii. Dual therapy with a preventative CGRP antagonist if **ONE** of the following applies:
            a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
            b) Patient has completed an adequate 3-month trial **of** a preventative CGRP antagonist in combination with a triptan agent

Prior–Approval *Renewal* Requirements

Nurtec ODT

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Preventive treatment of episodic migraine **AND ALL** of the following:
    a. Documented decrease in migraine days from baseline **OR** improvement in daily activities due to the reduction of debilitating migraine
    b. Patient has **ONE** of the following:
        i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
        ii. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
            a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
            b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent
2. Acute treatment of migraine with or without aura **AND ALL** of the following:
    a. **NO** dual therapy with Triptan Agents at Prior Authorization quantities
    b. Patient has **ONE** of the following:
        i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
        ii. Dual therapy with a preventative CGRP antagonist if **ONE** of the following applies:
            a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
            b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Qulipta

Age 18 years of age or older

Diagnosis

Patient must have the following:

Migraine

AND ALL of the following:

1. Used for the prevention of migraine
2. Documented decrease in migraine days from baseline **OR** improvement in daily activities due to the reduction of debilitating migraine
3. Patient has **ONE** of the following:
    a. **NO** dual therapy with another CGRP antagonist (see Appendix 1)
    b. Dual therapy with a CGRP antagonist for acute treatment of migraine if **ONE** of the following applies:
        i. Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
        ii. Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Ubrelvy *Prior authorization for Ubrelvy applies only to formulary exceptions due to being a non-covered medication*

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Acute treatment of migraine with or without aura **AND ALL** of the following:
    a. **NOT** used for the prevention of migraines
    b. **NO** dual therapy with Triptan Agents at Prior Authorization quantities
    c. Patient has **ONE** of the following:
        i. **NO** dual therapy with another CGRP antagonist (see Appendix 1)

ii. Dual therapy with a preventative CGRP antagonist if **ONE** of the following applies:
   a) Patient has completed an adequate 3-month trial of at least 2 preventative CGRP antagonists (i.e., Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta, and Vyepti)
   b) Patient has completed an adequate 3-month trial of a preventative CGRP antagonist in combination with a triptan agent

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity

Medication/Strength	Diagnosis	Quantity
Nurtec ODT 75 mg	Preventative treatment	48 tablets per 90 days **OR**
Nurtec ODT 75 mg	Acute treatment	56 tablets per 90 days **OR**
Qulipta 10 mg, 30 mg, 60 mg	Preventative treatment	90 tablets per 90 days **OR**

Medication/Strength ***with Approved Formulary Exception (FE) Only***	Diagnosis	Quantity
Ubrelvy 50 mg tablets	Acute treatment	96 tablets per 90 days **OR**
Ubrelvy 100 mg tablets	Acute treatment	48 tablets per 90 days

Duration 6 months

Prior–Approval *Renewal* Limits

Quantity

Medication/Strength	Diagnosis	Quantity
Nurtec ODT 75 mg	Preventative treatment	48 tablets per 90 days **OR**
Nurtec ODT 75 mg	Acute treatment	56 tablets per 90 days **OR**
Qulipta 10 mg, 30 mg, 60 mg	Preventative treatment	90 tablets per 90 days **OR**

Medication/Strength ***with Approved Formulary Exception (FE) Only***	Diagnosis	Quantity
Ubrelvy 50 mg tablets	Acute treatment	96 tablets per 90 days **OR**
Ubrelvy 100 mg tablets	Acute treatment	48 tablets per 90 days

Duration 12 months

Rationale

Summary

Nurtec ODT (rimegepant), Qulipta (atogepant), and Ubrelvy (ubrogepant) are calcitonin gene-related peptide receptor (CGRP) antagonists. CGRP is a neuropeptide widely distributed in the nervous system, particularly at anatomical areas thought to be involved with migraine, including the trigeminovascular nociceptive system. In studies, CGRP has been shown to be released during severe migraine attacks. CGRP mechanism blockade either by small molecule receptor antagonists or by monoclonal antibodies can have an abortive or preventive effect in migraine. Nurtec ODT and Ubrelvy are indicated for the acute treatment of migraine with or without aura in adults. Nurtec ODT is indicated for the preventative treatment of episodic migraine in adults, while Qulipta is indicated for the preventative treatment of migraine in adults. The safety and effectiveness of Nurtec ODT, Qulipta, and Ubrelvy in pediatric patients less than 18 years of age have not been established (1-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of CGRP antagonists oral while maintaining optimal therapeutic outcomes.

References

1. Ubrelvy [package insert]. Madison, NJ: Allergan USA, Inc.; March 2021.
2. Qulipta [package insert]. Dublin, Ireland. Forest Laboratories Ireland Ltd.; April 2023.

3. Nurtec ODT [package insert]. New Haven, CT: Biohaven Pharmaceuticals Inc.; April 2022.
4. Karsan N, Goadsby PJ. “Calcitonin gene-related peptide and migraine.” Curr Opin Neurol. 2015 Jun;28(3):250-4.
5. (2019), The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice. Headache: The Journal of Head and Face Pain, 59: 1-18. https://doi.org/10.1111/head.13456

Policy History

Date	Action
January 2020	Addition to PA
March 2020	Annual review. Addition of Nurtec ODT and renamed policy Migraine CGRP Antagonists Oral
April 2020	Addition of requirement of no dual therapy with another CGRP antagonist per FEP
June 2020	Annual review and reference update
June 2021	Annual review and reference update
July 2021	Added indication for Nurtec ODT: prevention of migraines. Increased quantity limit for acute treatment with Nurtec ODT to 18 days per 30-day period per package insert.
September 2021	Annual review
March 2022	Annual review and reference update. Addition of Qulipta to policy. Per SME, removed renewal requirement of “no dual therapy with Triptan Agents at PA quantities” for prophylactic treatment and removed requirement of “no dual therapy with Botox for migraine prevention”
January 2023	Prevention of migraines indication: removed the failure of triptans requirement and increased the failure of oral prophylaxis from 1 to 2 agents, per SME. Added nortriptyline and duloxetine to the list of t/f options per AAN/AHS guidelines. Per FEP, added initiation option for patients to have taken a preventative CGRP in the past or switching from another preventative CGRP in order to bypass the t/f of prophylactics. Changed policy number to 5.70.077
March 2023	Annual review and reference update
April 2023	Per PI update, removed “episodic” migraine requirement for Qulipta
June 2023	Annual review
September 2023	Annual review

October 2023	Per FEP, revised criteria to allow dual therapy between CGRP antagonists if patient is using one preventative and one acute treatment together after an adequate trial and failure of other CGRPs and triptans either alone or in combination
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.

Appendix 1 - List of CGRP Antagonists

Generic Name	Brand Name
atogepant	Qulipta
eptinezumab-jjmr	Vyepti
erenumab-aooe	Aimovig
fremanezumab-vfrm	Ajovy
galcanezumab-gnlm	Emgality
rimegepant	Nurtec ODT
ubrogepant	Ubrelvy
zavegepant	Zavzpret