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Coverage Policy Number **IP0029**

Migraine Treatment

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for Formulary Exceptions to the following Non-Covered Anti-Migraine Products:

- **Amerge®** (naratriptan tablets)
- **Cambia®** (diclofenac powder packet)
- **D.H.E. 45®** (dihydroergotamine mesylate injection)
- **Diclofenac powder packet**
- **dihydroergotamine** 4 mg/mL nasal spray
- **Elyxyb™** (celecoxib 120 mg/4.8 mL solution)
- **Ergomar®** (ergotamine 2 mg sublingual tablet)
- **Frova®** (frovatriptan tablets)
- **Imitrex®** (sumatriptan injection)
- **Imitrex®** (sumatriptan nasal spray)
- **Imitrex®** (sumatriptan tablets)
- **Maxalt®** (rizatriptan tablets)
- **Maxalt MLT®** (rizatriptan orally-disintegrating tablets)

- **Migranal®** (dihydroergotamine mesylate nasal solution)
- **Onzetra® Xsail®** (sumatriptan nasal powder)
- **Relpax®** (eletriptan tablets)
- **Tosymra™** (sumatriptan nasal spray)
- **Treximet®** (sumatriptan and naproxen sodium tablets)
- **Trudhesa™** (dihydroergotamine mesylate nasal spray)
- **Zembrace™ SymTouch™** (sumatriptan injection)
- **Zomig®** (zolmitriptan nasal spray)
- **Zomig®** (zolmitriptan tablets)
- **Zomig-ZMT®** (zolmitriptan orally-disintegrating tablets)

Coverage for Anti-Migraine Products varies across plans and requires the use of preferred products in addition to the criteria listed below. Refer to the customer's benefit plan document for coverage details.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Non-Covered Product	Criteria
Amerge (naratriptan tablets)	Naratriptan (Amerge) is considered medically necessary for the treatment of Acute Migraine when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **naratriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral rizatriptan e. oral sumatriptan f. oral zolmitriptan Naratriptan (Amerge) is considered medically necessary for the prevention of menstrually-associated migraine (MAM) when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **naratriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. oral frovatriptan b. oral zolmitriptan
Cambia (diclofenac powder packet)	Diclofenac powder packet (Cambia) is considered medically necessary for the treatment of Acute Migraine when the individual meets **ALL** of the following criteria: 1. 18 years of age or older

Non-Covered Product	Criteria
	2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. diclofenac tablets b. diclofenac delayed release tablets
Diclofenac powder packet	Diclofenac powder packet is considered medically necessary for the treatment of Acute Migraine when the individual meets **ALL** of the following criteria: 1. 18 years of age or older 2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. diclofenac tablets b. diclofenac delayed release tablets
D.H.E. 45 (dihydroergotamine mesylate injection)	**BOTH** of the following: 1. Documentation the individual has tried **dihydroergotamine mesylate injection** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to sumatriptan injection (generic for Imitrex injection)
Dihydroergotamine 4 mg/mL nasal spray	Documentation of failure, contraindication, or intolerance to **BOTH** of the following: 1. sumatriptan nasal spray (generic for Imitrex nasal spray) 2. Trudhesa (dihydroergotamine mesylate nasal spray) [may require prior authorization]
Elyxyb (celecoxib 120 mg/4.8 mL solution)	Celecoxib 120 mg/4.8 mL solution (Elyxyb) is considered medically necessary for the treatment of Acute Migraine when the individual meets **ALL** of the following criteria: 1. 18 years of age or older 2. **BOTH** of the following: a. Inability to swallow celecoxib capsules b. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: i. **ONE** (1) nonsteroidal anti-inflammatory drug (excluding celecoxib) ii. **ONE** (1) triptan medication OR **ONE** (1) Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist indicated to treat acute migraine
Ergomar (ergotamine sublingual tablet)	Documentation of failure, contraindication, or intolerance to **FIVE** of the following: 1. oral almotriptan 2. oral eletriptan 3. oral frovatriptan 4. oral naratriptan 5. oral rizatriptan 6. oral sumatriptan 7. oral zolmitriptan
Frova (frovatriptan tablets)	Frovatriptan (Frova) is considered medically necessary for the treatment of Acute Migraine when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **frovatriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Non-Covered Product	Criteria
	2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral naratriptan d. oral rizatriptan e. oral sumatriptan f. oral zolmitriptan Frovatriptan (Frova) is considered medically necessary for the for the prevention of menstrually-associated migraine (MAM) when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **<u>frovatriptan tablets</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. oral naratriptan b. oral zolmitriptan
Imitrex (sumatriptan injection)	Documentation the individual has tried **<u>sumatriptan injection</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Imitrex (sumatriptan nasal spray)	Documentation the individual has tried **<u>sumatriptan nasal spray</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Imitrex (sumatriptan tablets)	**BOTH** of the following: 1. Documentation the individual has tried **<u>sumatriptan tablets</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral naratriptan e. oral rizatriptan f. oral zolmitriptan
Maxalt (rizatriptan tablets)	**BOTH** of the following: 1. Documentation the individual has tried **<u>rizatriptan tablets</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral naratriptan e. oral sumatriptan

Non-Covered Product	Criteria
	f. oral zolmitriptan
Maxalt MLT (rizatriptan orally-disintegrating tablets)	**BOTH** of the following: 1. Documentation the individual has tried **rizatriptan orally-disintegrating tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral naratriptan e. oral sumatriptan f. oral zolmitriptan
Migranal (dihydroergotamine mesylate nasal solution)	Documentation of failure, contraindication, or intolerance to **BOTH** of the following: 1. sumatriptan nasal spray (generic for Imitrex nasal spray) 2. Trudhesa (dihydroergotamine mesylate nasal spray) [may require prior authorization]
Onzetra Xsail (sumatriptan nasal powder)	Documentation of failure, contraindication, or intolerance to sumatriptan nasal spray (generic for Imitrex nasal spray)
Relpax (eletriptan tablets)	**BOTH** of the following: 1. Documentation the individual has tried **eletriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral frovatriptan c. oral naratriptan d. oral rizatriptan e. oral sumatriptan f. oral zolmitriptan
Tosymra (sumatriptan nasal spray)	Documentation of failure or intolerance to sumatriptan nasal spray (generic for Imitrex nasal spray)
Treximet (sumatriptan and naproxen sodium tablets)	Documentation the individual has tried **sumatriptan and naproxen sodium tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Trudhesa (dihydroergotamine mesylate) nasal spray	Documentation of failure, contraindication, or intolerance to sumatriptan nasal spray (generic for Imitrex nasal spray)
Zembrace SymTouch (sumatriptan succinate auto-injector)	Documentation of failure or intolerance to sumatriptan injection (generic for Imitrex injection)
Zomig	**ONE** of the following:

Non-Covered Product	Criteria
(zolmitriptan nasal spray)	1. Individual is 12 to 17 years of age: approve 2. Individual is 18 years of age or older: a. Documentation of failure, contraindication, or intolerance to sumatriptan nasal spray (generic for Imitrex nasal spray)
zolmitriptan nasal spray	**ONE** of the following: 1. Individual is 12 to 17 years of age: approve 2. Individual is 18 years of age or older: a. Documentation of failure, contraindication, or intolerance to sumatriptan nasal spray (generic for Imitrex nasal spray)
Zomig (zolmitriptan tablets)	Zolmitriptan (Zomig) is considered medically necessary for the treatment of Acute Migraine when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **zolmitriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral naratriptan e. oral rizatriptan f. oral sumatriptan Zolmitriptan (Zomig) is considered medically necessary for the for the prevention of menstrually-associated migraine (MAM) when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **zolmitriptan tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. oral frovatriptan b. oral naratriptan
Zomig ZMT (zolmitriptan orally-disintegrating tablets)	Zolmitriptan orally-disintegrating tablets (Zomig ZMT) is considered medically necessary for the treatment of Acute Migraine when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **zolmitriptan orally-disintegrating tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **FOUR** of the following: a. oral almotriptan b. oral eletriptan c. oral frovatriptan d. oral naratriptan e. oral rizatriptan f. oral sumatriptan

Non-Covered Product	Criteria
	Zolmitriptan orally-disintegrating tablets (Zomig ZMT) is considered medically necessary for the for the prevention of menstrually-associated migraine (MAM) when the individual meets **BOTH** of the following criteria: 1. Documentation the individual has tried **zolmitriptan orally-disintegrating tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction 2. Documentation of failure, contraindication, or intolerance to **BOTH** of the following: a. oral frovatriptan b. oral naratriptan

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of anti-migraine products is considered medically necessary when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Migraine is a chronic condition marked by paroxysmal, unilateral attacks of moderate-to-severe throbbing headache with associated symptoms that may include nausea, vomiting, and photophobia or phonophobia.[1] Migraine affects approximately 15% of US adults. Migraine headaches usually begin in late childhood or early adolescence and are more common in preadolescent boys than girls. However, they become three times more common in adult women than men. Migraine headache is preceded by focal neurologic symptoms, termed “aura” in up to 30% of individuals. Aura is typically characterized by any combination of visual, hemisensory, or language abnormalities, with the most common being visual. Visual aura symptoms include a flashing light or an enlarged blind spot rimmed with a shimmering edge or jagged lines in the peripheral vision. The associated headache usually occurs within 1 hour, but auras do not always progress to headache pain. The five criteria that are most predictive of migraine using the mnemonic “POUND” are Pulsatile quality (pounding or throbbing headache), One day duration (headache episode last 4 to 72 hours if untreated), Unilateral location, Nausea or vomiting, and Disabling intensity (daily activities typically altered during headache). The group of medications referred to as “triptans” (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) play an important role in the acute treatment of migraines.

Guidelines

An updated assessment of the preventive and acute treatment of migraine by the American Headache Society (2018) reaffirms previous migraine guidelines.[17] The current update lists the triptans and dihydroergotamine (DHE) as effective treatments for moderate or severe acute migraine attacks and mild to moderate attacks that respond poorly to nonsteroidal anti-inflammatory drugs (NSAIDs) or caffeinated combinations (e.g., aspirin + acetaminophen + caffeine). Opioid medications are probably effective; however, they are not recommended for regular use. The recommendation remains that clinicians must consider medication efficacy, potential side effects, and potential medication-related adverse events (AEs) when prescribing acute medications for migraine. Treat at the first sign of pain to improve the probability of achieving freedom from pain and reduce attack-related disability. Use a non-oral formulation in individuals whose attacks are associated with severe nausea or vomiting or who have trouble swallowing orally administered medications. When first-line acute treatment is not adequate, individuals may require rescue medication. Depending on the initial treatment, options for outpatient rescue include SC sumatriptan, DHE injection or intranasal spray, or corticosteroids (e.g., dexamethasone, IM ketorolac). Migraine individuals who need to use acute treatments on a regular basis should limit treatment to an average of 2 headache days per week, and individuals who exceed this limit should be offered preventive treatment.

The American Academy of Neurology (AAN) published an evidence-based guideline update for the prevention of episodic migraine (2012) stating that divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, and timolol are effective for migraine prevention and should be offered to individuals with migraine to reduce migraine attack frequency and severity (Level A).[18] Frovatriptan is effective for prevention of menstrually-associated migraine (MAM) (Level A). Lamotrigine is ineffective for migraine prevention (Level A). Evidence to support pharmacologic treatment strategies for migraine prevention indicates which treatments might be effective but does not provide guidance on selecting an optimal therapy. Although Level A recommendations can be made for migraine-preventive medications, evidence is unavailable to help the practitioner choose one therapy over another. Treatment regimens need to be designed on a case-by-case basis taking into account efficacy, AEs, coexisting/comorbid conditions, and personal considerations. Often trial and error is required.

Cambia and Elyxyb are indicated for the acute treatment of migraine with or without aura in adults.[19,20] Cambia is labeled to be used at the lowest effective dose for the shortest duration that is consistent with the individual's treatment goals, while Elyxyb should be used for the fewest number of days per months as possible.

Use of acute treatments for migraine headache can potentially lead to medication-overuse headache (generally defined as use for 10 or more days per month for 3 months or more), therefore, they are not intended for regular use.[17] Guidelines for the management of migraine headache recommend limiting acute (abortive) therapy to less than 2 days per week on a regular basis or 8 treatment days per month. If individuals require abortive therapies more frequently, then re-evaluation of the diagnosis and assessment for the use of preventive therapy may be needed.

Safety
The triptans are all well-tolerated. Some adverse events (AEs) are difficult to distinguish from migraine symptoms.[1] Atypical sensations, including tingling, numbness, heaviness/tightness of the chest and throat, heat, burning, cold, or pressure are reported in individuals taking triptans. Chest pain/pressure is one of the most concerning of these AEs and appears to be low with the oral triptans. The differences in frequency of these symptoms associated with the oral products are difficult to determine based on the information available. However, these symptoms are most commonly associated with injectable sumatriptan compared with the other agents. The incidence of AEs appears to be dose-related.

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