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 a 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. Patients 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.

### Medical Necessity

The medications covered by this policy may be considered medically necessary for the treatment of migraine and cluster headaches when one or more of the following conditions is/are met:

- The quantity dispensed is in accordance with the table below

**OR**

- The prescription is for an oral or intranasal formulation NOT in excess of 30 doses per 30 day time period, AND the patient has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the Appendix section (unless such are contraindicated).

Prescriptions to treat headaches not meeting the above criteria may be considered medically necessary based on the clinical circumstances of an individual patient.

Brand name oral, injectable, nasal spray, nasal powder, or patch triptan products (other than Treximet®) will be considered medically necessary in quantities not exceeding 18 tablets, 8 injections, 18 nasal sprays, 8 nasal powder inhalations, or 4 patches (respectively) per 30 days when the patient has had a trial and failure of at least two different generic triptan products in any dosage form (ie, oral, injectable, or nasal spray).

If the requested medication is a multisource brand and has a generic equivalent, then one of the required generic trials must be the generic version of the brand name medication that is being requested.

**Note:** For quantities in excess of 18 tablets, 8 injections, 18 nasal sprays, 8 nasal powder inhalations, or 4 patches per 30 days, please see Criteria for Approving Additional Quantities below.

Treximet® (sumatriptan/naproxen combination) may be considered medically necessary in quantities not exceeding 18 tablets per 30 days when the patient has failed a trial of generic sumatriptan in combination with two generic NSAIDs, one of which MUST be generic naproxen.

**Note:** For quantities in excess of 18 tablets per 30 days, please see Criteria for Approving Additional Quantities.
Medical Necessity

All other uses of the medications addressed by this policy are considered not medically necessary.

Criteria for Approving Additional Quantities

Criteria for Approving Additional Quantities of Triptans for Migraine
- Patient has failed a trial of a different triptan prior to dose escalation
  AND
- Doses are not exceeding FDA labeled maximum daily doses
  AND
- Patient is not experiencing medication overuse headache(s)
  AND
- Patient has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the Appendix (unless contraindicated)

Criteria for Approving Additional Quantities of Triptans for Cluster Headache
- Patient has unsuccessfully tried at least three categories of other cluster headache therapy relievers from Headache Treatment Overview listed in the Appendix
  AND
- Patient has used at least three categories of prophylactic cluster headache therapies (unless contraindicated)
  AND
- Doses are not exceeding FDA labeled maximum daily doses

Criteria for Approving Additional Quantities of Migranal (dihydroergoatamine) Nasal Spray for Migraine
- Doses are not exceeding FDA labeled maximum daily doses
  AND
- Patient is not experiencing medication overuse headache(s)
  AND
- Patient has unsuccessfully tried at least three categories of prophylactic migraine headache therapies listed in the Appendix (unless contraindicated)

Maximum standard quantities of the listed medications in a rolling 30-day time period are provided in the following table. These quantities are based on national guidelines and standard of care as indicated by local expert opinion. It is important to note that the American
Headache Society recommends the use of triptans not exceeding 10 days/month to prevent the development of medication overuse headache.

### Dosage and Quantity Limits

<table>
<thead>
<tr>
<th>Drug Name, Strength and Dosage Form(s)</th>
<th>Maximum Quantity of Medication in a 30 Day Time Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>All oral triptans (including oral dissolving tablet dosage form)</td>
<td>18 tablets</td>
</tr>
<tr>
<td>Migranal® (dihydroergotamine) Nasal Spray</td>
<td>8 ampules</td>
</tr>
<tr>
<td>Zomig 2.5mg and 5 mg Nasal Spray</td>
<td>18 nasal sprays</td>
</tr>
</tbody>
</table>
| Sumatriptan injection | 4 injectable kits (8 injections)  
8 single-dose vials (8 injections)  
8 needle-free delivery devices (8 injections) |
| Sumatriptan nasal spray | 18 nasal sprays |
| Sumatriptan patch | 1 carton (4 patches) |
| Sumatriptan nasal powder | 8 doses (16 capsules for inhalation; 1 per each nostril) |

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>J3030</td>
<td>Injection, sumatriptan succinate, 6 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)</td>
</tr>
</tbody>
</table>

### Related Information

**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 patient 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**

**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 patients and often even among attacks within a single patient. 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 a patient 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 patient includes several components:

- Accurate diagnosis of the patient’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 patients with more frequent headaches.
Patients 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 patient’s functional status.

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

The “triptan” medications, including almotriptan (Axert®), eletriptan (Relpax®), frovatriptan (Frova®), naratriptan (Amerge), rizatriptan (Maxalt®), sumatriptan (Imitrex®), sumitriptan 85mg/naproxen 500mg (Treximet®), and zolmitriptan (Zomig®), are specific 5-hydroxytryptamine (5-HT1B/1D) receptor agonists used in the abortive treatment of acute migraine or cluster headaches with or without aura. Triptans selectively bind to the 5-HT1D receptors on T6 sensory afferent neurons and 5-HT1B 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-HT1B/1D, 1A, 2A, 2C as well as to Alphaa1 2a, 2b and DopamineD2, D3 receptors. Therapeutic activity is thought to be due to binding at the 5-HT1D receptor, preventing neuropeptide release from the trigeminal afferent terminals and blocking neurogenic inflammation. 5 HT1D activity leads to vasoconstriction that is more prolonged than that of the triptan class, due to a relatively longer T1/2 = 10 hours. In addition, the serotonin-stimulating effect of DHE at the 5-HT1D and 5-HT1A 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 patients 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. Patients 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 patients became completely headache-free after day 3, and 1 patient had no improvement. An average 86% reduction in headache frequency was observed on follow up and all but one patient 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 patient'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.

Medication overuse

Medication overuse continues to be a concern. Prophylaxis with an expanding variety of drugs, eg, valproate, topiramate and levetiracetam, is reported. The traditional pharmacologic classes of beta-blockers, calcium channel blockers and antidepressants continue to be popular. Calcitonin gene-related peptide receptor antagonists are a new pharmacologic class that appears promising and is being investigated for migraine prophylaxis. 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 patients 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 patients, but a significant proportion of migraine patients do not achieve adequate control with these measures.

Botulinum toxin products may benefit some patients. BOTOX® (onabotulinumtoxinA) is now FDA-approved to prevent headaches in adults with chronic migraine (headache lasting ≥4 hours on ≥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. Patients were randomized to receive placebo or 155 Units to 195 Units BOTOX injections every 12 weeks for the 2-cycle, double-blind phase. Patients 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. The first two agents in this class, erenumab (Aimovig) and fremanezumab, are pending final FDA approval in mid-2018. They represent a new option for patients that have failed other means of prophylaxis.

**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.

**References**

1. Product information for the various agents described; data on file with the manufacturers.


31. Policy was reviewed by a board certified practicing neurologist with specialty in headache management. Approved by the independent P&T Committee May 30, 2018.

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, Calcium channel blockers, Naproxen, Ergotamine preparations, Divalproex sodium, Topiramate, Botulinum toxin (Botox®), Calcitonin gene-related peptide (CGRP) antagonists, Others (cyproheptadine, clonidine, other anticonvulsants)

**Cluster Headaches**

**Abortive Therapy**

Ergotamine preparations, Local anesthetic agents, Oxygen, Triptans, Butorphanol nasal spray
**Prophylactic Therapy**

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

### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/05/97</td>
<td>New Policy – Add to Prescription Drug section.</td>
</tr>
<tr>
<td>12/07/99</td>
<td>Replace policy – Policy revised and updated.</td>
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<tr>
<td>12/21/00</td>
<td>Replace policy – Policy reviewed and revised to incorporate P5.01.107, DHE-45.</td>
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<tr>
<td>02/12/02</td>
<td>Replace policy – Policy reviewed and policy statement unchanged; added Frova® as acceptable triptan.</td>
</tr>
<tr>
<td>01/13/03</td>
<td>Replace policy – Policy revised; references updated.</td>
</tr>
<tr>
<td>02/10/04</td>
<td>Replace policy – Policy reviewed; policy statement unchanged.</td>
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<tr>
<td>09/01/04</td>
<td>Replace policy – Policy renumbered from 5.01.103 to 5.01.503; no other changes.</td>
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<tr>
<td>05/10/05</td>
<td>Replace policy – Policy reviewed by P&amp;T 3/22/05; policy statement remains unchanged.</td>
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<tr>
<td>02/14/06</td>
<td>Replace policy – Policy reviewed by P&amp;T 1/31/06; policy statement remains unchanged.</td>
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<tr>
<td>06/16/06</td>
<td>Update Scope and Disclaimer; no other changes.</td>
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<tr>
<td>10/10/06</td>
<td>Replace policy – Policy updated with literature review. Policy statement remains unchanged.</td>
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<tr>
<td>03/13/07</td>
<td>Replace policy – Policy updated with literature review; references added. No change in policy statement.</td>
</tr>
<tr>
<td>02/02/08</td>
<td>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 guidelines. References and codes updated. Policy was review by P&amp;T and recommended for adoption on January 22, 2008.</td>
</tr>
<tr>
<td>05/13/08</td>
<td>Replace policy – Policy updated with literature search; no change to the policy statement. Description and Policy guidelines were updated to include sumitriptan 85mg/naproxen 500mg (Treximet®).</td>
</tr>
<tr>
<td>05/12/09</td>
<td>Replace policy – References added; no change in policy statement.</td>
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<tr>
<td>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>07/29/09</td>
<td>Update Benefit Application; no other changes.</td>
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<tr>
<td>03/09/10</td>
<td>Replace policy – Policy updated with literature search; references added. Reviewed by P&amp;T January 26, 2010. No change to the policy statement.</td>
</tr>
<tr>
<td>11/09/10</td>
<td>Replace policy – Policy updated with current names for brand-name drugs</td>
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<tr>
<td>04/08/11</td>
<td>Replace policy – Policy J7335 added to policy.</td>
</tr>
<tr>
<td>05/17/11</td>
<td>Coding updated; J7335 removed from policy.</td>
</tr>
<tr>
<td>11/13/12</td>
<td>Replace policy - Policy updated with literature review; reference 37 added. No change in policy statement.</td>
</tr>
<tr>
<td>07/08/13</td>
<td>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.</td>
</tr>
<tr>
<td>12/09/13</td>
<td>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.</td>
</tr>
<tr>
<td>11/20/14</td>
<td>Annual Review. Policy updated with literature review; no change in policy statements. References 47-50 added.</td>
</tr>
<tr>
<td>03/01/17</td>
<td>Updated Related Policies. Removed 5.01.512 as it was archived.</td>
</tr>
<tr>
<td>07/04/17</td>
<td>Policy moved into new format, no changes to policy statement.</td>
</tr>
<tr>
<td>01/01/18</td>
<td>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 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.</td>
</tr>
<tr>
<td>08/01/18</td>
<td>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.</td>
</tr>
<tr>
<td>05/01/19</td>
<td>Interim Review, approved April 2, 2019. Added criteria for approving additional</td>
</tr>
</tbody>
</table>
Date | Comments
---|---
| quantities of Migranal® (dihydroergotamine) Nasal Spray.

**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). ©2019 Premera All Rights Reserved.

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You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
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