



Medication Policy Manual

Policy No: dru438

Topic: High-cost triptan products:

Date of Origin: December 11, 2015

- Alsuma[®]
- almotriptan (generic, Axert[®])
- frovatriptan (generic, Frova[®])
- Onzetra[™] Xsail[™]
- Relpax[®]
- Sumavel[®]
- Treximet[®]
- Zecuity[®] patch
- Zembrace[™] SymTouch
- zolmitriptan oral (generic, Zomig[®] oral)
- Zomig[®] nasal

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Next Review Date: December 2016

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IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Triptans are a rescue treatment for immediate pain relief of an acute migraine headache attack or cluster headaches. This policy applies to high-cost triptan products, many of which are branded products without a therapeutically-equivalent generic. Low-cost triptan products are covered under a separate policy.

Policy/Criteria

- I. Most contracts require prior authorization approval of high-cost triptan products (almotriptan, Axert[®], Alsuma[™], frovatriptan, Frova[®], Onzetra[™] Xsail[™], Relpax[®], Sumavel[®], Treximet[®], Zecuity[™] patch, Zembrace[™], zolmitriptan oral, Zomig[®] oral, Zomig[®] nasal) prior to coverage.
- A. High-cost triptan oral tablets, nasal spray, or transdermal patch may be considered medically necessary when generic sumatriptan **AND** one other low-cost generic triptan (naratriptan or rizatriptan) have been ineffective, not tolerated, or contraindicated.
- OR**
- B. High-cost branded sumatriptan injection products (Alsuma, Sumavel, and Zembrace) may be considered medically necessary when generic sumatriptan injection has been ineffective, not tolerated, or contraindicated.
- II. Administration, Quantity Limitations, and Authorization Period
- A. OmedaRx considers high-cost triptan products to be self-administered medications.
- B. When criteria IA or IB above are met and prior authorization is approved, high-cost triptan products may be authorized in quantities of 12 oral tablets, 6 nasal spray canisters, 6 injections, or 6 transdermal patches per month. Due to package size, Onzetra Xsail may be authorized in a quantity of 1 box (8 doses) per month.
- C. High-cost triptan oral tablets in quantities of 13 to 24 tablets per month may be considered medically necessary for treatment of cluster or migraine headaches when both criteria IA above is met **AND** either criterion 1 or 2 below is met.
1. Diagnosis of **cluster headache**.
- OR**
2. Diagnosis of **migraine headache** and both criteria a and b below are met.
- a. Prophylaxis with medications from three of the different therapy classes listed in Appendix 1 has been ineffective, not tolerated, or contraindicated.
- AND**
- b. There is documentation of migraine prophylaxis continuously for the last four months.
- D. High-cost triptan products in quantities of 7 to 12 nasal spray canisters/ injections/ transdermal patches per month or Onzetra Xsail in quantities of 9 to 16 doses per month (2 boxes) may be considered medically necessary for treatment of cluster or migraine headaches when criteria IA or IB above are met **AND** either criterion 1 or 2 below is met.
1. Diagnosis of **cluster headache**.
- OR**

2. Diagnosis of **migraine headache** and both criteria a and b below are met.
 - a. Prophylaxis with medications from three of the different therapy classes listed in Appendix 1 has been ineffective, not tolerated, or contraindicated.

AND

- b. There is documentation of migraine prophylaxis continuously for the last four months.
- E. Quantities exceeding 24 oral tablets, 12 nasal spray canisters/ injections/ transdermal patches, or 2 boxes on Onzetra Xsail per month in any combination of triptan products or dosage forms are considered not medically necessary.
- F. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

Summary

- The intent of this policy is to encourage the use of the lowest-cost generic sumatriptan for the treatment of migraine headaches, as well as ensure appropriate use of all triptans, to minimize risk of medication overuse headache.
- For the treatment of migraine headache, generic sumatriptan is the best-value triptan, along with other relatively low-cost generic triptans (naratriptan and rizatriptan tablets). Generic sumatriptan and rizatriptan have the best evidence of effectiveness.
- All triptans are effective and relatively safe for the acute treatment of moderate to severe migraine headaches.
- All forms of sumatriptan are used for the acute treatment of migraine attacks with or without aura and sumatriptan injection is used for the acute treatment of cluster headache episodes.
- When an injectable triptan is required, generic sumatriptan injection is the best value. There is no clinically significant difference between the various injectable sumatriptan products.
- Frequent use of abortive therapies, including triptans, may lead to medication overuse headache. Use should be limited to twice per week.
- Triptans may be covered at the doses at which they have been shown to be safe and effective. Up to 12 triptan tablets, 6 nasal sprays or 6 injections per month may be covered per month. Coverage of quantities exceeding these limits is allowed only when specific criteria are met.
- There is moderate certainty in the evidence that preventive medications help gain control of migraine headaches by reducing how often they occur and the severity, as well as need for abortive therapies.
- Low-cost triptans are available as oral disintegrating tablets (ODTs), nasal sprays and injectable dosage forms, which provide additional clinical value for patients who cannot tolerate swallowing tablets or have nausea associated with migraines.

Clinical Efficacy

- There is moderate certainty in the evidence that several low-cost nasal and oral triptans are effective for the acute treatment of migraine attacks. [1-4,7]. There is low certainty in the evidence for the treatment of other types of headaches. [1-7]
- There is insufficient evidence that demonstrates that one triptan is more efficacious than another in the treatment of migraine headache.
 - * Among the available triptans, there is insufficient evidence that almotriptan, frovatriptan, or naratriptan offer additional clinical benefits over sumatriptan: [17-21, 26-28]
 - In headache relief at two hours
 - In headache recurrence rates
 - * There is some evidence that eletriptan has a lower migraine recurrence rate at two hours than oral sumatriptan. [31-32]
 - * There are no trials to establish superiority of high-cost branded sumatriptan injection (Alsuma, Sumavel) over lower-cost generically-available sumatriptan injection or any other triptan for the acute treatment of migraine.
- A triptan taken at the first sign of a migraine yields the best response (pain free, or significant decrease in pain).
- Sumatriptan injection has the best evidence for the treatment of cluster headaches. [1] There are no trials to establish superiority of high-cost branded sumatriptan injection (Alsuma, Sumavel) over lower-cost generically-available sumatriptan injection for the treatment of cluster headache.

Safety

PREVENTIVE (PROPHYLACTIC) THERAPY

- Patients who suffer very severe or frequent migraine attacks may benefit from preventive therapy. [10]
- Current medical literature suggests that preventive therapy should be considered in patients experiencing greater than two migraine attacks per month. [10, 11]
- Preventive medication can help most people decrease the number of migraine headaches by half. Approximately one in ten patients becomes migraine-free with preventive medication. [11, 14]
- Consultation with a specialist experienced in the evaluation and treatment of refractory headache patients may be beneficial when three or more successive preventive drugs have not been effective. [14]
- The American Academy of Neurology (AAN) states that preventive medication may be indicated when a patient is experiencing one or more migraines per week. Severe may be defined as headache causing work loss.
- Frequent use of quick-relief (“abortive”) medication may cause medication overuse headache (MOH), including triptans, NSAIDs, acetaminophen and opioids.

- Many experts limit quick-relief therapy to two headaches per week on a regular basis. Patients with medication overuse headache should use preventive medication. [15]
- The American Academy of Neurology has suggests the best evidence for preventative drug efficacy is for amitriptyline, propranolol, timolol, and divalproex sodium. Evidence of efficacy also exists for other beta-blockers, tricyclic antidepressants (TCAs), and verapamil, a calcium channel blocker (CCB). [15]
- Triptans do not prevent migraines. [1-8, 22, 29, 33-34]
- All triptans carry warnings concerning the risk of serotonin syndrome when used with serotonergic medications, such as selective serotonin reuptake inhibitors (SSRIs) including fluoxetine.

MAXIMUM QUANTITIES

- Most people who have migraine headaches need fewer than 12 tablets per month.
- Approximately 85% of patients with migraine headaches suffer fewer than three to four attacks per month. [9] The median frequency of migraine attacks among migraine sufferers is 1.5 per month. [11]
- Frequent use of quick relief medications can lead to medication overuse headache and eventually chronic daily headache. Medication overuse headache is defined as headache frequency of more than 15 days per month after the frequent intake of quick relief medications for a minimum of three months. [10]
- Frequent use of triptans may lead to medication overuse headache. [12, 13]
- Medication overuse headache is the most common factor in patients referred to tertiary headache clinics. [14]
- The safety of treating more than four headaches with almotriptan, naratriptan, sumatriptan, frovatriptan, rizatriptan, or zolmitriptan (nasal spray) in a 30-day period has not been established. [1-7, 32-33, 39]
- The safety of treating more than three headaches with zolmitriptan tablets or eletriptan in a 30-day period has not been established. [4, 33]
- The safety of treating an average of more than 5 migraine headaches in a 30-day period has not been established for sumatriptan/naproxen. [38]
- The manufacturer's recommended dose for sumatriptan/naproxen is one tablet per attack. The efficacy of taking a second dose has not been established. [38]
- The prescribing information states not to take more than two sumatriptan/naproxen tablets or use two sumatriptan transdermal patches (Zecuity) in 24 hours. [38, 41]

Appendix 1: Migraine Prophylaxis Drug Therapy Classes

The following are examples of medication classes used for migraine prophylaxis:

- Anticonvulsants (a.k.a. anti-epileptic drugs, AEDs) (e.g. divalproex sodium, topiramate).
- Beta Blockers (e.g. propranolol, atenolol, metoprolol).
- Antidepressants (TCAs, e.g. amitriptyline; venlafaxine).
- Other antihypertensives (ACEIs, ARBs, alpha-agonists) [e.g. candesartan, clonidine (Catapres[®]), guanfacine, lisinopril]

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; TCAs: tricyclic antidepressants.

Appendix 2: Product Availability

Brand Name	Generic Name	Dosage Form	Doses per Headache	Doses per Month (4 headaches) ^[b]	Strengths Available	Doses per package
LOW-COST TRIPTANS						
naratriptan	naratriptan	Tablet	1 to 2	4 to 8	1 mg, 2.5 mg	9 tablets
rizatriptan tabs and orally dissolving tablet (ODT)	rizatriptan	Tablet, ODT	1 to 3 ^[a]	4 to 12	5mg, 10mg	various
sumatriptan	sumatriptan	Tablet	1 to 2 ^[a]	4 to 8	25mg, 50mg, 100mg	9 tablets; multi-dose bottles
sumatriptan	sumatriptan	Nasal Spray	1 to 2 ^[a]	4 to 8	5mg, 20mg	6 sprays
sumatriptan	sumatriptan	Injection	1	4	6mg/0.5ml	2 syringes, vial, cartridges
HIGH-COST TRIPTANS						
Axert [®]	almotriptan	Tablet	1	4	6.25mg, 12.5mg	6 tablets 12 tablets
Alsuma [™]	sumatriptan	Injection	1 to 2 ^[a]	4	6mg/0.5ml	2 syringes
Amerge [®]	naratriptan	Tablet	1 to 2 ^[a]	4 to 8	1mg, 2.5mg	9 tablets
Frova [®]	frovatriptan	Tablet	1 to 3 ^[a]	4 to 12	2.5mg	9 tablets
Relpax [®]	eletriptan	Tablet	1 to 2 ^[a]	4 to 8	20mg, 40mg	6 tablets 12 tablets
Sumavel [®] DosePro [®]	sumatriptan	Injection	1	4	6mg/0.5ml	6 syringes
Treximet [®]	sumatriptan/ naproxen	Tablet	1 to 2 ^[a]	5 to 10	85mg/500mg	9 tablets
Zecuity	sumatriptan	transdermal patch	1	4	6.5 mg over 4 hours	6 patches
Zembrace [™] SymTouch [™]	sumatriptan	Injection	4	16	3mg	1 autoinjector
Zomig [®] tablets and ODT	zolmitriptan	Tablet, ODT	1	4	2.5mg, 5mg	1, 3 or 6 tabs
Zomig [®]	zolmitriptan	Nasal Spray	1 to 2	4 to 8	5mg	6 sprays
<p>a. Dose may be repeated if first dose was not completely effective.</p> <p>b. Headache recurs in less than 46% of patients within 24 hours. ^[16]</p>						

Appendix 3: Cluster Headache Diagnostic Criteria

1.	Severe unilateral orbital, supraorbital, and/or temporal pain lasting 15-180 minutes untreated.	
AND		
2.	Headache is associated with at least one of the following signs on the pain side:	
	a.	Conjunctival injection
	b.	Lacrimation
	c.	Nasal congestion
	d.	Rhinorrhea
	e.	Forehead/facial sweating
	f.	Miosis
	g.	Ptosis
	h.	Eyelid edema
AND		
3.	Current frequency of attack is at least 1 every other day.	
AND		
4.	At least five attacks have occurred fulfilling the criteria listed above.	

Appendix 4: Subpopulation Consideration for Use of Triptans		
	Age	Pregnancy Category
<i>Low-cost triptans</i>		
almotriptan tablet	≥ 12 years ^a	C
naratriptan tablet	Not established	C
rizatriptan tabs and orally dissolving tablet (ODT)	≥ 6 years ^a	C
sumatriptan tablet	≥ 12 years ^{b,c}	C
sumatriptan nasal spray	≥ 12 years ^b	C
sumatriptan injection (generic)	Not established	C
<i>High-cost products</i>		
almotriptan tablet	≥ 12 years ^a	C
eletriptan tablet (Relpax)	Not established	C
frovatriptan tablet (Frova)	Not established	C
sumatriptan injection (Alsuma, Sumavel Dose Pro)	Not established	C
sumatriptan transdermal patch (Zecuity)	≥ 12 years ^a	C
sumatriptan/naproxen (Treximet)	Not established	C
zolmitriptan tablets and ODT	≥ 12 years ^b	C
zolmitriptan nasal spray (Zomig)	≥ 12 years ^b	C

^a FDA approved for use in the listed age groups

^b Supported by the AAN Practice Guidelines for treatment of migraines in children. ^[41]

^c Trials in patients as young as 8 years of age. ^[41]

Cross References
Low-cost triptan products, naratriptan, rizatriptan, and sumatriptan-containing oral products, Medication Policy Manual, Policy No. dru439

Codes	Number	Description
N/A		

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Revision History

Revision Date	Revision Summary
3/28/2016	Added generic frovatriptan and Zembrace SymTouch to policy.
12/11/2015	Rename the “Branded triptan” policy to reflect intent of step therapy with low cost triptans, including step therapy for the high-priced generic options.