Triptan Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	06-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
almotriptan Tablet	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 Important limitations: • Use only after a clear diagnosis of migraine has been established • In adolescents age 12 to 17 years, efficacy of almotriptan tablets on migraine-associated symptoms was not established • Not intended for the prophylactic therapy of migraine • Not indicated for the treatment of cluster headache		
Amerge® (naratriptan)* Tablet	Acute treatment of migraine attacks with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	1
Frova® (frovatriptan)* Tablet	Acute treatment of migraine attacks with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	3
IMITREX® (sumatriptan)* Nasal spray	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine headache has been established • Not indicated for the prophylactic therapy of migraine attacks	*generic available	5

Agent(s)	FDA Indication(s)	Notes	Ref#
	• Not indicated for the treatment of cluster headache		
IMITREX® (sumatriptan) * Subcutaneous injection	Acute treatment of migraine with or without aura in adults Acute treatment, cluster headache episodes in adults Limitations of Use: • Use only if a clear diagnosis of migraine or cluster headache has been established • Not indicated for the prophylactic therapy of migraine or cluster headache attacks	*generic available	4
IMITREX® (sumatriptan) * Tablet	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine headache has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	6
Maxalt® MLT/Maxalt® (rizatriptan)* Orally disintegrating tablet Tablet	Acute treatment of migraine with or without aura in adults and in pediatric patients 6 to 17 years old Limitations of Use: • Use only after clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine • Not indicated for the treatment of cluster headache	*generic available	7
ONZETRA® Xsail® (sumatriptan) Nasal powder	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache		8
RELPAX® (eletriptan)* Tablet	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	9
Tosymra® (sumatriptan) Nasal spray	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established		11

Agent(s)	FDA Indication(s)	Notes	Ref#
	• Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache		
Treximet® (sumatriptan/ naproxen sodium)* Tablet	Acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	12
Zembrace® SYMTOUCH® (sumatriptan) Subcutaneous injection	Acute treatment of migraine with or without aura in adults Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks		13
Zomig® (zolmitriptan) * Nasal spray	Acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache • Not recommended in patients with moderate to severe hepatic impairment	*generic available	15
Zomig® (zolmitriptan) * Tablet	Acute treatment of migraine with or without aura in adults and pediatric patients 12 years of age and older Limitations of Use: • Use only if a clear diagnosis of migraine has been established • Not indicated for the prophylactic therapy of migraine attacks • Not indicated for the treatment of cluster headache	*generic available	14

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Migraine and Cluster Headache Management	Migraine is a common disabling primary headache disorder with high prevalence, ranking second globally in terms of years lost to disability.(22) Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity, and association with nausea and/or photophobia and phonophobia. Migraines can present with or without aura, unilateral fully reversible visual, sensory, or other central nervous system symptoms that usually develop gradually and are most-often followed by headache and associated migraine symptoms.(25)

The International Classification of Headache Disorders 3rd Edition (ICHD-3) Diagnostic Criteria:(25)

Indication	Diagnostic Criteria
Migraine without aura	A. At least five attacks fulfilling criteria B-D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least TWO of the following: 1. unilateral location 2. pulsating quality 3. moderate to severe pain intensity 4. aggravation by causing avoidance of routine physical activity D. During headache at least ONE of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not better accounted for by another ICHD-3 diagnosis
Migraine with aura	A. At least two attacks fulfilling criteria B and C B. One or more of the following fully reversible aura symptoms: 1. visual 2. sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal C. At least THREE of the following: 1. at least one aura symptom spreads gradually over 5 minutes or more 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within 60 minutes, by headache D. Not better accounted for by another ICHD-3 diagnosis
Chronic Migraine	A. Headache (migraine-like or tension-type-like) on greater than or equal to 15 days/month

		for greater than 3 months AND fulfilling B and C B. Occurring in patient who has had at least 5 attacks fulfilling 1. criteria B-D for migraine without aura (noted above) and/or 2. criteria B and C for migraine with aura (noted above) C. On greater than or equal to 8 days/month for greater than 3 months, fulfilling any of the following: 1. criteria C and D for migraine without aura (noted above) 2. criteria B and C for migraine with aura (noted above) 3. believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative D. Not better accounted for by another ICHD-3 diagnosis
	Cluster Headache	A. At least 5 attacks fulfilling criteria B-D B. Severe to very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (untreated) C. At least one of the following: 1. At least one of the following signs or symptoms, ipsilateral to the headache a. conjunctival injection and/or lacrimation b. nasal congestion and/or rhinorrhea c. eyelid edema d. forehead and facial sweating e. miosis and/or ptosis 2. Sense of restlessness or agitation D. Occurring with frequency between one every other day and 8 per day E. Not better accounted for by another ICHD-3 diagnosis
	Episodic Cluster Headache	A. Attacks fulfilling criteria for Cluster Headache (noted above) occurring in bouts (cluster periods)

	B. At least two cluster periods lasting 7 days to 1 years (untreated) and separated by pain-free remission periods of at least 3 months

The IHS notes that cluster periods usually last between 2 weeks and 3 months.(25)

Migraine prevention may be of benefit in those with the following:(20,22,30)

- Frequent or long-lasting migraine headaches (greater than 4 headaches/month or headaches lasting greater than 12 hours)
- Attacks interfere significantly with patients' daily routines despite acute treatment
- Contraindicationto acute therapies
- Failure of acute therapies
- Adverse effects with acute therapies
- Risk of medication overuse headache (MOH)
- Patient preference

The American Headache Society (AHS) and the American Academy of Neurology (AAN) suggest the following agents for the prevention of migraine:(17)

- Established as effective (Level A)
    - Antiepileptic drugs (AEDs)
        - Divalproex
        - Valproate
        - Topiramate
    - Beta blockers
        - Metoprolol
        - Propranolol
        - Timolol
    - Triptans
        - Frovatriptan for short term menstrually associated migraines (MAMs) prevention
- Probably effective (Level B)
    - Antidepressants
        - Amitriptyline
        - Venlafaxine
    - Beta blockers
        - Atenolol
        - Nadolol
    - Triptans
        - Naratriptan, zolmitriptan for short term MAMs prevention

The 2021 American Headache Society Consensus Statement recommends the following indications for initiating treatment acute treatment with gepants and ditans agents:(30)

- Prescribed by a licensed clinician
- Patient is at least 18 years of age
- Diagnosis of ICHD-3 migraine with aura, migraine without aura, or chronic migraine
- Either of the following:
    - Contraindication to or inability to tolerate triptans
    - Inadequate response to two or more oral triptans, as determined by either of the following:

	▪ Validated acute treatment patient-reported outcoming questionnaire (mTOQ, Migraine-ACT, PPMQ-R, FIS, PGIC) ▪ Clinician attestation Lasmiditan is a selective serotonin 5HT-1F receptor agonist that lacks vasoconstrictor activity. Lasmiditan is structurally different than triptans and therefore constitutes a new class of drugs called "ditans".(30) Ditans are selective for the 5HT-1F receptor and its mechanism of action is neuronal without evidence of vasoactive effects.(26) Triptans non-specifically bind to the 5HT-1B and 5HT-1D receptors and with varying affinity bind the 5HT-1F receptors, causing direct vascular vasoconstriction. The safety, tolerability, and efficacy of co-administering lasmiditan with a triptan or a gepant has not been assessed.(30) Patients who do not respond to initial therapy with a triptan, may benefit from a second triptan or different therapy such as use of a gepant (ubrogepant or rimegepant) or a ditan (lasmiditan).(22) The 2021 American Headache Society Consensus Statement recommends the following indications for initiating treatment with a Calcitonin Gene-Related Peptide (CGRP) agent:(30) • Prescribed by a licensed clinician • Patient is at least 18 years of age • ONE of the following: o Diagnosis of migraine with or without aura (4-7 monthly headache days) and both of the following: ▪ Inability to tolerate (due to side effects) or inadequate response to an 8-week trial of at least two of the following: • Topiramate • Divalproex sodium/valproate sodium • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol • Tricyclic antidepressant: amitriptyline, nortriptyline • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine • Other Level A or B treatment according to AAN-AHS guideline ▪ At least moderate disability (Migraine Disability Assessment Questionnaire [MIDAS] greater than or equal to 11, Headache Impact Test-6 [HIT]-6 greater than 50) o Diagnosis of migraine with or without aura (8-14 monthly headache days [MHDs]) and inability to tolerate (due to side effects) or inadequate response to an 8-week trial of at least two of the following: ▪ • Topiramate • Divalproex sodium/valproate sodium • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol • Tricyclic antidepressant: amitriptyline, nortriptyline • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine • Other Level A or B treatment according to AAN-AHS guideline o Diagnosis of chronic migraine and one of the following: ▪ Inability to tolerate (due to side effects) or inadequate response to an 8-week trial of at least two of the following: • Topiramate • Divalproex sodium/valproate sodium • Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol • Tricyclic antidepressant: amitriptyline, nortriptyline • Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine

	• Other Level A or B treatment according to AAN-AHS guideline ▪ Inability to tolerate or inadequate response to a minimum of two quarterly injection (6 months) of onabotulinum toxin A The Medical Letter Treatment Guidelines (2023) and Institute for Clinical Systems Improvement Guideline Diagnosis and Treatment of Migraine Headache - Drugs for Migraine states that a triptan is the drug of choice for moderate to severe migraine. The short-acting oral serotonin (5-HT1B/1D) receptor agonists (triptans) sumatriptan (IMITREX, and others), almotriptan (Axert, and generics), eletriptan (RELPAX), rizatriptan (Maxalt, and generics), and zolmitriptan (Zomig, and generics) are similar in efficacy.(18,19) Onset of pain relief generally occurs 30-60 minutes after administration. The longer-acting oral triptans naratriptan (Amerge, and generics) and frovatriptan (Frova, and generics) have a slower onset of action and lower initial response rate than other triptans, but they are better tolerated. Patients with migraine who have nausea or vomiting may not be able to take an oral triptan. Intranasal triptan formulations have a more rapid onset of action than oral tablets, but their efficacy is partially dependent on GI absorption of the portion of the dose that is swallowed. Use of sumatriptan nasal powder (ONZETRA Xsail) results in a faster rise in sumatriptan plasma concentrations and higher peak concentrations than use of a similar dose of sumatriptan nasal spray, suggesting that a larger portion of the dose is absorbed intranasally with the powder. Subcutaneously administered sumatriptan relieves pain faster (in about 10 minutes) and more effectively than other triptan formulations, but it causes more adverse effects.(19) American Headache Society (AHS) (2015): The Acute Treatment of Migraine in Adults: The AHS Evidence Assessment of Migraine Pharmacotherapies: Triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A) and considered by AHS guidelines (2015) to be the gold standard for acute treatment of moderate to severe migraine headaches.(20) Dihydroergotamine is recommended for use as a second- or third-line therapy for select patients or for those with refractory migraine. Intranasal dihydroergotamine has strong evidence of effectiveness but more adverse effects than triptans because of its decreased receptor specificity.(10) An assessment of new migraine treatments by the AHS (2018; updated 2021) reaffirms previous migraine guidelines. The update lists triptans, dihydroergotamine, the oral gepants (Nurtec ODT [rimegepant] and UBRELVY [ubrogepant]), and REYVOW (lasmiditan) as effective treatment of moderate or severe acute attacks and mild to moderate attacks that respond poorly to non-specific nonsteroidal anti-inflammatory drugs (NSAIDs), non-opioid analgesics, acetaminophen, or caffeinated combinations (e.g., aspirin/acetaminophen/caffeine). The recommendation remains that prescribers must consider medication efficacy and potential medication-related adverse effects, potential adverse events, patient-specific contraindications to use with a particular medication, and drug-drug interactions when prescribing acute medications for migraine.(20,22,30) The American Academy of Neurology (AAN) 2010 Guideline: Acute and preventive pharmacologic treatment of cluster headache (CH) state that sumatriptan subcutaneous injection and zolmitriptan nasal spray first-line options for acute treatment of CH.(16,18) American Headache Society (2016): Treatment of CH: Since the publication of the 2010 AAN review, there are no new data from randomized, double-blind, controlled trials that contribute to determining the efficacy or safety for a number of acute treatments, including specifically sumatriptan and zolmitriptan. For acute treatment, sumatriptan subcutaneous, zolmitriptan nasal spray, and high flow oxygen remain the treatments with a Level A recommendation.(21) Guidelines suggest that prophylactic therapy should be started and continued for the duration of the CH period. Prophylactic pharmacological therapy includes verapamil, corticosteroids, lithium, topiramate, melatonin, gabapentin, valproic acid, ergotamine, and capsaicin. Verapamil is commonly considered the first option for prophylactic therapy in practice.(16,31,32) Corticosteroids can be used as transitional or bridging therapy until another prophylaxis agent is established.(32) Corticosteroids may be used by some practitioners for short periods of CH.(16,31) The American Academy Neurology

	lists the following agents as option that maybe considered or should be advised as preventative treatments: • Civamide • Suboccipital steroid injection • Melatonin • Verapamil • Lithium The European Headache Federation and WHO consensus article (2019) states the following:(23) • Individuals with migraine headaches should always be managed in primary care with the exception being chronic migraine, which likely requires specialist management • Any headache not responding satisfactorily in primary care or chronic migraine, should be referred to a specialist • In adults and children, regular high frequency use (greater than 2 day/week) of acute medication risks the development of MOH • Treatment of episodic acute migraine headaches should be approached in a step wise manner and should treat three attacks at each step before moving to the next step if needed: o Step 1: ▪ Use non-opioid analgesics, plus an antiemetic when needed o Step 2 for adults: ▪ Use triptan products ▪ Triptans should not be used regularly for 10 or more days per month to avoid the risk of MOH ▪ Triptan efficacy is highly variable between individuals, so patients should try different triptans and formulations. Sumatriptan subcutaneous injection should be considered when all other triptans are ineffective. ▪ When vomiting is present, zolmitriptan nasal spray or sumatriptan subcutaneous injection may be preferred o Step 2 for children and adolescents: ▪ Failure of Step 1 in children should lead to specialist referral. No specific anti-migraine drugs have shown efficacy in children under 12 years of age. ▪ Failure of Step 2 in adolescents (12-17 years of age), the following have shown efficacy and are approved: • Sumatriptan nasal spray • Zolmitriptan nasal spray • Episodic migraine prophylaxis: o Indication for migraine prophylaxis include: ▪ Attacks cause disability on two or more days per month, and ▪ Acute therapy has been optimized but does not prevent this, or is poorly tolerated, or there is a risk of over-frequent use of acute therapy, even when it is effective, and ▪ Patient is willing to take daily medication ▪ Failure of acute therapy is an indication for migraine prophylaxis ▪ For children, frequent absence from school is an additional indication for prophylaxis o Migraine prophylaxis agents may take 2-3 months to show efficacy o Children requiring prophylactic medication should be referred to a specialist o Medications which are effective in adult prophylaxis of episodic migraine include: ▪ Beta blockers: • Atenolol, bisoprolol, metoprolol, propranolol ▪ Amitriptyline

	▪ Topiramate ▪ Candesartan ▪ Sodium valproate ▪ Flunarizine ▪ CGRP o Onabotulinum toxin A is not effective in episodic migraine and not recommended o When prophylaxis therapy fails: ▪ May be due to subtherapeutic dosage or duration of therapy ▪ Failure of one therapy does not predict the failure of another therapy in a different class ▪ Review of the following are recommended: • Diagnosis • Adherence • Other medications, especially for MOH causes ▪ The prophylaxis therapy should be discontinued if it fails to show clear benefit ▪ If all prophylaxis therapies fail, a specialist should be referred • Chronic migraine management: o Chronic migraine patients should be referred to a specialist o Medications with efficacy in chronic migraine include: ▪ Topiramate ▪ Onabotulinum A ▪ CGRP • Cluster Headache management: o Patients should be referred to a specialist o Acute therapies include: ▪ Triptans: • Sumatriptan subcutaneous injection • Sumatriptan nasal spray • Zolmitriptan nasal spray ▪ Oxygen o Transition and maintenance therapies include: ▪ Prednisone ▪ Greater occipital nerve blockade ▪ Verapamil ▪ Lithium carbonate ▪ Topiramate o Neuromodulation is another treatment option o Failure of one prophylactic therapy does not predict the failure of other therapies o Combination prophylaxis therapy can be considered though the potential for toxicity is high o Long-term prophylaxis therapy may need to be continued The European Headache Federation guideline states the following on combining migraine prophylaxis therapy:(24) • In episodic migraine, guidelines suggest to stop oral prophylaxis migraine agents before starting CGRPs, unless the patient previously had chronic migraine prior to prophylaxis. In such patients, the suggestion is to add CGRP to the ongoing oral prophylaxis therapy • In chronic migraine, guidelines suggest to add CGRP to ongoing oral prophylaxis therapy • In chronic migraine patients on onabotulinum A therapy and are receiving inadequate treatment response, guidelines suggest to stop onabotulinum A therapy before starting CGRPs • In patients with chronic migraine who are on treatment with CGRP and may benefit from additional prevention, guidelines suggest to add on oral preventative agents

	• In patients with medication overuse, guidelines suggest to use CGRPs before or after withdrawal of acute medications The clinical trials referenced in FDA labeled package inserts for the preventative CGRP agents excluded patients that had received botulinum toxin within 4 months prior to receiving the CGRP agent.(27,28,29) However the 2021 American Headache Society consensus statement states that CGRP monoclonal antibody treatment (e.g., eptinezumab-jjmr, erenumab, fremanezumab, galcanezumab) may be added to greater than or equal to one established preventative treatment, based on clinical judgement, in adults who meet the ICHD-3 criteria for the following conditions:(25,30) • Migraine with/without aura (4–7 monthly migraine days [MMDs]) with at least moderate disability (Migraine Disability Assessment greater than or equal to 11 or 6-item Headache Impact Test greater than 50) and failure of an 8-week trial of greater than or equal to 2 preventive treatments with established efficacy (e.g., topiramate, divalproex sodium, beta-blocker, tricyclic antidepressant, and others) • Migraine with/without aura (8–14 MMDs) and failure of an 8-week trial of greater than or equal to 2 established preventive treatments • Chronic migraine (greater than or equal to 15 MMDs) with any level of disability and either failure of an 8-week trial of greater than or equal to two established preventive treatments or inadequate tolerability or response to onabotulinum toxin A for two quarterly injections

Medication overuse headache (MOH)	The European Headache Federation and WHO consensus article (2019) states the following:(23)
	
	• Prevention is preferred
	• The four objectives of management are:
	  ○ Stop the overused medication
	  ○ Recovery from MOH
	  ○ Review and reassess the underlying headache disorder
	  ○ Prevent relapse while allowing acceptable use of medications
	• Comorbidities may require management

Safety	Almotriptan has the following contraindications:(2) • Ischemic heart disease, coronary artery vasospasm, or other significant underlying cardiovascular disease • Cerebrovascular syndromes (e.g., history of stroke or TIA) • Peripheral vascular disease (including ischemic bowel disease) • Uncontrolled hypertension • Do not use almotriptan tablets within 24 hours of an ergotamine-containing, or ergot-type medication, or of another 5-HT1 agonist, e.g., another triptan • Hemiplegic or basilar migraine • Known hypersensitivity to almotriptan tablets Eletriptan has the following contraindications:(9) • History of coronary artery disease (CAD) or coronary artery vasospasm • Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or history or current evidence of hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension

	• Within 24 hours of treatment with another 5-HT1 agonist, or an ergotamine-containing medication • Hypersensitivity to RELPAX (angioedema and anaphylaxis seen) • Within at least 72 hours of treatment with the following potent CYP3A4 inhibitors: ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, or nelfinavir Frovatriptan has the following contraindications:(3) • History of coronary artery disease or coronary artery vasospasm • Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension • Recent (within 24 hours) use of treatment with another 5-HT1 agonist, or an ergotamine-containing medication • Hypersensitivity to Frova (angioedema and anaphylaxis seen) Naratriptan has the following contraindications:(1) • History of coronary artery disease or coronary artery vasospasm • Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension • Recent (within 24 hours) use of another 5-HT 1 agonist (e.g., another triptan) or an ergotamine-containing medication • Hypersensitivity to Amerge (angioedema and anaphylaxis seen) • Severe renal or hepatic impairment Rizatriptan has the following contraindications:(7) • History of ischemic heart disease or coronary artery vasospasm • History of stroke or transient ischemic attack • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension • Recent (within 24 hours) use of another 5-HT1 agonist (e.g., another triptan), or of an ergotamine-containing medication • Hemiplegic or basilar migraine • MAO-A inhibitor used in the past 2 weeks • Hypersensitivity to rizatriptan or any of the excipients Sumatriptan subcutaneous injection, tablet, nasal spray, and nasal powder have the following contraindications:(4-6,8,11) • History of coronary artery disease or coronary artery vasospasm • Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension

	• Recent (within 24 hours) use of treatment with another 5-HT1 agonist, or an ergotamine-containing medication • Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor Hypersensitivity to sumatriptan (angioedema and anaphylaxis seen). • Severe hepatic impairment Sumatriptan/naproxen sodium tablet has the following contraindications:(12) • History of coronary artery disease or coronary vasospasm • In the setting of CABG surgery • Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension • Recent (within 24 hours) use of another 5-HT1 agonist (e.g., another triptan) or of ergotamine-containing medication • Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor • History of asthma, urticaria, other allergic type reactions, rhinitis, or nasal polyps syndrome after taking aspirin or other NSAID/analgesic drugs • Known hypersensitivity to sumatriptan, naproxen, or any components of Treximet (angioedema and anaphylaxis seen) • Severe hepatic impairment Sumatriptan/naproxen sodium tablet has the following boxed warning:(12) • Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use. • Treximet is contraindicated in the setting of coronary artery bypass graft (CABG) surgery • NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events. Zolmitriptan has the following contraindications:(14-15) • History of coronary artery disease or coronary artery vasospasm • Symptomatic Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders • History of stroke, transient ischemic attack, or hemiplegic or basilar migraine • Peripheral vascular disease • Ischemic bowel disease • Uncontrolled hypertension • Recent (within 24 hours) use of treatment with another 5-HT1 agonist, or an ergotamine-containing medication • MAO-A inhibitor used in the past 2 weeks • Hypersensitivity to zolmitriptan

REFERENCES

Number	Reference
1	Amerge Tablets prescribing information. GlaxoSmithKline. October 2020.

Number	Reference
2	Almotriptan malate prescribing information. Ajanta Pharma USA Inc. March 2023.
3	Frova prescribing information. Endo Pharmaceuticals, Inc. August 2018.
4	IMITREX Injection prescribing information. GlaxoSmithKline LLC. February 2023.
5	IMITREX Nasal Spray prescribing information. GlaxoSmithKline LLC. December 2017.
6	IMITREX Tablets prescribing information. GlaxoSmithKline LLC. December 2020.
7	Maxalt Tablets/Maxalt-MLT Tablets prescribing information. Organon LLC. June 2021.
8	ONZETRA Xsail prescribing information. Currax Pharmaceuticals LLC. December 2019.
9	RELPAX Tablets prescribing information. Roerig. March 2020.
10	Mayans L, Walling A. Acute Migraine Headache: Treatment Strategies. *Am Fam Physician.* 2018; 97(4): 243-251.
11	Tosymra prescribing information. Promius Pharma, LLC. January 2019.
12	Treximet prescribing information. Currax Pharmaceuticals LLC. October 2021.
13	Zembrace SYMTOUCH prescribing information. Promius Pharma, LLC. June 2019.
14	Zomig Tablets/Zomig ZMT Tablets prescribing information. Amneal Pharmaceuticals. March 2022.
15	Zomig Nasal Spray prescribing information. Amneal Pharmaceuticals. May 2019.
16	Francis GJ, Becker WJ, Prinsheim TM. Acute and preventive treatment of cluster headache. *Neurology* 2010; 75(5): 463-473.
17	Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2012; 78(17): 1337-1345.
18	Beithon J, Gallenberg M, Johnson K, Kildahl P, Krenik J, Liebow M, Linbo L, Myers C, Peterson S, Schmidt J, Swanson J. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. ICSI. Updated January 2013. https://www.icsi.org/wp-content/uploads/2019/01/Headache.pdf.
19	Drugs for Migraine. *Med Lett Drugs Ther.* 2023 Jun 12; 65(1678):89-96. doi:10.58347/tml.2023.1678a.
20	Marmura MJ, Silberstein SD, Schwedt TJ. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. *Headache.* 2015; 55: 3-20. https://doi.org/10.1111/head.12499.
21	Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. *Headache.* 2016; 56: 1093-106. doi:10.1111/head.12866.
22	American Headache Society. The American Headache Society Position Statement: Update on Integrating New Migraine Treatments Into Clinical Practice. *Headache.* 2021; 61(7): 1021-1039. doi: 10.1111/head.14153.
23	Steiner TJ, Jensen R, Katsarava Z, et al. Aids to management of headache disorders in primary care (2nd edition). *Journal of Headache and Pain.* 2019; 20:57. https://doi.org/10.1186/s10194-018-0899-2.
24	Sacco S, Bendtsen L, Ashina M, et al. European headache federation guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention. *The Journal of Headache and Pain*. 2019; 20:6. https://doi.org/10.1186/s10194-018-0955-y.
25	International Classification of Headache Disorders-3 (ICHD-3). *International Headache Society.* 2018.
26	Oswald JC, Schuster NM. Lasmiditan for the treatment of acute migraine: a review and potential role in clinical practice. *J Pain Res.* 2018; 11: 2221-2227.
27	Tepper S, Ashina M, Reuter U, Brandes JL, Dolezil D, Silberstein S, Winner P, Leonardi D, Mikol D, Lenz R. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomized, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol.* 2017 Jun; 16(6): 425-434. doi: 10.1016/S1474-4422(17)30083-2.

Number	Reference
28	Detke HC, Goadsby PJ, Wang S, Friedman DI, Selzler KJ, Aurora SK. Galcanezumab in chronic migraine: The randomized, double-blind, placebo-controlled REGAIN study. *Neurology*. 2018 Dec 11; 91(24): e2211-e2221. doi: 10.1212/WNL.0000000000006640.
29	Lipton RB, Cohen JM, Gandhi SK, Yang R, Yeung PP, Buse DC. Effect of fremanezumab on quality of life and productivity in patients with chronic migraine. *Neurology.* 2020 Aug 18; 95(7): e878-e888. doi: 10.1212/WNL.0000000000010000.
30	Ailani J, Burch RC, Robbins MS; the Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache*. 2021; 61: 1021-1039. https://doi.org/10.1111/head.14153.
31	Goadsby PJ. Information for Health Care Professionals: Treatments for Cluster Headache. *American Headache Society.* 2018 June. https://americanheadachesociety.org/wp-content/uploads/2018/06/Goadsby-Cluster-Headache.docx.
32	Weaver-Agostoni, J. Cluster headache. *American Family Physician.* 2013 Jul 15; 88(2): 122-128.

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	almotriptan malate tab	12.5 MG ; 6.25 MG	12	Tablets	30	DAYS			
	Sumatriptan Succinate Inj 6 MG/0.5ML	6 MG/0.5 ML	10	Vials	30	DAYS			
	zolmitriptan orally disintegrating tab	2.5 MG ; 5 MG	12	Tablets	30	DAYS			
Amerge	naratriptan hcl tab	1 MG ; 2.5 MG	18	Tablets	30	DAYS			
Frova	frovatriptan succinate tab	2.5 MG	18	Tablets	30	DAYS			
Imitrex	sumatriptan nasal spray	20 MG/ACT	12	Units	30	DAYS			
Imitrex	Sumatriptan Nasal Spray 5 MG/ACT	5 MG/ACT	12	Units	30	DAYS			
Imitrex	sumatriptan succinate tab	100 MG ; 25 MG ; 50 MG	18	Tablets	30	DAYS			
Imitrex statdose refill	Sumatriptan Succinate Solution Cartridge 4 MG/0.5ML	4 MG/0.5 ML	12	Doses	30	DAYS			
Imitrex statdose refill	Sumatriptan Succinate Solution Cartridge 6 MG/0.5ML	6 MG/0.5 ML	12	Doses	30	DAYS			
Imitrex statdose system	sumatriptan succinate solution auto-injector	6 MG/0.5 ML	12	Doses	30	DAYS			
Imitrex statdose system	Sumatriptan Succinate Solution Auto-injector 4 MG/0.5ML	4 MG/0.5 ML	12	Doses	30	DAYS			
Maxalt	rizatriptan benzoate tab	10 MG ; 5 MG	18	Tablets	30	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Maxalt-mlt	rizatriptan benzoate oral disintegrating tab	10 MG ; 5 MG	18	Tablets	30	DAYS			
Onzetra xsail	Sumatriptan Succinate Exhaler Powder 11 MG/NOSEPIECE	11 MG/NOSEPC	2	Kits	30	DAYS			
Relpax	eletriptan hydrobromide tab	20 MG ; 40 MG	12	Tablets	30	DAYS			
Tosymra	Sumatriptan Nasal Spray 10 MG/ACT	10 MG/ACT	18	Sprays	30	DAYS			
Treximet	sumatriptan-naproxen sodium tab	85-500 MG	18	Tablets	30	DAYS			
Zembrace symtouch	sumatriptan succinate solution auto-injector	3 MG/0.5 ML	24	Pens	30	DAYS			
Zomig	zolmitriptan nasal spray	2.5 MG ; 5 MG	2	Boxes	30	DAYS			
Zomig	zolmitriptan tab	2.5 MG ; 5 MG	12	Tablets	30	DAYS			

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	almotriptan malate tab	12.5 MG ; 6.25 MG	Medicaid
	Sumatriptan Succinate Inj 6 MG/0.5ML	6 MG/0.5ML	Medicaid
	zolmitriptan orally disintegrating tab	2.5 MG ; 5 MG	Medicaid
Amerge	naratriptan hcl tab	1 MG ; 2.5 MG	Medicaid
Frova	frovatriptan succinate tab	2.5 MG	Medicaid
Imitrex	sumatriptan nasal spray	20 MG/ACT	Medicaid
Imitrex	Sumatriptan Nasal Spray 5 MG/ACT	5 MG/ACT	Medicaid
Imitrex	sumatriptan succinate tab	100 MG ; 25 MG ; 50 MG	Medicaid
Imitrex statdose refill	Sumatriptan Succinate Solution Cartridge 4 MG/0.5ML	4 MG/0.5ML	Medicaid
Imitrex statdose refill	Sumatriptan Succinate Solution Cartridge 6 MG/0.5ML	6 MG/0.5ML	Medicaid
Imitrex statdose system	sumatriptan succinate solution auto-injector	6 MG/0.5ML	Medicaid
Imitrex statdose system	Sumatriptan Succinate Solution Auto-injector 4 MG/0.5ML	4 MG/0.5ML	Medicaid
Maxalt	rizatriptan benzoate tab	10 MG ; 5 MG	Medicaid
Maxalt-mlt	rizatriptan benzoate oral disintegrating tab	10 MG ; 5 MG	Medicaid
Onzetra xsail	Sumatriptan Succinate Exhaler Powder 11 MG/NOSEPIECE	11 MG/NOSEPC	Medicaid
Relpax	eletriptan hydrobromide tab	20 MG ; 40 MG	Medicaid
Tosymra	Sumatriptan Nasal Spray 10 MG/ACT	10 MG/ACT	Medicaid
Treximet	sumatriptan-naproxen sodium tab	85-500 MG	Medicaid
Zembrace symtouch	sumatriptan succinate solution auto-injector	3 MG/0.5ML	Medicaid
Zomig	zolmitriptan nasal spray	2.5 MG ; 5 MG	Medicaid
Zomig	zolmitriptan tab	2.5 MG ; 5 MG	Medicaid

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. ALL of the following: A. The patient has a diagnosis of migraine headache **AND** B. ONE of the following: 1. The patient is currently using migraine prophylactic medication (i.e., anticonvulsants [i.e., divalproex, valproate, topiramate], beta blockers [i.e., atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e., amitriptyline, venlafaxine], candesartan, prophylactic use CGRP [i.e., Aimovig, AJOVY, Emgality, Nurtec, QULIPTA, Vyepti], onabotulinum toxin A (Botox]) **OR** 2. The patient has an intolerance or hypersensitivity to an anticonvulsant, a beta blocker, an antidepressant, candesartan, prophylactic use CGRP, or onabotulinum toxin A listed above **OR** 3. The patient has an FDA labeled contraindication to ALL anticonvulsants, beta blockers, antidepressants, candesartan, prophylactic use CGRP, or onabotulinum toxin A listed above **OR** 4. BOTH of the following: A. The patient's medication history includes a migraine prophylactic medication (i.e., anticonvulsants [i.e., divalproex, valproate, topiramate], beta blockers [i.e., atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e., amitriptyline, venlafaxine], candesartan, prophylactic use CGRP [i.e., Aimovig, AJOVY, Emgality, Nurtec, QULIPTA, Vyepti], onabotulinum toxin A (Botox]), or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following: 1. Evidence of a paid claim(s) **OR** 2. The prescriber has stated that the patient has tried a migraine prophylactic medication (i.e., anticonvulsants [i.e., divalproex, valproate, topiramate], beta blockers [i.e., atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e., amitriptyline, venlafaxine], candesartan, prophylactic use CGRP [i.e., Aimovig, AJOVY, Emgality, Nurtec, QULIPTA, Vyepti], onabotulinum toxin A (Botox]), or a drug in the same pharmacological class with the same mechanism of action **AND** B. ONE of the following: 1. Migraine prophylactic medication was discontinued due to lack of effectiveness or an adverse event **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over migraine prophylactic medication **OR** 5. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 6. The prescriber has provided documentation that migraine prophylactic medication cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease

Module	Clinical Criteria for Approval
	ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** C. Medication overuse headache has been ruled out **AND** D. The patient will NOT be using the requested agent in combination with another acute migraine therapy (e.g., triptan, 5HT-1F [REYVOW], ergotamine, acute use CGRP [e.g., Nurtec, UBRELVY, Zavzpret]) **AND** E. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **OR** 2. BOTH of the following: A. The patient has a diagnosis of cluster headache **AND** B. The requested agent is an injection or nasal spray **Length of Approval:** up to 12 months [For a diagnosis of migraine, the quantity requested up to the FDA labeled maximum dose allowed per 24 hours will be approved.]