

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
- sumatriptan nasal spray

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_{1B/1D} agonists that likely possess activity at the 5-HT_{1B/1D} receptors on the extracerebral, intracranial blood vessels that become dilated during a migraine attack.
- The exact mechanism by which Reyvow, a 5-HT_{1F} 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:**

Medication	Retail Edit Limit (limit per 30 days)	Mail Order Edit Limit (limit per 90 days)
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 (total for all dosage forms) 48 mg (injection)	2700 mg oral dose equivalents (total for all dosage forms)
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. Amerge, Frova, Maxalt MLT, Relpax, Zomig ZMT

When a benefit, coverage of Amerge, Frova, Maxalt MLT, Relpax, or Zomig ZMT 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 plan-preferred products **(a., b., and c.)**:
 - a. generic oral sumatriptan
 - b. generic oral rizatriptan
 - c. generic oral zolmitriptan

B. D.H.E 45 Injection and Imitrex Injection for Migraine

When a benefit, coverage of D.H.E 45 or Imitrex Injection 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 injection.

C. D.H.E 45 Injection and Imitrex Injection for Cluster Headaches

When a benefit, coverage of D.H.E 45 or Imitrex Injection 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.

D. Elyxyb and Cambia

When a benefit, coverage of Elyxyb or 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 plan-preferred NSAIDs (e.g. ibuprofen, naproxen, celecoxib).

E. Ergomar

When a benefit, coverage of Ergomar 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

F. Imitrex tablets

When a benefit, coverage of brand Imitrex tablets 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. plan-preferred generic oral rizatriptan
 - c. plan-preferred generic oral zolmitriptan

G. Imitrex Nasal Spray, Migranal (dihydroergotamine), Trudhesa, and Zomig (zolmitriptan) Nasal Spray

When a benefit, coverage of Imitrex Nasal Spray, Migranal (dihydroergotamine), Trudhesa, or Zomig (zolmitriptan) Nasal Spray 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.

H. Maxalt

When a benefit, coverage of brand Maxalt 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. plan-preferred generic oral sumatriptan
 - b. generic oral rizatriptan
 - c. plan-preferred generic oral zolmitriptan

I. Onzetra Xsail and Tosymra

When a benefit, coverage of Onzetra Xsail or Tosymra 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 plan-preferred generic sumatriptan nasal spray.

J. Reyvow

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

K. 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 plan-preferred products **(a., b., and c.)**:
 - a. generic oral sumatriptan + generic naproxen

- b. generic oral rizatriptan + generic naproxen
- c. generic oral zolmitriptan + generic naproxen

L. Zembrace SymTouch

When a benefit, coverage of Zembrace SymTouch 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 plan-preferred generic sumatriptan injection.

M. Zomig tablets

When a benefit, coverage of brand Zomig tablets 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. plan-preferred generic oral sumatriptan
 - b. plan-preferred generic oral rizatriptan
 - c. generic oral zolmitriptan

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

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 End Begin:

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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.
26. Ailani J, Burch R, Robbins M, et al. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache* 2021.

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