



**Medication Policy Manual**

**Policy No:** dru052

**Topic:** Amerge<sup>®</sup>, naratriptan

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**Next Review Date:** November 2010

**Effective Date:** December 1, 2009

### **IMPORTANT REMINDER**

This Medical 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 medical policy is to provide a guide to coverage. Medical 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**

Naratriptan (Amerge<sup>®</sup>) is a rescue treatment for immediate pain relief of an acute migraine headache attack.

## Policy/Criteria

- I. Most contracts require prior authorization approval of naratriptan (Amerge®) prior to coverage. Naratriptan (Amerge®) may be considered medically necessary when both criteria A and B below are met.

- A. Sumatriptan has been ineffective, not tolerated, or contraindicated.

### AND

- B. One preferred formulary triptan has been ineffective, not tolerated, or contraindicated. (see Appendix 2).

## II. Administration, Quantity Limitations, and Authorization Period

- A. Regence considers naratriptan (Amerge®) to be a self-administered medication.

- B. When criteria I A and I B above are met and prior authorization is approved, naratriptan (Amerge®) may be authorized in quantities of 12 tablets per month.

- C. Naratriptan in quantities of 13 to 24 tablets per month may be considered medically necessary for treatment of cluster or migraine headaches when both criteria I A and I B above are met AND either criterion 1 or 2 below are met.

1. Diagnosis of **cluster headache**.

### OR

2. Diagnosis of **migraine headache** and both criterion 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 within the last four months.

- D. Quantities exceeding 24 tablets per month in any combination of triptan products or dosage forms are considered not medically necessary.

- E. Authorization maybe reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

## Position Statement

### *Summary*

- For the treatment of migraine headache, the preferred triptan medications sumatriptan (Imitrex<sup>®</sup>), rizatriptan (Maxalt<sup>®</sup>), and eletriptan (Relpax<sup>®</sup>), are the best value and have the best evidence of effectiveness.
- There is reliable evidence that almotriptan (Axert<sup>®</sup>) and zolmitriptan (Zomig<sup>®</sup>) stops migraines, but they have no proven additional benefit over formulary options to justify the higher cost.
- Naratriptan (Amerge<sup>®</sup>) is used for the acute treatment of migraine attacks
- All triptans are effective and relatively safe for the acute treatment of moderate-to-severe migraine headaches. [1-8, 22, 29, 33-34]
- There is reliable evidence that preventive medications help gain control of migraine headaches by reducing how often they occur and the severity.

### *Clinical Efficacy*

- The evidence for the preferred nasal and oral triptans is reliable for the acute treatment of migraine attacks. [1-7] There is not reliable evidence for the treatment of other types of headaches. [1-8]
- Sumatriptan (Imitrex) injection has the best evidence for the treatment of cluster headaches. [1]
- Among the available triptans, there is no reliable evidence that almotriptan, frovatriptan or naratriptan offer additional clinical benefits: [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 is reliable evidence that almotriptan, sumatriptan, rizatriptan, eletriptan, and zolmitriptan abort migraine headaches and treat the associated symptoms. Approximately three to five patients need to be treated for one to have a response.
- The clinical value of naratriptan, frovatriptan and sumatriptan/naproxen is uncertain because there is not reliable evidence to determine how well they treat migraines.
- Because migraines are often accompanied by nausea, products with multiple dosage forms such as oral disintegrating tablets, nasal sprays and injectables provide additional clinical value for patients who can not tolerate swallowing tablets.

- There is insufficient evidence to demonstrate that one triptan is more efficacious than another in the treatment of migraine headache.
- A triptan taken at the first sign of a migraine yields the best response (elimination or significant decrease of pain).
- There is no reliable evidence that the addition of naproxen to sumatriptan is effective.

### *Safety*

#### PREVENTIVE (PROPHYLACTIC) THERAPY

- Patients who suffer very severe or frequent migraine attacks may benefit from preventative therapy.<sup>[10]</sup>
- Current medical literature suggests that preventative therapy should be considered in patients experiencing greater than two migraine attacks per month.<sup>[10, 11]</sup>
- Preventative medication can help most people decrease the number of migraine headaches by half. Approximately one in ten patients become migraine free with preventative medication.<sup>[11, 14]</sup>
- Consultation with a specialist experienced in the evaluation and treatment of refractory headache patients may be beneficial when three or more successive preventative drugs have not been effective.<sup>[14]</sup>
- The American Academy of Neurology states that preventative 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 medication may cause medication overuse headache.
- Many experts limit quick relief therapy to two headaches per week on a regular basis. Patients with medication overuse headache should use preventive medication to reduce the need for quick relief medication.<sup>[15]</sup>
- 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, tricyclics, and verapamil.<sup>[15]</sup>
- Triptans do not prevent migraines.<sup>[1-8, 22, 29, 33-34]</sup>

#### 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.<sup>[9]</sup> The median frequency of migraine attacks among migraine sufferers is 1.5 per month.<sup>[11]</sup>
- 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).<sup>[10]</sup>
- Frequent use of triptans may lead to medication overuse headache.<sup>[12, 13]</sup>
- Medication overuse headache is the most common factor in patients referred to tertiary headache clinics.<sup>[14]</sup>
- 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.<sup>[1-7, 34-35]</sup>
- The safety of treating more than three headaches with zolmitriptan tablets or eletriptan in a 30-day period has not been established.<sup>[4, 33]</sup>
- The safety of treating an average of more than 5 migraine headaches in a 30-day period has not been established for sumatriptan/naproxen.<sup>[38]</sup>
- The manufacturer's recommended dose for sumatriptan/naproxen is one tablet. The efficacy of taking a second dose has not been established.<sup>[38]</sup>
- The prescribing information states not to take more than two sumatriptan/naproxen tablets in 24 hours.<sup>[38]</sup>

### Appendix 1: Migraine Prophylaxis Drug Therapy Classes

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

-	Anticonvulsants (divalproex sodium).
-	Beta Blockers (propranolol, atenolol, metoprolol).
-	Calcium Channel Blockers (verapamil).
-	Tricyclic Antidepressants (amitriptyline).

**Appendix 2: Product Availability**

<b>Brand Name</b>	<b>Generic Name</b>	<b>Dosage Form</b>	<b>Doses per Headache</b>	<b>Doses per Month (4 headaches)<sup>[b]</sup></b>	<b>Strengths Available</b>	<b>Doses per package</b>
<b>FORMULARY/PREFERRED TRIPTANS</b>						
sumatriptan	sumatriptan	Tablet	1 to 2 <sup>[a]</sup>	4 to 8	25mg, 50mg, 100mg	9 tablets
sumatriptan	sumatriptan	Nasal Spray	1 to 2 <sup>[a]</sup>	4 to 8	5mg, 20mg	6 sprays
sumatriptan	sumatriptan	Injection	1	4	6mg/0.5ml	2 syringes
Maxalt <sup>®</sup> , Maxalt MLT <sup>®</sup>	rizatriptan	Tablet	1 to 3 <sup>[a]</sup>	4 to 12	5mg, 10mg	6 tablets
Relpax <sup>®</sup>	eletriptan	Tablet	1 to 2 <sup>[a]</sup>	4 to 8	20mg, 40mg	6 tablets, 12 tablets

Brand Name	Generic Name	Dosage Form	Doses per Headache	Doses per Month (4 headaches) <sup>[b]</sup>	Strengths Available	Doses per package
<b>NON-FORMULARY/NON-PREFERRED TRIPTANS</b>						
Amerge <sup>®</sup>	naratriptan	Tablet	1 to 2 <sup>[a]</sup>	4 to 8	1mg, 2.5mg	9 tablets
Axert <sup>®</sup>	almotriptan	Tablet	1	4	6.25mg, 12.5mg	6 tablets 12 tablets
Frova <sup>®</sup>	frovatriptan	Tablet	1 to 3 <sup>[a]</sup>	4 to 12	2.5mg	9 tablets
Imitrex <sup>®</sup>	sumatriptan	Tablet	1 to 2 <sup>[a]</sup>	4 to 8	25mg, 50mg, 100mg	9 tablets
Imitrex <sup>®</sup>	sumatriptan	Nasal Spray	1 to 2 <sup>[a]</sup>	4 to 8	5mg, 20mg	6 sprays
Imitrex <sup>®</sup>	sumatriptan	Injection	1	4	6mg/0.5ml	2 syringes
Treximet <sup>™</sup>	sumatriptan/naproxen	Tablet	1 to 2 <sup>[a]</sup>	5 to 10	85mg/500mg	9 tablets
Sumavel <sup>™</sup> DosePro <sup>™</sup>	sumatriptan	Injection	1	4	6mg/0.5ml	6 syringes
Zomig <sup>®</sup>	zolmitriptan	Nasal Spray	1 to 2	4 to 8	5mg	6 sprays
Zomig <sup>®</sup> , Zomig ZMT <sup>®</sup>	zolmitriptan	Tablet	1	4	2.5mg, 5mg	6 tablets 3 tablets
a. Dose may be repeated if first dose was not completely effective.						
b. Headache recurs in less than 46% of patients within 24 hours. <sup>[16]</sup>						

### 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.

### References

1. Imitrex<sup>®</sup> Tablets (sumatriptan) prescribing information. GlaxoSmithKline; Research Triangle Park, NC; April 2007.
2. Imitrex<sup>®</sup> Nasal Spray (sumatriptan) prescribing information. GlaxoSmithKline; Research Triangle Park, NC; April 2007.
3. Amerge<sup>®</sup> Tablets (naratriptan) prescribing information. GlaxoSmithKline; Research Triangle Park, NC; October 2007.

4. Zomig<sup>®</sup> Tablets (zolmitriptan) prescribing information. AstraZeneca Pharmaceuticals LP; Wilmington, DE; October 2008.
5. Axert<sup>®</sup> Tablets (almotriptan) prescribing information. Ortho-McNeil Pharmaceuticals, Inc; Raritan, NJ; April 2009.
6. Frova<sup>®</sup> Tablets prescribing information. Elan Pharmaceuticals South San Francisco, CA. April 2007.
7. Maxalt<sup>®</sup> Tablets (rizatriptan) prescribing information. Merck and Co., Inc.; Whitehouse Station, NJ; February 2008.
8. Imitrex<sup>®</sup> Injection (sumatriptan) prescribing information. GlaxoSmithKline; Research Triangle Park, NC; April 2007.
9. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001; 41:646-57.
10. Pryse-Phillips WE, Dodick DW, Edmeads JG, et al. Guidelines for the diagnosis and management of migraine in clinical practice. Canadian Headache Society. *CMAJ*. 1997; 156:1273-87.
11. Goadsby PJ, Lipton RB, Ferrari MD. Migraine--current understanding and treatment. *N Engl J Med*. 2002;346:257-70.
12. Katsarava Z, Fritsche G, Muessig M, et al. Clinical features of withdrawal headache following overuse of triptans and other headache drugs. *Neurology*. 2001;57:1694-8.
13. Fritsche G, Eberl A, Katsarava Z, et al. Drug-induced headache: long-term follow-up of withdrawal therapy and persistence of drug misuse. *Eur Neurol*. 2001;45:229-35.
14. Noble SL, Moore KL. Drug treatment of migraine: Part II. Preventive therapy. *Am Fam Physician*. 1997;56:2279-86.
15. Silberstein SD, et al. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review). Report on the Quality Standards Subcommittee of the American Academy of Neurology. *Neurol* 2000; 55:754-63.
16. Welch KMA. A 27 year-old woman with migraine headaches. *JAMA* 1997;278:322-328
17. Ferrari MD, Roon KI, Lipton R, Goadsby PJ. Oral triptans (serotonin 5-HT 1b-1d agonists) in acute migraine treatment: a meta-analysis of 53 trials. *Lancet* 2001 Nov;358:1668-75.
18. Ryan R, Geraud G, Golstein J, Cady R, Keywood C. Clinical efficacy of frovatriptan: placebo controlled studies. *Headache* 2002 April;42(Suppl2):S84-92.
19. Geraud G, Spierings LH, Keywood C. Tolerability and safety of frovatriptan with short and long term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002 April;42(Suppl2):S93-9.

20. Speirings ELH, et al. Oral almotriptan vs sumatriptan in the abortive treatment of migraine. A double-blind, randomized, parallel-group, optimum-dose comparison. *Arch Neurol* 2001 June;58:944-50.
21. Pascual J, et al. Consistent efficacy and tolerability of almotriptan in the acute treatment of multiple migraine attacks: results of a large, randomized, double-blind, placebo-controlled study. *Cephalalgia* 2000:588-96.
22. Zomig<sup>®</sup> Nasal Spray (zolmitriptan) prescribing information. AstraZeneca Pharmaceuticals LP; Wilmington, DE; October 2008.
23. Syrett N, Abu-Shakra S, Yates R. zolmitriptan nasal spray: advances in migraine treatment. *Neurology* 2003;61(suppl 4):S27-S30.
24. Dowson AJ, Charlesworth BR, Purdy A, Becker WJ, Boes-Hansen S, Farkkila M. Tolerability and consistency of effect of zolmitriptan nasal spray in a long-term migraine treatment trial. *CNS Drugs* 2003;17(11):839-51.
25. Charlesworth BR, Dowson AJ, Purdy A, Becker WJ, Boes-Hansen S, Farkkila M. Speed of onset and efficacy of zolmitriptan nasal spray in the acute treatment of migraine: a randomised, double-blind, placebo-controlled, dose-ranging study versus zolmitriptan tablet. *CNS Drugs* 2003;17(9):653-67.
26. Dalhof C, Winter P, Whitehouse H, Hassani H. Randomized, double-blind, placebo controlled comparison of oral naratriptan and oral sumatriptan in acute treatment of migraine. *Neurology* 1997;48:A85.
27. Mathew NT, Asgharnejad M, Peykamain M, Laurenza A. Naratriptan is effective and well tolerated in the acute treatment of migraine. *Neurology* 1997 Nov;49(6):1485-90.
28. Klassen A, Elkind A, Asgharnejad M, Webster C, Laurenza A. Naratriptan is effective and well tolerated in the acute treatment of migraine. Results of a double-blind, placebo-controlled, parallel-group study. *Headache* 1997 Nov/Dec:640-5.
29. Relpax<sup>®</sup> (eletriptan) prescribing information. Pfizer, Inc.; New York, NY; May 2008.
30. Fuseau E, et al. Effect of encapsulation on absorption of sumatriptan tablets: data from healthy volunteers and patients during migraine. *Clin Therapeutics* 2001 Nov 1;23(1):127-45.
31. Sandrini G et al. Eletriptan vs sumatriptan; a double blind, placebo-controlled, multiple migraine attack study. *Neurology* 2002;59(8):1210-7.
32. Mathew NT, Schoenen J, Winner P, Muirhead N, Kikes CR. Comparative efficacy of eletriptan 40mg versus sumatriptan 100mg. *Headache* 2003;43:214-22.
- 33.

34. International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain. [cited 2004 Oct 11]; Available at: <http://www.i-h-s.org>.
35. Marcus DA, Furman JM. Prevention of motion sickness with rizatriptan: a double-blind, placebo controlled pilot study. *Med Sci Monit.* 2006;12(1):PI1-7.
36. Rapoport AM, Mathew NT, Silberstein SD, Dodick D, Tepper SJ, Sheftell FD, Bigal ME. Zolmitriptan nasal spray in the acute treatment of cluster headache: a double-blind study. *Neurology.* 2007 Aug 28;69(9):821-6.
37. Cittadini E, May A, Straube A, Evers S, Bussone G, Goadsby PJ. Effectiveness of intranasal zolmitriptan in acute cluster headache: a randomized, placebo-controlled, double-blind crossover study. *Arch Neurol.* 2006 Nov;63(11):1537-42.
38. Treximet™ (sumatriptan and naproxen sodium) Tablets Prescribing Information. June 2009. GlaxoSmithKline, Research Triangle Park, NC.
39. Sumavel™ DosePro™ (sumatriptan injection) for subcutaneous use prescribing information. July 2009. Zogenix, Inc., San Diego, CA.

Cross References
Axert®, almotriptan dru053
Frova®, frovatriptan dru078
Imitrex®, sumatriptan dru055
Maxalt®/Maxalt MLT®, rizatriptan dru056
Relpax®, eletriptan dru092
Sumavel™ DosePro™, sumatriptan injection, dru191
Treximet®, sumatriptan/naproxen dru165
Zomig®/Zomig ZMT®, zolmitriptan dru057

Codes	Number	Description
N/A		