

TREXIMETTM
UTILIZATION MANAGEMENT CRITERIA

DRUG CLASS:	5HT1 agonists
BRAND (generic) NAME:	Treximet (sumatriptan/naproxen sodium) 85 mg / 500 mg tablet

FDA INDICATIONS:

Sumatriptan/naproxen is indicated for the acute treatment of migraine attacks with or without aura. Sumatriptan/naproxen is not intended for prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.

ICD-9 CODES:	Migraine – with aura (“classic”)	346.0
	Migraine – idiopathic/without aura (“common”)	346.1

QUANTITY LIMITATIONS (QL) CRITERIA:

QL CRITERIA:	SHORT TERM:	EXTENDED SUPPLY:
Treximet (sumatriptan 85 mg / naproxen sodium 500 mg)	765 mg sumatriptan per 30 days 9 tablets	2295 mg sumatriptan per 90 days 27 tablets

If patient requires amounts in excess of these limits, please follow Quantity Limitations (QL) criteria for Treximet.

RATIONALE: Treximet tablets: Treximet is a fixed combination tablet containing doses of sumatriptan 85 mg and naproxen sodium 500 mg. The recommended dose is one tablet. The maximum recommended adult dose that may be given in 24 hours is two doses separated by at least two hours.

The safety of treating an average of more than 5 migraine headaches in a 30-day period with Treximet has not been established. Most people using these medications for migraine treatment do not need quantities in amounts exceeding that necessary to treat a maximum of 4 migraine attacks in a 30-day period. For this reason, the benefit plan provides coverage only for amounts up to those listed.

CRITERIA FOR EXCEEDING QL:

1. Convey to physician the amount of the drug that the patient has already received (refer to QL criteria) and ask if the patient needs more than that amount. **AND**
2. Patient must have diagnosis of moderate to severe migraine headache. (Cluster, tension-type, and chronic daily headaches are NOT appropriate diagnoses.) **AND**
3. Must have tried and failed at least 2 other abortive migraine therapies. Examples of medications used for abortive therapy include:
 - Diclofenac (Voltaren, Cataflam)
 - Ergotamine-containing products (Cafergot, Wigraine, Ergomar, etc)
 - Flurbiprofen (Ansaid)
 - Ibuprofen (Motrin)
 - Isometheptene mucate/Dichloralphenazone/Acetaminophen (Midrin, etc.)
 - Naproxen sodium (Anaprox DS) **AND**

4. If patient experiences > 4 migraine headaches per month, prophylactic therapy has been given an adequate trial (see table below). **AND**
5. The possibility of medication-induced, rebound, or chronic daily headache should be considered. **AND**
6. **DENY** if to be used in combination with another triptan (e.g., Imitrex, Amerge, Maxalt, Axert, Frova, Relpax, Zomig) or an ergotamine (e.g., Migranal, Cafergot) due to the possibility of increased blood pressure effect.

BLACK BOX WARNINGS:

Cardiovascular risk: Sumatriptan/naproxen may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Gastrointestinal (GI) risk: Sumatriptan/naproxen contains a nonsteroidal anti-inflammatory drug (NSAID).

NSAID-containing products cause an increased risk of serious GI adverse reactions, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These reactions can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious GI reactions.

RATIONALE:

- Aspirin, acetaminophen, and NSAIDs are generally considered first-line abortive therapy for migraine.
- Prophylactic migraine therapy may reduce the frequency and severity of migraine attacks.
- Quantity limitations criteria are intended to prevent inappropriate use of the triptans.

NURSING ASSESSMENT:

1. Gather a complete medical history; note any contributing factors (i.e., smoker, diet alcohol consumption, use of OTC medications, stress, etc.). Include migraine history and any precipitating factors.
2. Determine any history of NSAID or aspirin allergy, cardiac problems or evidence of cardiovascular disease as drug is contraindicated.
3. Ensure that a neurological examination has been performed to identify appropriate migraine category.
4. Obtain baseline ECG, liver (AST, ALT) and renal function tests.

PROVIDER EDUCATION:

1. Review appropriate method for administration (oral).
2. GlaxoSmithKline Drug Information 800-245-1040.

MISUSE AND CHRONIC DAILY HEADACHE:

Chronic Daily Headache (CDH) is a syndrome that consists of a group of disorders that can be sub-classified into primary and secondary types. Drug-induced daily headache frequently arises during headache therapy. It can result from the daily use of ergotamines and excessive amounts of common analgesics. CDH usually manifests itself as a constant dull pressure in the frontal and occipital areas. Most patients will complain of headache upon awakening in the morning. The symptomatic medications used for the immediate relief of headache may actually perpetuate the headache if used frequently and in excessive amounts. Therapy for drug-induced headache is withdrawal of the responsible medication.

CLINICAL OUTCOME:

Reversal of acute migraine attack and relief of associated symptoms.

DOSAGE AND ADMINISTRATION:

The recommended dose is sumatriptan 85 mg / naproxen sodium 500 mg (one tablet). If the patient responds, but satisfactory relief is not obtained within 2 hours, a second dose of up to sumatriptan 85 mg / naproxen sodium 500 mg (one tablet) can be given. Treatment can be repeated up to a maximum of two oral doses (up to sumatriptan 170 mg/day) per 24-hour period with a minimum of 2 hours between doses. If no relief is experienced after the initial dose, a second dose should not be administered. The first dose of the medication should be given in a physician's office or medical clinic if there is a risk of coronary artery disease.

RISK FACTORS/CONTRAINDICATIONS:

1. Do not use with ergotamine-containing products or within 2 weeks of an MAO-A inhibitor.
2. Do not use in patients with cardiovascular or cerebrovascular disease or uncontrolled blood pressure.
3. Do not use as a prophylactic agent.
4. Give only where diagnosis of migraine is clearly established.
5. Contraindications: late pregnancy, peripheral vascular disease (e.g., thromboangitis, leucic arteritis, Raynaud's Syndrome, thrombophlebitis, arteriosclerosis, ischemic bowel disease), hepatic or renal impairment, coronary artery disease, uncontrolled hypertension, allergy to NSAIDs, GI ulcer or bleeding.
6. Advise that if a patient experiences chest, jaw, throat, or neck pain a physician should conduct further medical evaluation.
7. Do not use in patients with significant renal disease (creatinine clearance < 30 ml/min).

DRUG INTERACTIONS:

- Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because there is a theoretical basis that these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine) and 5-HT₁ agonists within 24 hours of each other should be avoided.
- MAO-A inhibitors increase the systemic exposure of the 5-HT₁ agonists and concomitant use is contraindicated.
- Concomitant use of more than one 5-HT₁ agonist within 24 hours of each other is not recommended.
- Selective serotonin reuptake inhibitors (SSRIs) have been reported to cause weakness, hyperreflexia, and incoordination when coadministered with 5-HT₁ agonists.
- Caution should be used with administration of Treximet with the following drugs: aspirin, diuretics and other medications for treating hypertension, high-dose methotrexate, lithium, and warfarin.

Migraine therapy options:

Examples of prophylactic therapy for migraine headaches (the list below may not be complete). An adequate trial of 2-3 months of treatment should be given before a drug is considered ineffective.

DRUG CLASS	NAME
Beta Blockers	Propranolol Atenolol Metoprolol Timolol
Antidepressants	Amitriptyline Fluoxetine

Calcium Channel Blockers	Nifedipine Verapamil Diltiazem
Anticonvulsants	Divalproex sodium/sodium valproate Carbamazepine Gabapentin Topiramate
NSAIDs	Naproxen Aspirin Ketoprofen
Other	Feverfew Magnesium Vitamin B2 (Riboflavin)

Initial Date: 6/2008

Review Date: 9/2009

REFERENCES:

1. Treximet (sumatriptan/naproxen sodium) package insert. GlaxoSmithKline, Research Triangle Park, NC. April, 2008.
2. Snow V, Weiss K, Wall EM, et al. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. *Annals of Internal Med.* 2002; 137(10):840-9.
3. 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. *Neurology.* 2000; 55:754-63.
4. Seema M, Lowder DM. Medications for migraine prophylaxis. *Am Fam Physician.* 2006; 73:72-8.
5. Drugdex editorial staff. Micromedex, Inc. Volume 92, 1997.
6. Edmeads JG, Gawal MJ, Vickers J. Strategies for diagnosing and managing medication-induced headache. *Can Fam Physician.* 1997; 15(1):167-86.
7. Mathew NT. Transformed migraine, analgesic rebound, and other chronic daily headaches. *Neurol Clin.* 1997; 15(1):167-86.
8. Moore KL, Noble SL. Drug treatment of migraine: Part 1. Acute therapy and drug-rebound headache. *Am Fam Physician.* 1997; 56(8):2039-48.
9. Edmeads J. Headaches in older people. *Postgrad Med.* 1997; 101(5):91-100.
10. Cady RK, Dexter J, Sargent JD, et al. Easy therapeutic management of sumatriptan-induced daily headache. *Neurology* 1996; 47:297-8.
11. PDR Nurse's Handbook; 3rd edition. 1998.
12. Saunders' Nursing Drug Handbook; W.S. Saunders Co. 1999.

References supporting average number of migraine attacks per month:

13. Solomon GD, et al. *Neurology.* 1997; 49:1219-25. (n=327): 3+/- 1.37 per month.
14. Zagami AS, et al. *Neurology.* 1997; 48 (suppl 3):S25-8. (n=2,058).
15. Geraud GEA. *Eur Neurol.* 1996; 32 (suppl 2): 24-7. (n=606): 2.9-3.2 per month.
16. Fletcher PE, et al. *Headache treatment: Trial methodology and new drugs.* Lippincott-Raven, Publishers. 1997. (n=710): 2.9-3.2 per month.
17. Visser WH, et al. *Neurology.* 1996; 46:522-6. (n=84): 3-4 per month.
18. Dowson A. *Eur Neurol.* 1996; 36 (suppl 2):28-31. (n=40): 2 per month.

General References:

19. Beckett B. Headache disorder, in Dipiro J (ed): *Pharmacotherapy: a Pathophysiologic Approach.* Stamford, Simon & Schuster. 1997; pp 1279-91.

20. Diener HC, Limmroth V. A practical guide to the management and prevention of migraine. *Drugs*. 1998; 56:811-24.
21. Gaist D, et al. Misuse of sumatriptan. *Lancet*. 1997; 344:1090.
22. Gaist D, Tsiropoulos I, Sindrup SH. Inappropriate use of sumatriptan: population-based register and interview study. *BMJ*. 1998; 316:1352-3.
23. Goadsby PJ, Olesen J. Increasing the options for effective migraine management. *Neurology*. 1997; 48:s1-s3.
24. Greiner DI, et al. Sumatriptan use in a large group-model health maintenance organization. *Am J Health Syst Pharm*. 1996; 53:633-8.
25. Honkasalo ML, et al. A population-based survey of headache and migraine in 22,809 adults. *Headache*. 1993; 33:403-12.
26. Peroutka S. Drugs effective in the therapy of migraine. Hardman J, Goodman A, Gilman, Limbird L (eds): *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. New York, 1996, pp 487-502.
27. Salonen R, Ashford E, Dathlof C, et al. Intranasal sumatriptan for the acute treatment of migraine. *Neurology*. 1994; 241:463-9.
28. 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. *Neurology*. 2000; 55:754-63.
29. The Finnish Sumatriptan Group and the Cardiovascular Clinical Research Group. A placebo-controlled study of intranasal sumatriptan for the acute treatment of migraine. *Eur Neurol*. 1991; 31:332-8.
30. Touchon J, Bertin L, Pilgrim AJ, et al. A comparison of subcutaneous sumatriptan and dihydroergotamine nasal spray in the acute treatment of migraine. *Neurology*. 1996; 47:361-5.
31. Visser WH, et al. Sumatriptan in clinical practice: a 2-year review of 453 migraine patients. *Neurology*. 1996; 47:46-51.
32. Visser WH, Terwindt GM, Reines SA, et al. Rizatriptan vs. sumatriptan in the acute treatment of migraine. *Arch Neurol*. 1996; 53:1132-7.
33. <http://headaches.about.com/>