curative

Triptan
Quantity Limit Criteria

FDA APPROVED INDICATIONS AND DOSAGE [1-15]

Agent(s)	Indication(s)			Dosage
	Acute treatment, migraine attacks with/without aura (adults)	Acute treatment, migraine headaches (pediatrics)	Acute treatment, cluster headache episodes (adults)	
almotriptan Tablet	✓	✓ (12 years or older)		Initial dose: 6.25 mg or 12.5 mg Min time before repeat dose: 2 hours Max dose/24 hours: 25 mg The safety of treating an average of more than 4 migraines in a 30-day period has not been established
Amerge® (naratriptan) Tablet	✓			Initial dose: 1 mg or 2.5 mg Min time before repeat dose: 4 hours Max dose/24 hours: 5 mg The safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established
Frova® (frovatriptan) Tablet	✓			Initial dose: 2.5 mg Min time before repeat dose: 2 hours Max dose/24 hours: 7.5 mg The safety of treating an average of more than 4 migraine attacks in a 30-day period has not been established

Agent(s)	Indication(s)			Dosage
	Acute treatment, migraine attacks with/without aura (adults)	**Acute treatment, migraine headaches (pediatrics)**	**Acute treatment, cluster headache episodes (adults)**	
Imitrex®, Sumatriptan Tablet	✓			Initial dose: 25 mg to 100 mg Min time before repeat dose: 2 hours Max dose/24 hours: 200 mg The safety of treating an average of more than 4 headaches in a 30-day period has not been established
Imitrex® (sumatriptan) Nasal spray	✓			Initial dose: 5 mg to 20 mg Min time before repeat dose: 2 hours Max dose/24 hours: 40 mg The safety of treating an average of more than 4 headaches in a 30-day period has not been established
Imitrex®, Sumatriptan Subcutaneous injection	✓		✓	Initial dose: 4 mg or 6 mg SC Min time before repeat dose: 1 hour Max dose/24 hours: 12 mg
Maxalt®, Maxalt MLT® (rizatriptan) Tablet	✓	✓ (6 years or older)		Initial dose: 5 mg or 10 mg Min time before repeat dose: 2 hours Max dose/24 hours: 30 mg The safety of treating, on average, more than 4 headaches in a 30-day period has not been established

Agent(s)	Indication(s)			Dosage
	Acute treatment, migraine attacks with/without aura (adults)	Acute treatment, migraine headaches (pediatrics)	Acute treatment, cluster headache episodes (adults)	
Onzetra® Xsail® (sumatriptan nasal powder) Nosepiece	✓			Initial dose: 22 mg Min time before repeat dose: 2 hours Max dose/24 hours: 44 mg The safety of treating an average of more than 4 headaches in a 30-day period has not been established
Relpax® (eletriptan) Tablet	✓			Initial dose: 20 mg or 40 mg Min time before repeat dose: 2 hours Max dose/24 hours: 80 mg The safety of treating an average of more than 3 migraine attacks in a 30-day period has not been established
Tosymra™ (sumatriptan) Nasal spray	✓			Initial dose: 10 mg Minimum time before repeat dose: 1 hour Maximum dose/24 hours: 30 mg

Agent(s)	Indication(s)			Dosage
	Acute treatment, migraine attacks with/without aura (adults)	**Acute treatment, migraine headaches (pediatrics)**	**Acute treatment, cluster headache episodes (adults)**	
Treximet® (sumatriptan/naproxen) Tablet	✓	✓ (12 years or older)		Adults: Initial dose: 85/500 mg Min time before repeat dose: 2 hours Max Dose/24 hours: 170/1000 mg Pediatric: Initial dose: 10/60 mg Maximum dose/24 hours: 85/500 mg The safety of treating an average of more than 5 migraine headaches in adults, or more than 2 migraine headaches in pediatric patients, in a 30-day period has not been established
Zembrace SymTouch™ (sumatriptan) Injection	✓			Initial dose: 3 mg Min time before repeat dose: 1 hour Max dose/24 hours: 12 mg
Zomig®, Zomig ZMT® (zolmitriptan) Tablet	✓			Initial dose: 1.25 mg to 5 mg Min time before repeat dose: 2 hours Max dose/24 hours: 10 mg The safety of treating an average of more than 3 migraines in a 30-day period has not been established

Agent(s)	Indication(s)			Dosage
	Acute treatment, migraine attacks with/without aura (adults)	Acute treatment, migraine headaches (pediatrics)	Acute treatment, cluster headache episodes (adults)	
Zomig®, Zolmitriptan) Nasal spray	✓	✓ (12 years or older)		Initial dose: 2.5 mg Maximum single dose: 5 mg Min time before repeat dose: 2 hours Max dose/24 hours: 10 mg The safety of treating an average of more than 4 headaches in a 30-day period has not been established

All products in the above chart are indicated for the acute treatment of migraine attacks with or without aura in adults.[1-15]

- Use only after a clear diagnosis of migraine has been established
- These products are not intended for prophylactic therapy of migraine attacks, or for management of hemiplegic or basilar migraine.

While the incidence is rare, the triptans have been associated with angina, myocardial infarction (MI), cardiac arrhythmias, hypertension, or stroke, particularly when they were used in patients with vascular risk factors. Triptans should be used with extreme caution in these patients or those with a suspected history of coronary artery disease. Triptans should not be used in patients with uncontrolled hypertension, ischemic heart disease, peripheral vascular disease, or cerebrovascular disease. Triptans should not be used within 24 hours of treatment with another 5-HT1 agonist, or an ergotamine-containing or ergot-type medication like dihydroergotamine or methysergide.[1-15]

CLINICAL RATIONALE

The Medical Letter Treatment Guidelines (2017) – 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. 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]

The American Academy of Neurology and the American Headache Society guidelines (2012,

reaffirmed 2015) on pharmacologic treatment for episodic migraine prevention in adults state that frovatriptan is established as effective and should be offered for short-term menstrually associated migraine (MAMs) prevention (Strong Evidence). Naratriptan and zolmitriptan are probably effective and should be considered for short-term MAMs prevention (Moderate Evidence).[17]

The Institute for Clinical Systems Improvement Guideline Diagnosis and Treatment of Migraine Headache states that triptans are considered to have equal efficacy and are more effective at halting migraine pain at mild levels than if the headache is more severe. Clinicians should consider using subcutaneous sumatriptan or intranasal zolmitriptan as a first line option for the treatment of cluster headaches.[18]

The American Academy of Neurology 2010 Guideline: Acute and preventive pharmacologic treatment of cluster headache state that sumatriptan subcutaneous injection and zolmitriptan nasal spray are recommended for acute treatment of cluster headaches.[16]

American Headache Society (2015): The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies: The specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A). The evidence base for medication efficacy should be considered along with potential medication side effects, potential adverse events, patient-specific contraindications to use of a particular medication, and drug-to-drug interactions when deciding which medication to prescribe for acute therapy of a migraine attack.[20]

American Headache Society (2016): Treatment of Cluster Headaches: Since the publication of the 2010 American Academy of Neurology 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]

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 European Headache Federation and WHO consensus article (2019) states the following:[23]

- Individuals with migraine headaches should almost always be managed in primary care. The exception being chronic migraine, which likely requires specialist management.
- Any headache not responding satisfactorily in primary care should be referred to a specialist
- In adults and children, regular high frequency use (>2 day/week) of acute medication risks the development of medication-overuse headache
- 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:
    - Step 1:
        - Use non-opioid analgesics, plus an antiemetic when needed.
    - Step 2 for adults:
        - Use triptan products.
        - Triptans should not be used regularly on ≥10 days/month to avoid the risk of medication overuse headaches.
        - 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 nausea is present, zolmitriptan nasal spray or sumatriptan subcutaneous injection may be preferred.
    - 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
- For episodic migraine prophylaxis:
    - 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 the patient is willing to take daily medication.
        - Failure of acute therapy is an indication for migraine prophylaxis.
        - For children: frequent absence from school.
    - Migraine prophylaxis agents may take 2-3 months to show efficacy.
    - Children requiring prophylactic medication should be referred to a specialist.
    - Medications which are effective in adult prophylaxis of episodic migraine include:
        - Beta blockers:
            - Atenolol, bisoprolol, metoprolol, propranolol
        - Amitriptyline
        - Topiramate
        - Candesartan
        - Sodium valproate
        - Flunarizine
        - CGRP
    - Onabotulinum toxin A is not effective in episodic migraine.
    - When prophylaxis therapy fails:
        - Failure may be due to subtherapeutic dosage or duration of therapy.
        - Failure of one therapy does not predict the failure of another therapy.
        - Review of the following are recommended:
            - Diagnosis
            - Adherence
            - Other medications, especially for medication overuse headache

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:
    - Chronic migraine patients should be referred to a specialist.
    - Medications with efficacy in chronic migraine include:
        - Topiramate
        - Onabotulinum A
        - CGRP
- Cluster headache patients should be referred to specialists.
    - Acute therapies include:
        - Triptans:
            - Sumatriptan subcutaneous injection
            - Sumatriptan nasal spray
            - Zolmitriptan nasal spray
        - Oxygen
    - Transition and maintenance therapies include:
        - Prednisone
        - Greater occipital nerve blockade
        - Verapamil
        - Lithium carbonate
        - Topiramate
    - Neuromodulation is another treatment option.
    - Failure of one prophylactic therapy does not predict the failure of other therapies
    - Combination prophylaxis therapy can be considered though the potential for toxicity is high.
    - For chronic cluster headache patients, long-term prophylaxis therapy may be needed.
- Medication overuse headache (MOH)
    - 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 also require management

The European Headache Federation guideline states the following on combining migraine prophylaxis therapy:[24]

- In episodic migraine, it's suggested 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, it's suggested to add CGRP to ongoing oral prophylaxis therapy.
- In chronic migraine patients on onabotulinum A therapy and are receiving inadequate treatment response, it's suggested 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, it's suggested to add on oral preventative agents.
- In patients with medication overuse, it's suggested to use CGRPs before or after withdrawal of acute medications

Based on published data from a 1989 survey the median frequency of migraine attacks is 1.5 per month, and the median duration of an attack is 24 hours; at least 10% of patients have weekly attacks, and 20% have attacks lasting two to three days.[25] Additional surveys from the mid to late 1990's have confirmed these data.[26-29] Survey results continue to report a median

attack duration of 24 hours; 54% to 63% of patients report monthly attacks and 13% to 25% report weekly attacks.[26-29]

For additional clinical information see Capital Rx Therapeutics Formulary Chapter 10.4A: Migraine Products: Triptans.

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Triptan Quantity Limit

Target Agents:
Rizatriptan (tab)
Naratriptan (tab)
Sumatriptan (soln./tab)
Zolmitriptan (tab)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Quantities above the program quantity limit for **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:
        i. The patient is currently using a migraine prophylactic medication (i.e. anticonvulsants [divalproex, valproate, topiramate], beta blockers [i.e. atenolol, metoprolol, nadolol, propranolol, timolol], antidepressants [i.e. amitriptyline, venlafaxine], candesartan, CGRP [i.e. Aimovig, Ajovy, Emgality], onabotulinum toxin A [Botox])
        OR
        ii. The patient has an intolerance or hypersensitivity to an anticonvulsant, a beta blocker, an antidepressant, candesartan, CGRP, or onabotulinum toxin A listed above
        OR
        iii. The patient has an FDA labeled contraindication to ALL anticonvulsants, beta blockers, antidepressants, candesartan, CGRP, or onabotulinum toxin A listed above
    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 5HT agent (i.e., triptan, 5HT-1F, ergotamine, acute CGRP)
    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: 12 months
For a diagnosis of migraine, the quantity requested up to the FDA labeled maximum dose allowed per 24 hours will be approved.]

DOCUMENT HISTORY

Approval Date MM/YYYY	Approved By	Notes
08/2022	P&T UM Committee	Initial Criteria Review