

# Pharmacy Policy Bulletin

## Acute Migraine Therapies – Commercial and Healthcare Reform

**Number:** J-0714

**Category:** Managed Rx Coverage

**Line(s) of Business:**

- Commercial
- Healthcare Reform
- Medicare

**Benefit(s):**

**Commercial:**

**Prior Authorization (1. or 2.):**

1. Rx Mgmt Step Therapy = Preferred
2. Rx Mgmt Performance = MRXC = Yes

**Quantity Limits (1., 2., 3., or 4.):**

1. Rx Mgmt Quantity Limits = Safety/Specialty
2. Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt
3. Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful
4. Rx Mgmt Performance = MRXC = Yes

**Healthcare Reform:** Not Applicable

**Region(s):**

- All
- Delaware
- New York
- Pennsylvania
- West Virginia

**Additional Restriction(s):**

Excluding plans with the Commercial National Select Formulary for Prior Authorization (Step Therapy for Non-Preferred Medications)

Excluding members with the HCR Essential Formulary for Prior Authorization (Step Therapy for Non-Preferred Medications)

**Drugs Products**

**Preferred Oral Therapies**

- sumatriptan
- rizatriptan
- zolmitriptan

#### ***Preferred Non-Oral Therapy***

- sumatriptan injection

#### ***Non-Preferred Therapies***

- Amerge (naratriptan) – *Brand only*
- Cambia (diclofenac) powder for oral solution
- H.E. 45 (dihydroergotamine) injection
- Elyxyb (celecoxib) oral solution
- Ergomar (ergotamine) sublingual tablet
- Frova (frovatriptan) – *Brand only*
- Imitrex (sumatriptan) oral tablet – *Brand only*
- Imitrex (sumatriptan) nasal spray and injection – *Brand only*
- Maxalt and Maxalt MLT (rizatriptan) – *Brand only*
- Migranal (dihydroergotamine) nasal spray
- Onzetra Xsail (sumatriptan) nasal pieces
- Relpax (eletriptan) – *Brand only*
- Reyvow (lasmiditan) (*see Limitations of Coverage*)
- Tosymra (sumatriptan) nasal spray
- Treximet (sumatriptan/naproxen) (*see Limitations of Coverage*)
- Trudhesa (dihydroergotamine mesylate) nasal spray
- Zembrace SymTouch (sumatriptan) injection
- Zomig, Zomig ZMT (zolmitriptan) – *Brand only*
- Zomig nasal spray (zolmitriptan)

**FDA-Approved Indications:**

- **Amerge, Cambia, Elyxyb, Frova, Imitrex tablets, Imitrex nasal spray, Onzetra Xsail, Relpax, Reyvow, Tosymra, Trudhesa, Zembrace SymTouch, Zomig, Zomig-ZMT, Zomig Nasal Spray**
  - Acute treatment of migraine with or without aura in adults
- **Axert**
  - Acute treatment of migraine attacks in adults with a history of migraine with or without aura
  - Acute treatment of migraine headache pain in adolescents age 12 to 17 years with a history of migraine with or without aura, and who have migraine attacks usually lasting 4 hours or more
- **H.E. 45**
  - Acute treatment of migraine headaches with or without aura
  - Acute treatment of cluster headache episodes
- **Ergomar**
  - To abort or prevent vascular headache, e.g., migraine, migraine variants or so-called “histaminic cephalalgia”
- **Imitrex Injection**
  - Acute treatment of migraine with or without aura in adults
  - Acute treatment of cluster headache in adults
- **Maxalt, Maxalt-MLT**
  - Acute treatment of migraine with or without aura in adults and in pediatric patients 6 to 17 years of age
- **Migranal**
  - Acute treatment of migraine headaches with or without aura
- **Treximet**
  - Acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older

**Background:**

- Ergotamine derivatives possess partial agonist or antagonist activity against tryptaminergic, dopaminergic, and alpha-adrenergic receptors constricting peripheral and cranial blood vessels.
- Triptans are serotonin 5-HT<sub>1B/1D</sub> agonists that likely possess activity at the 5-HT<sub>1B/1D</sub> receptors on the extracerebral, intracranial blood vessels that become dilated during a migraine attack.
- The exact mechanism by which Reyvow, a 5-HT<sub>1F</sub> receptor agonist, exerts its therapeutic effect in the treatment of migraine is unknown.
- Elyxyb and Cambia are nonsteroidal anti-inflammatory drugs (NSAIDs). The mechanism by which it exerts therapeutic

effects in migraine is not fully understood. Elyxyb may inhibit prostaglandin synthesis primarily via inhibition of COX-2.

Cambia may inhibit prostaglandin synthesis via COX-1 and COX-2.

- The American Academy of Neurology (AAN) guideline supports the following medications for migraine prophylaxis:
  - Level A (established as effective): divalproex/sodium valproate, metoprolol, onabotulinumtoxinA, propranolol, timolol, and topiramate, and frovatriptan for menstrual migraine
  - Level B (probably effective): amitriptyline, venlafaxine, atenolol, and nadolol
  - Level C (possibly effective): lisinopril, clonidine, guanfacine, carbamazepine, nebivolol, pindolol, cyproheptadine, and candesartan
  - A cluster headache is a rare and disabling primary headache disorder characterized by attacks that are unilateral, short, and severe. The AAN assigned Level A recommendations for subcutaneous sumatriptan and zolmitriptan nasal spray for treatment of cluster headache.
- Prescribing Considerations:
  - The safety of treating more than 4 headache days in a 30-day period with a triptan product has not been established. As such, prescribers must weigh risks versus benefits when prescribing for additional quantities that would result in exceedance of studied limits.

• **Quantity Limitations:**

<b>Medication</b>	<b>Retail Edit Limit (limit per 30 days)</b>	<b>Mail Order Edit Limit (limit per 90 days)</b>
Almotriptan	100 mg	300 mg
Amerge (naratriptan)	20 mg	60 mg
Frova (frovatriptan)	30 mg	90 mg

Imitrex (sumatriptan tablets)	900 mg oral dose equivalents ( <b>total for all dosage forms</b> )  48 mg (injection)	2700 mg oral dose equivalents ( <b>total for all dosage forms</b> )
Imitrex (sumatriptan injection)  Imitrex or Tosymra nasal spray solution	160 mg (Imitrex nasal spray) or 120 mg (Tosymra nasal spray)	
Maxalt, Maxalt-MLT (rizatriptan)	120 mg	360 mg
Onzetra Xsail	16 units	48 units
Relpax (eletriptan)	240 mg	720 mg
Treximet tablets (sumatriptan/naproxen) (see <i>Limitations of Coverage</i> )	9 tablets	27 tablets
Zomig, Zomig-ZMT (zolmitriptan)	40 mg	120 mg

\*Refer to policies J-0645 or J-0646 for the quantity limits of Cambia, D.H.E, Elyxyb, Ergomar, Migranal, Reyvow, Trudhesa, and Zembrace

### Approval Criteria

#### I. Step Therapy for Non-Preferred Medications

##### A. Oral Single-Agent Triptans and Oral Ergotamines Treatment for Migraine

When a benefit, coverage of a non-preferred oral triptan or ergotamine may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura.( ICD-10: G43)
2. The member has experienced therapeutic failure, contraindication, or intolerance to all of the following products **(a., b., and c.)**:
  - a. generic oral sumatriptan
  - b. generic oral rizatriptan
  - c. generic oral zolmitriptan

#### **B. Reyvow Treatment for Migraine**

When a benefit, coverage of Reyvow may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura (ICD-10:G43)
2. The member has experienced therapeutic failure, contraindication, or intolerance to two (2) of the following products **(a., b., and c.)**:
  - a. generic oral sumatriptan
  - b. generic oral rizatriptan
  - c. generic oral zolmitriptan

#### **C. Oral Single-Agent NSAID Treatment for Migraine**

When a benefit, coverage of Elyxyb and Cambia may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura (ICD-10:G43)
2. The member has experienced therapeutic failure, contraindication, or intolerance to three (3) generic NSAID tablets or capsules (e.g. ibuprofen, naproxen, celecoxib).

#### **D. Intranasal Treatment for Migraine**

When a benefit, coverage of a non-preferred nasal spray therapy for the treatment of migraine may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura (ICD-10:G43)
2. The prescriber attests that the member experiences significant nausea and vomiting and requires a non-oral route of administration.
3. The member has experienced therapeutic failure, contraindication, or intolerance to generic sumatriptan nasal spray.

#### **E. Injectable Treatment for Migraine**

When a benefit, coverage of a non-preferred injectable migraine therapy may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura (ICD-10:G43)
2. The prescriber attests that the member experiences significant nausea and vomiting and requires a non-oral route of administration.
3. The member has experienced therapeutic failure, contraindication, or intolerance to generic sumatriptan injection.

#### **F. Cluster Headaches**

When a benefit, coverage of a non-preferred therapy for the treatment of cluster headaches may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of cluster headache (ICD-10 G44.00, G44.01, G44.02)
2. The member has experienced therapeutic failure, contraindication, or intolerance to generic sumatriptan injection.

#### **G. Treximet (sumatriptan/naproxen)**

When a benefit, coverage of Treximet may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of acute migraine headaches with or without aura (ICD-10: G43)
2. The member has experienced therapeutic failure, contraindication, or intolerance to all of the following products **(a., b., and c.)**:
  - a. generic oral sumatriptan + generic naproxen
  - b. generic oral rizatriptan + generic naproxen
  - c. generic oral zolmitriptan + generic naproxen

## **II. Reauthorization of Step Therapy**

When a benefit, reauthorization of acute migraine or cluster headache treatment may be approved when the following criterion is met **(A.)**:

- A.** The prescriber attests that the member has experienced positive clinical response to therapy.

### **III. Quantity Level Limits for Migraine Therapies**

#### **A. Migraine**

When a benefit, coverage of additional quantities of acute triptan medications may be approved (up to two times the limit in the above table) when the following criterion is met **(1.)**:

- 1.** The member has a diagnosis of migraine (ICD-10: G43) and meets one (1) of the following criteria **(a., b., or c.)**:

- a.** The member is currently receiving one (1) of the following prophylactic migraine medications **(i. through ix.)**:

- i.** Alpha-agonists
- ii.** Angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers
- iii.** Anti-epileptic drugs
- iv.** Beta-blockers
- v.** Calcitonin gene-related peptide (CGRP) inhibitors indicated for prevention of migraine
- vi.** Calcium Channel Blockers
- vii.** OnabotulinumtoxinA
- viii.** Serotonin-norepinephrine reuptake inhibitors
- ix.** Tricyclic antidepressants

- b.** The member has experienced therapeutic failure or intolerance to one (1) agent from two (2) different prophylactic migraine medication classes or all are contraindicated **(i. through ix.)**:

- i.** Alpha-agonists
- ii.** Angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers
- iii.** Anti-epileptic drugs

- iv. Beta-blockers
  - v. Calcitonin gene-related peptide (CGRP) inhibitors indicated for prevention of migraine
  - vi. Calcium Channel Blockers
  - vii. OnabotulinumtoxinA
  - viii. Serotonin-norepinephrine reuptake inhibitors
  - ix. Tricyclic antidepressants
- c. The member has exceeded the retail limit and presents at the pharmacy with a current or impending migraine.
- i. *Note: Authorization is limited to a one time exception. A continual monthly override will not be permitted (see Limitations of Coverage).*

**B. Cluster Headache**

When a benefit, coverage of additional quantities of an acute medication may be approved medication (up to two times the limit in the above table) when the following criterion is met **(1.)**:

- 1. The member has a diagnosis of cluster headache (G44.00.G44.01.G44.02) and is receiving prophylactic therapy.
  - a. *Note: Members who are not on prophylactic therapy may receive a one-time exception for an additional quantity. A continual monthly override will not be permitted.*

**IV.** An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

**Limitations of Coverage**

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- I. A continual monthly override for treatment of a current or impending migraine and cluster headache will not be permitted.
  - II. Safety supporting use of more than 9 tablets per 30 days of Treximet or more than 4 doses per 30 days of Reyvow has not been established. Additional quantities of these products will not be approved.
  - III. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
  - V. For Commercial and HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

#### Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

*Note: Not applicable for members that meet a one-time exception.*

#### Automatic Approval Criteria

None

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Effective Date Begin: 12/03/2021

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#### References:

1. Amerge [package insert]. Research Triangle Park, NC: GlaxoSmithKline; November 2016.
2. Axert [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; May 2017.
3. Cambia [package insert]. Lake Forest, IL: Assertio Therapeutics, Inc.; April 2021.

4. D.H.E. 45 [package insert]. Aliso Viejo, CA: Valeant Pharmaceuticals North America; September 2009.
5. Elyxyb [package insert]. Telangana, India: Dr. Reddy's Laboratories Limited; May 2020.
6. Ergomar [package insert]. Lake Forest, IL: TerSera Therapeutics, LLC; May 2018.
7. Frova [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; August 2018.
8. Imitrex injection [package insert]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.
9. Imitrex tablets [package insert]. Research Triangle Park, NC: GlaxoSmithKline; December 2017.
10. Imitrex nasal spray [package insert]. Research Triangle Park, NC: GlaxoSmithKline; December 2017.
11. Maxalt and Maxalt-MLT [package insert]. Whitehouse Station, NJ: Merck & Co. Inc.; October 2019.
12. Migranal [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; August 2019.
13. Onzetra Xsail [package insert]. Morristown, NJ: Currax Pharmaceuticals LLC; December 2019.
14. Relpax [package insert]. New York, NY: Pfizer; March 2020.
15. Reyvow [package insert]. Indianapolis, Indiana: Eli Lilly and Company; June 2021.
16. Sumavel [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; July 2020.
17. Tosymra [package insert]. Princeton, NJ: Dr. Reddy's Laboratories Limited; January 2019.
18. Treximet [package insert]. Morristown, NJ: Currax Pharmaceuticals LLC; April 2021.
19. Trudhesa [package insert]. Seattle, WA: Impel NeuroPharma Inc.; September 2021.
20. Zembrace [package insert]. San Diego, CA: Dr. Reddy's Laboratories Limited; June 2019.
21. Zomig and Zomig-ZMT [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; December 2018.
22. Zomig nasal spray [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; December 2018.
23. Francis G, Becker W, Pringsheim T, et al. Acute and preventive pharmacologic treatment of cluster headache. 2010; 75(5)463-473.
24. Silberstine S. Practice Parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report on the quality standards subcommittee of the American Academy of Neurology. *Neurology*. 2000;55:754.
25. American Headache Society. The American Headache Society Position Statement on Integrating New Migraine Treatments into Clinical Practice. *Headache* 2019;59(1):1-18.

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