

## PHARMACY POLICY – 5.01.503

## Migraine and Cluster Headache Medications

Effective Date: May 1, 2025

Last Revised: Apr. 8, 2025


Replaces: N/A

RELATED MEDICAL POLICIES:

5.01.584 CGRP Inhibitors for Migraine Prophylaxis

Select a hyperlink below to be directed to that section.

[POLICY CRITERIA](#) | [CODING](#) | [RELATED INFORMATION](#)  
[EVIDENCE REVIEW](#) | [REFERENCES](#) | [APPENDIX](#) | [HISTORY](#)

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## Introduction

There are many different types of headaches. Tension headaches are the most common form and can be treated with over-the-counter pain relievers, like aspirin or ibuprofen. Migraine and cluster headaches are more severe and may need prescription medication.

Migraine is a debilitating disease, with severe headaches. Some people have other symptoms like seeing auras, experiencing nausea or vomiting, and suffering an inability to tolerate bright light or loud noises. About one in eight Americans has migraines. It's the seventh most disabling disease worldwide. Women are twice as likely as men to suffer from migraine.

Some people have just a few headaches a month. These may be treated with pills like ibuprofen or prescription medications like sumatriptan. These treatments stop the headaches after they've started. However, if people take too much of the headache-stopping medications, over time they may end up with more headaches. This is poor long-term strategy.

Cluster headaches are severe headaches that come on quickly, last 30 to 90 minutes, go away, and then come back a little while later. They are different from migraine headaches. Individuals with cluster headaches may need a different approach to treatment, though using many of the same drugs.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can

be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

**Note:** The medications addressed in this policy may be considered medically necessary for the FDA-approved ages.

Drug	Medical Necessity
<b>Generic triptans:</b> <ul style="list-style-type: none"><li>• Almotriptan (oral)</li><li>• Eletriptan (oral)</li><li>• Frovatriptan (oral)</li><li>• Rizatriptan (oral)</li><li>• Sumatriptan (oral; nasal spray; inj.)</li><li>• Zolmitriptan (oral; nasal spray)</li></ul>	<p><b>Generic triptan medications may be considered medically necessary for the acute treatment of migraine and cluster headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"><li>• The quantity dispensed does not exceed:<ul style="list-style-type: none"><li>○ 18 tablets per 30 days</li><li>○ 8 injections per 30 days</li><li>○ 18 nasal sprays per 30 days</li></ul></li></ul> <p><b>Additional quantities of generic triptan medications may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"><li>• The individual has failed a trial of a different triptan prior to dose escalation</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• The prescription is for less than 30 doses per 30 days</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Doses are not exceeding FDA labeled maximum daily doses</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• The individual is not experiencing medication overuse headache(s)</li></ul> <p><b>AND</b></p> <ul style="list-style-type: none"><li>• Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li></ul>

Drug	Medical Necessity
	<p><b>Additional quantities of generic triptan medications may be considered medically necessary for the acute treatment of cluster headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual has unsuccessfully tried at least three categories of other abortive cluster headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic cluster headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The prescription is for less than 30 doses per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The individual is not experiencing medication overuse headache(s)</li> </ul>
<p><b>Brand name triptans:</b></p> <ul style="list-style-type: none"> <li>Amerge (naratriptan; oral)</li> <li>Frova (frovatriptan; oral)</li> <li>Imitrex (sumatriptan; oral, nasal spray, inj.)</li> <li>Maxalt (rizatriptan; oral)</li> <li>Maxalt MLT (rizatriptan oral)</li> <li>Onzetra Xsail (sumatriptan; nasal powder)</li> <li>Relpax (eletriptan; oral)</li> <li>RizaFilm (rizatriptan; oral film)</li> <li>Tosymra (sumatriptan; nasal spray)</li> <li>Zembrace SymTouch (sumatriptan; inj.)</li> </ul>	<p><b>Brand name triptan medications may be considered medically necessary when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual requires acute treatment of migraines or cluster headaches</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The quantity dispensed does not exceed: <ul style="list-style-type: none"> <li>18 tablets per 30 days</li> <li>8 injections per 30 days</li> <li>18 nasal sprays per 30 days</li> <li>8 nasal powder inhalations per 30 days</li> <li>18 oral films per 30 days</li> </ul> </li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The individual has had a trial and failure of at least two different generic triptan products in any dosage form (i.e., oral, injectable, or nasal spray)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>If the requested medication is for Amerge, Frova, Imitrex, Maxalt, Relpax, or Zomig, one of the required generic trials must be the generic version of the brand name medication that is being requested</li> </ul>

Drug	Medical Necessity
<ul style="list-style-type: none"> <li><b>Zomig (zolmitriptan; oral, nasal spray)</b></li> </ul>	<p><b>Additional quantities of brand name triptan medications may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The prescription is for less than 30 doses per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The individual is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>Additional quantities of brand name triptan medications may be considered medically necessary for the acute treatment of cluster headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual has unsuccessfully tried at least three categories of other abortive cluster headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic cluster headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The prescription is for less than 30 doses per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The individual is not experiencing medication overuse headache(s)</li> </ul>



Drug	Medical Necessity
<b>Symbravo (rizatriptan/meloxicam)</b>	<p><b>Symbravo (rizatriptan/meloxicam) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Quantity prescribed does not exceed 18 tablets per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has failed a trial of generic rizatriptan in combination with two generic NSAIDs</li> </ul> <p><b>Additional quantities of Symbravo (rizatriptan/meloxicam) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has failed a trial of generic rizatriptan in combination with two generic NSAIDs</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The prescription is for less than 30 doses per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Doses are not exceeding FDA labeled maximum daily doses</li> </ul>
<b>Generic sumatriptan/naproxen, Treximet (sumatriptan/naproxen)</b>	<p><b>Generic sumatriptan/naproxen and brand Treximet (sumatriptan/naproxen) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• Quantity prescribed does not exceed 18 tablets per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The individual is aged 12 years or older</li> </ul> <p><b>AND</b></p>



Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>Has failed a trial of generic sumatriptan in combination with two generic NSAIDs, one of which MUST be generic naproxen.</li> </ul> <p><b>Additional quantities of generic sumatriptan/naproxen and brand Treximet (sumatriptan/naproxen) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 12 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has failed a trial of generic sumatriptan in combination with two generic NSAIDs, one of which MUST be generic naproxen.</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The prescription is for less than 30 doses per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul>
<p><b>Elyxyb (celecoxib oral solution)</b></p> <p><b>NSAID</b></p>	<p><b>Elyxyb (celecoxib oral solution) may be considered medically necessary for the acute treatment of migraine with or without aura when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 NSAID medication during previous migraine episode/s</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 2 triptan medications during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p>



Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>The quantity does not exceed 18 bottles (120 mg/4.8 mL per bottle) per 30 days</li> </ul> <p><b>Additional quantities of Elyxyb (celecoxib oral solution) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 NSAID medication during previous migraine episode/s</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 2 triptan medications during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul>
<ul style="list-style-type: none"> <li>Generic dihydroergotamine nasal spray</li> <li>Ergomar (ergotamine) oral</li> <li>Migranal (dihydroergotamine) nasal spray</li> <li>Trudhesa (dihydroergotamine) nasal spray</li> </ul> <p><b>Ergot Derivative</b></p>	<p><b>Generic dihydroergotamine may be considered medically necessary in quantities not exceeding 8 ampules per 30 days for the acute treatment of migraine.</b></p> <p><b>Migranal (dihydroergotamine) may be considered medically necessary when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual requires acute treatment of migraines</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The quantity dispensed does not exceed 8 ampules per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The individual has had a trial and failure of at least two different generic triptan products in any dosage form (i.e., oral, injectable, or nasal spray)</li> </ul>

Drug	Medical Necessity
	<p><b>Ergomar (ergotamine) may be considered medically necessary when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual requires acute treatment of migraines</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The quantity dispensed does not exceed 18 oral films per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The individual has had a trial and failure of at least two different generic triptan products in any dosage form (i.e., oral, injectable, or nasal spray)</li> </ul> <p><b>Trudhesa (dihydroergotamine) may be considered medically necessary when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual requires acute treatment of migraines</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The quantity dispensed does not exceed 18 nasal sprays per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The individual has had a trial and failure of at least two different generic triptan products in any dosage form (i.e., oral, injectable, or nasal spray)</li> </ul> <p><b>Additional quantities of generic dihydroergotamine, Ergomar (ergotamine), Migranal (dihydroergotamine), and Trudhesa (dihydroergotamine) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• Doses are not exceeding FDA labeled maximum daily doses</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The individual has had a trial and failure of at least two different generic triptan products in any dosage form (i.e., oral, injectable, or nasal spray)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p>





Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul>
<p><b>Nurtec ODT (rimegepant)</b></p> <p><b>CGRP Inhibitor</b></p>	<p><b>Nurtec ODT (rimegepant) may be considered medically necessary in quantities not exceeding 8 tablets per 30 days for the acute treatment of migraine with or without aura when the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Nurtec ODT (rimegepant) is not used concurrently with Ubrelvy (ubrogepant) or Zavzpret (zavegepant) for the acute treatment of migraine</li> </ul> <p><b>Additional quantities of Nurtec ODT (rimegepant) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least two categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The quantity prescribed is less than or equal to 16 tablets per 30 days</li> </ul> <p><b>AND</b></p>

Drug	Medical Necessity
	<ul style="list-style-type: none"> <li>Nurtec ODT (rimegepant) is not used concurrently with Ubrelvy (ubrogepant), or Zavzpret (zavegepant) for the acute treatment of migraine</li> </ul> <p><b>Note:</b> Please see Policy 5.01.584 CGRP Inhibitors for Migraine Prophylaxis when Nurtec ODT (rimegepant) is being requested for the preventive treatment of episodic migraine.</p>
<p><b>Reyvow (lasmiditan)</b></p> <p><b>Serotonin (5-HT) 1F receptor agonist</b></p>	<p><b>Reyvow (lasmiditan) may be considered medically necessary in quantities not exceeding 8 tablets per 30 days for the acute treatment of migraine with or without aura when the following conditions are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medications during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>Additional quantities of Reyvow (lasmiditan) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medications during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Is not experiencing medication overuse headache(s)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The quantity prescribed is less than or equal to 16 tablets per 30 days</li> </ul>

Drug	Medical Necessity
	<p><b>AND</b></p> <ul style="list-style-type: none"> <li>Doses are not exceeding FDA labeled maximum daily doses</li> </ul>
<p><b>Ubrelvy (ubrogepant)</b></p> <p><b>CGRP Inhibitor</b></p>	<p><b>Ubrelvy (ubrogepant) may be considered medically necessary in quantities not exceeding 10 tablets per 30 days for the acute treatment of migraine with or without aura when the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Ubrelvy (ubrogepant) is not used concurrently with Nurtec ODT (rimegepant), or Zavzpret (zavegepant) for the acute treatment of migraine</li> </ul> <p><b>Additional quantities of Ubrelvy (ubrogepant) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Has unsuccessfully tried at least two categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>The quantity prescribed is less than or equal to 16 tablets per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Ubrelvy (ubrogepant) is not used concurrently with Nurtec ODT (rimegepant), or Zavzpret (zavegepant) for the acute treatment of migraine</li> </ul>

Drug	Medical Necessity
<b>Zavzpret (zavegepant)</b>  <b>CGRP Inhibitor</b>	<p><b>Zavzpret (zavegepant) may be considered medically necessary for the acute treatment of migraine with or without aura when the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>• Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Zavzpret (zavegepant) is not used concurrently with Nurtec ODT (rimegepant) or Ubrelvy (ubrogepant) for the acute treatment of migraine</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Quantities do not exceed 8 sprays per 30 days</li> </ul> <p><b>Additional quantities of Zavzpret (zavegepant) may be considered medically necessary for the acute treatment of migraine headaches when all the following criteria are met:</b></p> <ul style="list-style-type: none"> <li>• The individual is aged 18 years or older</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has had inadequate response from greater than or equal to 1 triptan medication during previous migraine episode/s</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>• Has a contraindication to triptans</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has unsuccessfully tried at least two categories of prophylactic migraine headache therapies listed in the <a href="#">Appendix</a> section (unless contraindicated)</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The quantity prescribed is less than or equal to 16 sprays per 30 days</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Zavzpret (zavegepant) is not used concurrently with Nurtec ODT (rimegepant) or Ubrelvy (ubrogepant) for the acute treatment of migraine</li> </ul>

Drug	Not Medically Necessary
As listed	All other uses of the medications listed in this policy are considered not medically necessary.

Drug	Investigational
As listed	The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.

Length of Approval	
Approval	Criteria
Initial authorization	Non-formulary exception reviews and all other reviews for drugs listed in policy may be approved up to 12 months.
Re-authorization criteria	Non-formulary exception reviews and all other reviews for drugs listed in policy may be approved up to 12 months as long as the drug-specific coverage criteria are met, and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.

Documentation Requirements
<p>The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:</p> <ul style="list-style-type: none"> <li>Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history</li> </ul>

## Coding

N/A

## Related Information

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### Benefit Application

This policy is managed through the pharmacy benefit.

The limitation of migraine headache therapies in a rolling 30-day period is in conformance to member contracts, which state quantities may be limited based on medical necessity. Exceptions to pharmacy prior authorization duration/quantity limitations will be made on a case-by-case basis after review of individual medical records.

This policy is applicable to enrollees who are managed by the Company's Pharmacy Formulary. It does not apply to enrollees managed under the Express Scripts Formulary.

## Evidence Review

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### Description

Migraine headache is a common disorder seen in clinical practice. According to the U.S. National Center for Health Statistics, the overall age-adjusted 3-month prevalence of migraine is 19.1% in women and 9.0% in men in the United States, almost half of whom are undiagnosed or undertreated. Most headaches are caused by the primary headache disorders, which include migraine, cluster, and tension-type headaches. Secondary headaches, which are those with underlying pathologic causes, are far less common. Migraine is a chronic condition with recurrent acute attacks whose characteristics vary among individuals and often even among attacks within a single individual. Migraine is a syndrome with a wide variety of neurologic and non-neurologic manifestations. The International Headache Society has developed diagnostic criteria for migraine with and without aura. Clinicians should bear in mind that an individual may suffer from headaches arising from multiple etiologies. Most recently, attention has been focused on possible confusion between sinus headache and migraine, which often mimics sinus symptoms (congestion, rhinorrhea, etc.).

Appropriate management of the headache individual includes several components:

- Accurate diagnosis of the individual's condition.



- Effective pharmacological management of acute attacks, including a rescue strategy designed to minimize emergency department utilization.
- Prophylactic strategies to reduce attack frequency and mitigate their effect on function and quality of life. These should include trigger avoidance when possible, as well as maintenance pharmacotherapy in individuals with more frequent headaches.
- Individuals with frequent and severely disabling headaches may benefit from referral to a multidisciplinary headache specialty service where a holistic approach is applied to optimize the individual's functional status.

Individual self-management is an important strategy in migraine treatment. Numerous tools are available to the individual and primary care practitioner to facilitate this approach.

The "triptan" medications, including almotriptan (Axert), eletriptan (Relpax), frovatriptan (Frova), naratriptan (Amerge), rizatriptan (Maxalt), rizatriptan 10 mg/MoSEIC meloxicam 20 mg (Symbravo), sumatriptan (Imitrex), sumatriptan 85 mg/naproxen 500 mg (Treximet), and zolmitriptan (Zomig), are specific 5-hydroxytryptamine (5-HT<sub>1B/1D</sub>) receptor agonists used in the abortive treatment of acute migraine or cluster headaches with or without aura. Triptans selectively bind to the 5-HT<sub>1D</sub> receptors on T<sub>6</sub> sensory afferent neurons and 5-HT<sub>1B</sub> receptors on meningeal vasculature. While the etiology of migraine is still not completely understood, the use of 5-HT agonists results in cranial vasoconstriction and inhibition of pro-inflammatory neuropeptide release, which correlates with the relief of migraine.

Dihydroergotamines (Migranal Nasal Spray and DHE 45 injection) are thought to relieve migraine headaches by constricting peripheral and cranial blood vessels and depressing central vasomotor centers. Dihydroergotamine (DHE) is an alpha-adrenergic blocking agent with a direct stimulating effect on the smooth muscle of peripheral and cranial blood vessels, which produces depression of the central vasomotor centers. DHE is a mixed serotonin agonist/antagonist, and is thought primarily to compensate for insufficient plasma serotonin levels. DHE has a high affinity to 5-HT<sub>1B/1D</sub>, 1A, 2A, 2C as well as to Alpha<sub>1</sub> 2a, 2b and Dopamine D<sub>2</sub>, D<sub>3</sub> receptors. Therapeutic activity is thought to be due to binding at the 5-HT<sub>1D</sub> receptor, preventing neuropeptide release from the trigeminal afferent terminals and blocking neurogenic inflammation. 5-HT<sub>1D</sub> activity leads to vasoconstriction that is more prolonged than that of the triptan class, due to a relatively longer T<sub>1/2</sub> = 10 hours. In addition, the serotonin-stimulating effect of DHE at the 5-HT<sub>1D</sub> and 5-HT<sub>1A</sub> receptor sites counteracts the loss of tone of the extracranial vascular musculature seen in migraine headaches.

Charles and von Dohn reported results of a study of 31 individuals with chronic daily headache treated with outpatient home-based continuous intravenous dihydroergotamine for 3 days.



They administered 3 mg dihydroergotamine given continuously at a rate of 42 ml/hour on day 1 and 2, and administered 1.5 mg on day 3 at the rate of 21 ml/hour. Individuals reported an average of 63.4% reduction in pain intensity at the end of the 3-day infusion (11-point VAS). Side effects were minimal and no serious adverse effects occurred. Approximately one-third of individuals became completely headache-free after day 3, and 1 individual had no improvement. An average 86% reduction in headache frequency was observed on follow up and all but one individual converted to episodic migraine. The authors concluded that efficacy and safety of this home-based IV dihydroergotamine withdrawal protocol compared favorably to established inpatient protocols and provides an effective, safe and less expensive outpatient alternative.

Butorphanol NS is a potent analgesic with mixed opioid agonist/antagonist effects, but it is not for migraine-specific treatment. While this agent may be appropriately self-administered as a rescue medication in occasional cases where the individual's other medications have failed, overuse carries a significant risk of developing tolerance and dependence. It should be prescribed for self-administration with extreme caution. This information in no way supports butorphanol NS for the treatment of migraine.

Calcitonin-gene related peptide (CGRP) antagonists are believed to alleviate migraine headaches by regulating the activity of CGRP, which is responsible for transmitting trigeminal vascular pain in migraine. People who experience migraines typically have elevated levels of CGRP. When CGRP neuropeptides bind to their receptors, they trigger a series of events, including inflammation, vasodilation, mast-cell degranulation, and protein extravasation. CGRP antagonists, humanized monoclonal antibodies, bind to the CGRP receptor and inhibit the cascade events described above, thus preventing the onset of migraines. CGRP inhibitors include Nurtec ODT, Ubrovelvy (ubrogepant) and Zavzpret (zavegepant).

## Medication Overuse

Medication overuse continues to be a concern. Prophylaxis with an expanding variety of drugs, e.g., valproate, topiramate and levetiracetam, is reported. The traditional pharmacologic classes of beta-blockers, calcium channel blockers and antidepressants continue to be popular. Overuse of abortive treatments is worrisome because it creates feedback increasing headache frequency, which in turn increases the amount of medication used. The net result is decrease in control, function and quality of life, along with major increase in medication cost.





## Prophylaxis

Some individuals are able to reduce headache frequency by trigger identification and avoidance, but this strategy is of limited usefulness. Over the years a variety of small molecule drugs have been used in attempts to reduce migraine frequency. A Cochrane review found that **anticonvulsants**, specifically topiramate, sodium valproate and divalproex are effective prophylactic treatments for episodic migraine in adults. In contrast to previous reports, the authors found insufficient evidence to further support the use of gabapentin as a migraine prophylactic agent. **Antidepressants**, **beta blockers** and **calcium channel blockers** have been used with benefit to some individuals, but a significant proportion of migraine individuals do not achieve adequate control with these measures.

**Botulinum toxin** products may benefit some individuals. Botox (onabotulinumtoxinA) is FDA-approved to prevent headaches in adults with chronic migraine (headache lasting  $\geq 4$  hours on  $\geq 15$  days/month). Botox was evaluated in two randomized, multi-center, 24-week, 2 injection cycle, placebo-controlled double-blind studies in chronic migraine adults not using concurrent prophylaxis. Individuals were randomized to receive placebo or 155 Units to 195 Units Botox injections every 12 weeks for the 2-cycle, double-blind phase. Individuals were allowed to use acute headache treatments during the study. Botox treatment demonstrated statistically significant and clinically meaningful improvements from baseline compared to placebo; however, this treatment requires an office procedure that is unpleasant and must be repeated four times a year.

**Calcitonin gene-related peptide (CGRP) antagonists** are monoclonal antibodies that represent the latest approach to migraine prevention. There are four agents in this class which are Aimovig (erenumab), Ajovy (fremanezumab), Emgality (galcanezumab), and Vyepti (eptinezumab-jjmr). CGRP antagonists represent an option for individuals that have failed other means of prophylaxis.

## Acute Treatment of Migraine in Children and Adolescent

Migraine is a common and disabling condition in children, with population-based studies 2 showing a prevalence of 9.7% (95% confidence interval [CI], 9.4 to 9.9) in female children and 3 adolescents, and 6.0% (5.8–6.2) in male children and adolescents. The American Academy of Neurology (AAN) recently published (2019) an update to previous (2004) guideline on the treatment of migraine in children. The objective of this update is to provide evidence-based recommendations for the acute symptomatic treatment of children and adolescents with



migraine and to explore the efficacy of self-administered treatments in reducing headache duration and associated symptoms.

Many children and adolescents use 13 and benefit from nonprescription oral analgesics like acetaminophen, ibuprofen, and naproxen. Triptans are less commonly prescribed in children than in adults, and only the following triptans have FDA approved indication for use in individuals <18 years old.

**Table 1. Acute Treatment of Migraine in Children and Adolescent**

Drug Name	FDA Approved age limit
almotriptan tablet	≥ 12 years old
rizatriptan ODT	6-17 years old
sumatriptan/naproxen tablet	≥ 12 years old
zolmitriptan nasal spray	≥ 12 years old
rizatriptan oral film	≥ 12 years old

## 2018 Update

A literature search was conducted, and expert opinion of a practicing headache specialist in the area was consulted. As a result, the policy was updated and simplified, consolidating previous updates. The discussion of prophylaxis was updated to include the calcitonin gene-related peptide inhibitor class, including erenumab and fremanezumab, which are currently pending final FDA approval. Outdated references were deleted and replaced with recent guidance from AHS/AAN and other relevant organizations.

## 2019 Update

A literature search was conducted from October 1, 2018, through December 1, 2019, and reviewed package inserts for medications in this policy. Added background information regarding recent published guidelines by the American Academy of Neurology (AAN) and the American Headache Society (AHS) for acute treatment of migraine in children and adolescents. No information from this update requires changes to the policy. Added newly approved migraine treatment agent, Reyvow (lasmiditan) to policy.



## 2020 Update

Reviewed product information and availability of all medications listed in policy. Removed reference to triptan patch products. Zecuity (sumatriptan iontophoretic transdermal system) was the only triptan patch product available on the market and the manufacturer stopped selling the device. Treximet (sumatriptan/naproxen) was identified as a multisource product and generic sumatriptan/naproxen was added to policy with same criteria as brand Treximet.

## 2021 Update

Reviewed product information of all medications listed in policy. Updated Treximet and generic sumatriptan/naproxen criteria to include individual age, as reflected by package insert. Reviewed published guidelines from American Academy of Neurology (AAN) and the American Headache Society (AHS). No changes to guidelines since 2019, therefore no other changes to the policy are required.

## 2022 Update

Reviewed product information of all medications listed in policy. Reviewed published guidelines from American Academy of Neurology (AAN) and the American Headache Society (AHS). No changes to guidelines since 2019. Updated the migraine prophylactic therapy drugs in the appendix table by removing clonidine, cyproheptadine, and other anticonvulsants and added the drugs candesartan, gabapentin, and valproic acid.

## 2023 Update

Reviewed product information of all medications listed in policy. Added coverage criteria for Zavzpret (zavegepant). Removed the following criteria requirement from Nurtec ODT (rimegepant) and Ubrelvy (ubrogepant) criteria: "Individual is not experiencing medication overuse headache(s)." Added RizaFilm VersaFilm to the brand triptan medication lists. Updated existing criteria for CGRPs for acute use and preventive use. For acute use, updated requirement that trial and failure of 1 triptan, and for preventive use, updated requirement that trial and failure of 2 prophylactic medications.



## 2024 Update

Reviewed product information of all medications listed in policy. Added Maxalt MLT (rizatriptan) to brand triptans coverage criteria. Removed brand zolmitriptan nasal spray from the brand triptans coverage criteria as it is no longer on the market. Updated the brand ergot derivative coverage criteria for Migranal (dihydroergotamine) to include trial and treatment failure with two generic triptans. Added Ergomar (ergotamine) and Trudhesa (dihydroergotamine) to the brand ergot derivative coverage criteria.

## 2025 Update

Reviewed product information of all medications listed in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

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## Appendix

### Headache Treatment Overview: Summary of Migraine and Cluster Headache Management

#### Migraine

##### Abortive Therapy

Aspirin, Acetaminophen, Ergotamine preparations, NSAIDs, Midrin, Triptans, Dihydroergotamine IV/IM, SC, Butorphanol nasal spray, Others (chlorpromazine, prochlorperazine, metoclopramide)

##### Prophylactic Therapy

Antidepressants, Beta blockers, Botulinum toxin (Botox), Calcium channel blockers, CGRP inhibitors (when used for migraine prophylaxis), Candesartan, Divalproex sodium, Gabapentin, Naproxen (when used daily), Topiramate, Valproic acid.



## Cluster Headaches

### Abortive Therapy

Ergotamine preparations, Local anesthetic agents, Oxygen, Triptans, Butorphanol nasal spray

### Prophylactic Therapy

Calcium channel blockers, Corticosteroids, Lithium, Neurostabilizers, Methysergide, Others (capsaicin, leuprolide)

## History

Date	Comments
11/05/97	New Policy – Add to Prescription Drug section.
12/07/99	Replace policy – Policy revised and updated.
12/21/00	Replace policy – Policy reviewed and revised to incorporate P5.01.107, DHE-45.
02/12/02	Replace policy – Policy reviewed and policy statement unchanged; added Frova® as acceptable triptan.
01/13/03	Replace policy – Policy revised; references updated.
02/10/04	Replace policy – Policy reviewed; policy statement unchanged.
09/01/04	Replace policy – Policy renumbered from 5.01.103 to 5.01.503; no other changes.
05/10/05	Replace policy – Policy reviewed by P&T 3/22/05; policy statement remains unchanged.
02/14/06	Replace policy – Policy reviewed by P&T 1/31/06; policy statement remains unchanged.
06/16/06	Update Scope and Disclaimer; no other changes.
10/10/06	Replace policy – Policy updated with literature review. Policy statement remains unchanged.
03/13/07	Replace policy – Policy updated with literature review; references added. No change in policy statement.
02/02/08	Replace policy – Policy updated with literature search. Policy statement updated to include: The medications covered by this policy may be considered medically necessary for the treatment of migraine and cluster headache in accordance with the policy



Date	Comments
	guidelines. References and codes updated. Policy was review by P&T and recommended for adoption on January 22, 2008.
05/13/08	Replace policy – Policy updated with literature search; no change to the policy statement. Description and Policy guidelines were updated to include sumatriptan 85mg/naproxen 500mg (Treximet).
05/12/09	Replace policy – References added; no change in policy statement.
07/29/09	Update Benefit Application; no other changes.
03/09/10	Replace policy – Policy updated with literature search; references added. Reviewed by P&T January 26, 2010. No change to the policy statement.
11/09/10	Replace policy – Policy updated with current names for brand-name drugs
04/08/11	Replace policy – Policy J7335 added to policy.
05/17/11	Coding updated; J7335 removed from policy.
11/10/11	Replace policy – Policy updated with literature review; reference 35 added. No change in policy statement. Reviewed by P&T September 27, 2011. Codes J0585 – J0587 removed; not applicable to policy.
11/13/12	Replace policy - Policy updated with literature review; reference 37 added. No change in policy statement.
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
12/09/13	Replace policy. Sumatriptan patch added to the list of drugs considered medically necessary for treating migraine headaches; Policy Guidelines and Appendix updated to align with this addition.
11/20/14	Annual Review. Policy updated with literature review; no change in policy statements. References 47-50 added.
06/09/15	Annual Review. Policy updated with literature review. Medically necessary policy statement updated with clarifying criteria and specific indications for appropriate agents addressed. Approved by P&T, May 2015.
05/01/16	Annual Review, approved April 12, 2016. Change of the criteria for brand name triptan products (requiring 2 step therapies). Addition of 2 new agents: Zembrace and Onzetra Xsail. Edited quantity limit table for Zomig.
03/01/17	Updated Related Policies. Removed 5.01.512 as it was archived.
07/04/17	Policy moved into new format, no changes to policy statement.
01/01/18	Annual Review, approved December 20, 2017. A literature search was conducted, and an expert opinion of a practicing headache specialist in the area was consulted. Zecuity was deleted from the table due to discontinuation. Age specific dosing was added to





Date	Comments
	each triptan. Note added that the age criteria for the drugs addressed in this policy are based on the FDA-approved ages. Added HCPCS code J3030.
08/01/18	Annual Review, approved July 10, 2018. Literature search and expert consultation with a practicing headache specialist. Policy was updated and simplified, consolidating previous updates and discussion of prophylaxis was updated to include CGRP inhibitors. Bibliography was updated to reflect current guideline sources.
05/01/19	Interim Review, approved April 2, 2019. Added criteria for approving additional quantities of Migranal (dihydroergotamine) Nasal Spray.
07/01/19	Coding update, removed HCPCS code J3030.
01/01/20	Annual Review, approved December 17, 2019. Added Reyvow (lasmiditan) coverage criteria to policy.
02/01/20	Interim Review, approved January 9, 2020. Added Ubrelvy (ubrogepant) coverage criteria same as Reyvow.
05/01/20	Interim Review, approved April 23, 2020. Added Nurtec ODT (rimegepant) coverage criteria to policy.
01/01/21	Annual Review, approved December 1, 2020. Added prior authorization and quantity limits to generic sumatriptan/naproxen. Removed reference to triptan patch products due to manufacturer withdrawal from market.
10/01/21	Annual Review, approved September 23, 2021. Updated Treximet and generic sumatriptan/naproxen criteria adding requirement patient is 12 years of age or older.
02/01/22	Interim Review, approved January 11, 2022. Added coverage criteria for Elyxyb (celecoxib oral solution) for the acute treatment of migraine with or without aura. Removed ergotamine preparations from Appendix for prophylactic therapy.
06/01/22	Interim Review, approved May 10, 2022. Updated coverage criteria for Nurtec ODT (rimegepant) for quantity approved and added restriction on concurrent use with Ubrelvy (ubrogepant) for the acute treatment of migraine. Updated coverage criteria for Ubrelvy (ubrogepant) for quantity approved and added restriction on concurrent use with Nurtec ODT (rimegepant) for the acute treatment of migraine. Updated coverage criteria for Reyvow (lasmiditan) for quantity approved.
11/01/22	Annual Review, approved October 24, 2022. Updated the migraine prophylactic therapy drugs in the appendix table by removing clonidine, cyproheptadine, and other anticonvulsants and added the drugs candesartan, gabapentin, and valproic acid. Added Length of Approval table and Documentation Requirements table to policy. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/23	Interim Review, approved December 13, 2022. Added the names of generic and brand name triptan medications to the policy. Moved the criteria for approving additional quantities of headache therapies under each of the individual drugs. Removed the



Date	Comments
	separate dosage and quantity limits table and added the quantity limits under the respective drug categories.
06/01/23	Annual Review, approved May 9, 2023. Added coverage criteria for Zavzpret (zavegepant). Removed the following requirement from Nurtec ODT (rimegepant) and Ubrelvy (ubrogepant) criteria: "Individual is not experiencing medication overuse headache(s)". Added RizaFilm VersaFilm to the brand triptan medication lists.
10/01/23	Interim Review, approved September 12, 2023. Updated existing criteria for CGRPs for acute use and preventive use. For acute use, updated requirement that trial and failure of one triptan, and for preventive use, updated requirement that trial and failure of two prophylactic medications.
11/03/23	Minor correction made to reflect approved change, "For acute use, updated requirement that trial and failure of one triptan, and for preventive use, updated requirement that trial and failure of two prophylactic medications."
08/01/24	Annual Review, approved July 9, 2024. Added Maxalt MLT (rizatriptan) to brand triptans coverage criteria. Removed brand zolmitriptan nasal spray from the brand triptans coverage criteria as it is no longer on the market. Updated the brand ergot derivative coverage criteria for Migranal (dihydroergotamine) to include trial and treatment failure with two generic triptans. Added Ergomar (ergotamine) and Trudhesa (dihydroergotamine) to the brand ergot derivative coverage criteria.
03/01/25	Annual Review, approved February 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.
05/01/25	Interim Review, approved April 8, 2025. Added coverage for Symbravo (rizatriptan/meloxicam) for the acute treatment of migraine headaches. Corrected policy language for drugs with additional quantities from "at least 30 doses per 30 days" to "less than 30 doses per 30 days".

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2025 Premera All Rights Reserved.

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