

Treatment Guidelines

from The Medical Letter®

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, NY 10801 • A Nonprofit Publication

Volume 6 (Issue 67) March 2008
www.medicalletter.org

Tables

1. Triptans: Onset of Action	Page 17
2. Some Drugs for Treatment of Migraine	Page 18
3. Some Drugs for Prevention of Migraine	Page 20

Drugs for Migraine

Some drugs for treatment of migraine attacks are listed in table 2 on page 18. Drugs for prevention of migraine are listed in table 3 on page 20. Treatment of migraine in the emergency room, which may involve use of intravenous drugs, is not included here.

ANALGESICS

Treatment with a nonopioid analgesic may be sufficient for mild or moderate episodes of migraine without nausea, disability or a need for bed rest. **Aspirin** and **acetaminophen** alone have been shown to be effective for treatment of migraine; they are also marketed in combinations such as *Fiorinal* (aspirin, caffeine and butalbital) and *Fioricet* or *Esgic* (acetaminophen, caffeine and butalbital). Butalbital has not been shown to be effective for treatment of migraine in controlled trials and is associated with tolerance, dependence and analgesic rebound. *Midrin*, which contains acetaminophen, isometheptene (a sympathomimetic amine) and dichloralphenazone (a chloral hydrate compound) is also used for mild to moderate migraine. A combination of acetaminophen, aspirin and caffeine (*Excedrin Migraine*, and others) is available over the counter (OTC).

Ibuprofen 200 mg (*Advil*, *Motrin*, *Advil Migraine*, *Motrin Migraine Pain*, and others) is FDA-approved for OTC treatment of migraine.¹ Other nonsteroidal anti-inflammatory drugs (NSAIDs) such as **naproxen sodium** (*Anaprox*, and others) also have been effective in relieving migraine pain. In one study, the combination of acetaminophen 500 mg, aspirin 500 mg and caffeine 130 mg was more effective than ibuprofen 400 mg for treatment of an acute migraine attack and had a faster onset of action.²

Oral opioid combinations and injected opioids are effective for relief of pain, but they produce the usual opioid adverse effects (such as constipation), and frequent use can lead to drug dependence.³ In one study,

a single 2-tablet dose containing tramadol 75 mg combined with acetaminophen 650 mg (*Ultracet*, and others) was more effective than placebo in patients with moderate-to-severe acute migraine pain.⁴

Decreased gastric motility during an acute migraine attack may interfere with absorption of oral analgesics. **Metoclopramide** (*Reglan*, and others) taken promptly after the onset of symptoms can enhance absorption by increasing gastric motility and may prevent the nausea associated with many migraine attacks.

SEROTONIN (5-HT_{1B/1D}) RECEPTOR AGONISTS (“TRIPTANS”)

Sumatriptan was the first triptan marketed in the US. A selective serotonin-receptor agonist with a short duration of action, it is highly effective for treatment of acute migraine. Sumatriptan is available for subcutaneous self-injection, as a nasal spray, and for oral administration. The injection and nasal spray formulations have a more rapid onset of action than oral tablets. A subcutaneous injection of sumatriptan produces relief within 2 hours in 70% to 80% of patients

Table 1. Triptans: Onset of Action

	Onset of action	Elimination half-life
Almotriptan (<i>Axert</i>)	30-60 min	3-4 hrs
Eletriptan (<i>Relpax</i>)	30-60 min	3-4 hrs
Frovatriptan (<i>Frova</i>)	~2 hrs	~25 hrs
Naratriptan (<i>Amerge</i>)	1-3 hrs	~6 hrs
Rizatriptan (<i>Maxalt</i>)	30-60 min	2-3 hrs
Sumatriptan (<i>Imitrex</i>)		~2 hrs
tablets	30-60 min	
nasal spray	10-15 min	
SC injection	~10 min	
Zolmitriptan (<i>Zomig</i>)		2-3 hrs
tablets	30-60 min	
nasal spray	10-15 min	

Drugs for Migraine

Table 2. Some Drugs for Treatment of Migraine			
Drug	Formulations	Usual dosage	Cost ¹
Serotonin (5-HT_{1B/1D}) Receptor Agonists ("Triptans")			
Almotriptan – <i>Axert</i> (Ortho-McNeil)	6.25, 12.5 mg tabs	12.5 mg PO; can be repeated once after 2 hrs (max 2 doses/d)	\$21.15
Eletriptan – <i>Relpax</i> (Pfizer)	20, 40 mg tabs	20 or 40 mg PO; can be repeated after 2 hrs (max 80 mg/d)	19.95
Frovatriptan – <i>Frova</i> (Endo)	2.5 mg tabs	2.5 mg PO; can be repeated after 2 hrs (max 7.5 mg/d)	21.92
Naratriptan – <i>Amerge</i> (GlaxoSmithKline)	1, 2.5 mg tabs	2.5 mg PO; can be repeated once after 4 hrs (max 5 mg/d)	24.47
Rizatriptan – <i>Maxalt, Maxalt-MLT</i> (Merck)	5, 10 mg tabs; 5, 10 mg orally disintegrating tabs	5 or 10 mg PO; can be repeated after 2 hrs (max 30 mg/d) ²	21.06
Sumatriptan – <i>Imitrex</i> (GlaxoSmithKline)	25, 50, 100 mg tabs	50 or 100 mg PO; can be repeated after 2 hrs (max 200 mg/d)	22.88
	5, 20 mg nasal spray	5, 10 or 20 mg intranasally; can be repeated once after 2 hrs (max 40 mg/d)	34.71
	4, 6 mg/0.5 mL cartridges; 6 mg/0.5 mL vials	6 mg SC; can be repeated once after 1 hr (max 12 mg/d)	81.62
Zolmitriptan – <i>Zomig, Zomig ZMT</i> (AstraZeneca)	2.5, 5 mg tabs; 2.5, 5 mg orally disintegrating tabs	2.5 or 5 mg PO; can be repeated after 2 hrs (max 10 mg/d)	20.07
	5 mg/100 mL nasal spray	5 mg intranasally; can be repeated once after 2 hrs	29.25
Ergot Alkaloids			
Dihydroergotamine mesylate – generic <i>D.H.E. 45</i> (Valeant)	1 mg/mL ampules	1 mg IM or SC; can be repeated at 1 hr intervals (max 3 mg/24 hrs, 6 mg/wk)	33.99 81.93
	<i>Migranal Nasal Spray</i> (Valeant)	4 mg/mL nasal spray	1 spray (0.5 mg) into each nostril, repeated 15 min later (2 mg/dose; max 3 mg/24 hrs)
Ergotamine tartrate – <i>Ergomar</i> (Rosedale)	2 mg sublingual tabs	2 mg sublingually; can be repeated q30min PRN (max 6 mg/24 hrs, 10 mg/wk)	8.66
Ergotamine/cafeine – <i>Cafergot</i> (Novartis)	1 mg/100 mg tabs	2 tabs PO, then 1 q30min x 4 PRN (max 6 tabs/attack)	1.50
	2 mg/100 mg rectal suppositories	1 rectal suppository; can be repeated once 1 hr later	8.03

1. Average cost of one dose at the lowest usual dosage, according to the most recent data (December 31, 2007) from retail pharmacies nationwide available from Wolters Kluwer Health. Prices of generic drugs may vary widely.
2. Patients also taking propranolol should only use a 5-mg dose (max 15 mg/24 hrs).

with moderate to severe migraine. Sumatriptan nasal spray has produced relief in about 60% of patients after 2 hours. Oral sumatriptan has been effective in about 50% to 60% of patients with acute migraine after 2 hours and in about 70% after 4 hours.⁵

Sumatriptan nasal spray was effective and well tolerated in children 8-17 years old.⁶ The reformulated rapid-release sumatriptan tablets may produce pain relief sooner than the older formulation; direct comparisons with other triptans are lacking.⁷ In 2 randomized, double-blind studies, a fixed-dose combination tablet containing sumatriptan 85 mg and naproxen 500 mg, under review by the FDA, achieved better pain relief than either agent as monotherapy in patients with a moderate or severe migraine.⁸

Four other triptans (almotriptan, eletriptan, rizatriptan and zolmitriptan) are similar in efficacy to sumatriptan.⁹ **Zolmitriptan**, like sumatriptan, is available as a nasal spray as well as orally; compared to sumatriptan, fewer patients complain about its taste.¹⁰ **Naratriptan** and especially **frovatriptan** each have a longer half-life and appear to have a slower onset of action and lower initial response rate than other triptans.

Use of a triptan early in an attack, when pain is still mild to moderate in intensity, has been shown to improve outcomes compared to later use.¹¹ In patients with moderate or severe migraine, the rate of recurrence within 24 hours after treatment with a triptan is generally 20% to 40%; it is slightly lower with nara-

triptan and frovatriptan. Recurrences usually respond to a second dose of the triptan.

Adverse Effects – A burning sensation at the injection site is common with subcutaneous sumatriptan. Tingling, flushing, dizziness, drowsiness, fatigue, and a feeling of heaviness, tightness or pressure in the chest may occur with all triptans, but most commonly with injectable sumatriptan. CNS symptoms such as somnolence and asthenia following triptan therapy may be partly related to the resolution of a migraine attack.¹² Angina, myocardial infarction, cardiac arrhythmia, stroke and death have occurred rarely with these drugs. They are contraindicated in patients with coronary, cerebrovascular or other arterial disease, or uncontrolled hypertension.

Drug Interactions – A triptan should not be used within 24 hours after another triptan or an ergotamine-containing drug because vasoconstriction could be additive. Rizatriptan, sumatriptan and zolmitriptan are contraindicated in patients taking an MAO inhibitor or within two weeks of stopping one. Propranolol increases serum concentrations of eletriptan, rizatriptan and zolmitriptan.¹³ Inhibitors of CYP3A4, including verapamil, increase serum concentrations and may increase the toxicity of eletriptan; it should not be used within 72 hours of a strong CYP3A4 inhibitor such as clarithromycin (*Biaxin*, and others).¹⁴ Taking a triptan with an SSRI, or an SNRI such as venlafaxine (*Effexor*), can cause potentially life-threatening serotonin syndrome.¹⁵

ERGOT ALKALOIDS

Ergotamine tartrate, a non-specific serotonin agonist and a vasoconstrictor, has been used for many years for treatment of moderate to severe migraine headache. It is available alone in sublingual tablets and combined with caffeine in oral tablets and suppositories. Comparative studies have shown that oral ergotamine plus caffeine is less effective than a triptan for treatment of acute migraine.¹⁶

Dihydroergotamine mesylate, which can be injected subcutaneously, intramuscularly or intravenously, or sprayed intranasally, is also effective in treating migraine attacks. It is a weaker arterial vasoconstrictor than ergotamine. Dihydroergotamine nasal spray relieves migraine after 2 hours in about 50% of patients with a 15% incidence of headache recurrence within 24 hours. According to Medical Letter consultants, it can be effective in some patients who do not respond to triptans.

Adverse Effects – Nausea and vomiting are fairly common with ergotamine, but can be prevented by pretreat-

ment with or concurrent use of an antiemetic such as prochlorperazine (*Compazine*, and others). Serious adverse effects, such as vascular (including coronary) occlusion and gangrene, are rare and usually associated with overdosage (more than 6 mg in 24 hours or 10 mg per week). Liver disease or fever can accelerate development of severe vasoconstriction. In one retrospective case-control study in >17,000 patients, overuse of ergotamine (≥ 90 daily doses/yr), particularly in patients taking cardiovascular drugs, increased the risk of ischemic events, while overuse of a triptan did not.¹⁷ Long-term use of ergotamine has been associated with retroperitoneal, pleural and pericardial fibrosis and fibrotic thickening of cardiac valves. Dihydroergotamine causes fewer adverse effects than ergotamine; it can cause diarrhea.

Drug Interactions – The effects of ergot alkaloids may be potentiated by triptans, beta-blockers, dopamine, nicotine or CYP3A4 inhibitors. Ergot alkaloids and triptans should not be taken within 24 hours of each other. Use of ergot alkaloids is contraindicated with strong CYP3A4 inhibitors such as clarithromycin or itraconazole (*Sporanox*, and others).¹⁴

MEDICATION-OVERUSE HEADACHE

Overuse (two or more days a week for >3 months) of analgesics, ergot alkaloids (except dihydroergotamine) or triptans can cause medication-overuse headache, a dull or migraine-like headache that is present at least 15 days per month.¹⁸ Preventive measures include restricting use of these drugs (per attack, per week and per month) and initiating prophylactic treatment when necessary.¹⁹

PREVENTION

Patients with frequent or severe disabling migraine headaches and those who cannot take vasoconstrictors or are refractory to acute treatment should receive prophylactic treatment. Menstrual or other predictable migraine attacks may sometimes be prevented by a brief course of an NSAID, ergot alkaloid or triptan, particularly naratriptan or frovatriptan taken for several days before and during the first few days of menstruation.^{20,21}

For continuous prophylaxis, **beta-blockers** are commonly used. Propranolol and timolol are the only beta-blockers approved by the FDA for this indication, but metoprolol, nadolol (*Corgard*, and others) and atenolol (*Tenormin*, and others) also have been effective in preventing migraine.²² All beta-blockers can cause fatigue, exercise intolerance, depression and orthostatic hypotension, and should not be used in patients with

Drugs for Migraine

Table 3. Some Drugs for Prevention of Migraine			
Drug	Formulations	Usual dosage	Cost ¹
Beta-Blockers			
Metoprolol – generic ²	25, 50, 100 mg tabs	50-100 mg bid	\$29.40
<i>Lopressor</i> (Novartis) ²	50, 100 mg tabs		78.60
Extended-release – generic ²	25, 50, 100, 200 mg tabs	100-200 mg once/d	34.50
<i>Toprol-XL</i> (AstraZeneca) ²			42.30
Propranolol – generic	10, 20, 40, 60, 80 mg tabs	160-240 mg/d divided bid, tid or qid	33.60
<i>Inderal</i> (Wyeth)			84.60
Extended-release – generic	60, 80, 120, 160 mg caps	160-240 mg once/d	64.20
<i>Inderal LA</i> (Wyeth)			81.60
Timolol – generic	5, 10, 20 mg tabs	10-15 mg bid or 20 mg once/d	28.80
Antiepileptic Drugs			
Valproate ³ –	125, 250, 500 mg tabs;		
<i>Depakote</i> (Abbott)	125 mg sprinkle caps	250-500 mg bid	100.80
<i>Depakote ER</i>	250, 500 mg tabs	500-1000 mg once/d	82.20
Topiramate – <i>Topamax</i> (Ortho-McNeil)	25, 50, 100, 200 mg tabs; 15, 25 mg caps	50 mg bid	255.00
Tricyclic Antidepressants			
Amitriptyline ² – generic	10, 25, 50, 75, 100, 150 mg tabs	30-150 mg once/d	13.50
Calcium-Channel Blocker			
Verapamil ² – generic	40, 80, 120 mg tabs	80 mg tid or qid	27.90
<i>Calan</i> (Pfizer)			82.80
Extended-release – generic	120, 180, 240 mg tabs; 120, 180, 240 mg caps	240 mg once/d	32.70
<i>Calan SR</i>	120, 180, 240 mg caplets		76.20
Angiotensin-Converting Enzyme (ACE) Inhibitor			
Lisinopril ² – generic	5, 10, 20 mg tabs	5-40 mg once/d	24.90
<i>Prinivil</i> (Merck)			30.30
<i>Zestril</i> (AstraZeneca)	2.5, 5, 10, 20, 30, 40 mg tabs		39.30
Angiotensin Receptor Blocker (ARB)			
Candesartan ² –	4, 8, 16, 32 mg tabs	8-32 mg once/d	
<i>Atacand</i> (AstraZeneca)			55.80

1. Average cost for 30 days' treatment with the lowest usual dosage, according to the most recent data (December 31, 2007) from retail pharmacies nationwide, available from Wolters Kluwer Health. Prices of generic drugs may vary widely.
2. Not approved by the FDA for this indication.
3. Marketed as divalproex sodium (*Depakote*) and valproic acid (*Depakene*, and others). Only divalproex sodium is FDA-approved for prevention of migraine.

decompensated heart failure. All are relatively contraindicated in patients with asthma.

The antiepileptic drugs **valproate** and **topiramate** have been effective in decreasing migraine frequency; about 50% of patients achieve a $\geq 50\%$ reduction in headache frequency with these drugs.²³⁻²⁵ Other antiepileptic drugs such as gabapentin (*Neurontin*, and others) have also been tried for this indication with varying degrees of success.^{24,26} In randomized, placebo-controlled studies, topiramate and valproate have shown similar efficacy to propranolol for migraine prevention.²⁷ Topiramate has also reduced the number of migraines per month in patients with chronic migraine (≥ 15 headaches/month), with and without medication overuse.^{28,29}

Adverse effects of **valproate** include nausea, fatigue, tremor, weight gain and hair loss. Acute hepatic failure, pancreatitis and hyperammonemia (in patients with

urea cycle disorders) occur rarely. Rare complications include polycystic ovary syndrome, hyperinsulinemia, lipid abnormalities, hirsutism and menstrual disturbances. **Topiramate**, which is a carbonic anhydrase inhibitor, commonly causes paresthesias; other adverse effects include fatigue, language and cognitive impairment, taste perversion and weight loss.³⁰ Topiramate can rarely cause angle-closure glaucoma, oligohydrosis, nephrolithiasis and symptomatic metabolic acidosis. An analysis of data from clinical trials found that patients taking antiepileptic drugs, including valproate and topiramate, were more likely to report suicidal ideation or behavior than those taking a placebo (0.43% vs. 0.22%).³¹

Tricyclic antidepressants can prevent migraine in some patients and may be given concurrently with other prophylactic agents, but often cause sedation, dry mouth and weight gain. Amitriptyline has been shown to be effective.³² Nortriptyline (*Aventyl*, and others) is

also frequently used for this purpose and has fewer anticholinergic adverse effects.

Calcium-channel blockers are also used for prevention of migraine, but the evidence for their effectiveness is weak. Verapamil was somewhat more effective than placebo in some small studies.²² Calcium-channel blockers should not be used with beta-blockers because of the potential for heart block.

In small double-blind studies, the **angiotensin-converting enzyme (ACE) inhibitor** lisinopril and the **angiotensin receptor blocker (ARB)** candesartan cilexetil have reduced migraine frequency.^{33,34}

Nonsteroidal anti-inflammatory drugs (NSAIDs), particularly naproxen sodium and flurbiprofen (*Ansaid*, and others), have been used for short-term prevention of migraine, as in menstrual migraine, as well as for aborting acute attacks.

The dietary supplements petasites (butterbur) 100-150 mg per day, riboflavin 400 mg per day, magnesium citrate 600 mg per day, coenzyme Q10 300 mg per day, and feverfew 18.75 mg per day, have been reported to be effective in small randomized placebo-controlled trials.³⁵⁻³⁹

Pericranial injections of **botulinum toxin type A** (*Botox*) have been tried for prophylactic treatment of episodic migraine, but they are ineffective,⁴⁰⁻⁴² their use in chronic migraine is under investigation.

PREGNANCY

All ergot alkaloids are contraindicated in pregnancy. NSAIDs should not be used in the 3rd trimester because they can cause premature closure of the ductus arteriosus. The triptans are classified as category C (risk cannot be ruled out) for use in pregnancy, but sumatriptan, which has been used the longest, does not appear to be associated with an increased risk of birth defects.^{43,44} Preventive therapy is generally not recommended in pregnancy.

DRUGS OF CHOICE

A nonopioid analgesic may be effective for **treatment** of mild to moderate migraine. A triptan is the drug of choice for treatment of moderate to severe migraine headache. Oral ergot preparations cost less than the triptans, but are not as effective and are associated with more adverse events. Short-acting oral triptans are similar in their efficacy and speed of onset; naratriptan and especially frovatriptan have a slower onset and longer duration. The nasal spray forms of sumatriptan and

zolmitriptan have a faster onset of action than all the oral triptans and probably deserve wider use. Sumatriptan SC is expensive, but it is the fastest acting and most effective triptan formulation. Some patients may respond to one triptan and not to another.

For **prevention** of migraine attacks, the antiepileptics valproate and topiramate are increasingly being used, but there is no evidence that they are more effective than beta-blockers, which cost much less.

1. C Suthisisang et al. Efficacy of low-dose ibuprofen in acute migraine treatment: systematic review and meta-analysis. *Ann Pharmacother* 2007; 41:1782.
2. J Goldstein et al. Acetaminophen, aspirin, and caffeine in combination versus ibuprofen for acute migraine: results from a multicenter, double-blind, randomized, parallel-group, single-dose, placebo-controlled study. *Headache* 2006; 46:444.
3. Drugs for pain. *Treat Guidel Med Lett* 2007; 5:23.
4. SD Silberstein et al. Tramadol/acetaminophen for the treatment of acute migraine pain: findings of a randomized, placebo-controlled trial. *Headache* 2005; 45:1317
5. SD Silberstein. Migraine. *Lancet* 2004; 363:381.
6. K Ahonen et al. Nasal sumatriptan is effective in treatment of migraine attacks in children: a randomized trial. *Neurology* 2004; 62:883.
7. FD Sheftell et al. Two replicate randomized, double-blind, placebo-controlled trials of the time to onset of pain relief in the acute treatment of migraine with a fast-disintegrating/rapid-release formulation of sumatriptan tablets. *Clin Ther* 2005; 27:407
8. JL Brandes et al. Sumatriptan-naproxen for acute treatment of migraine: a randomized trial. *JAMA* 2007; 297:1443.
9. MD Ferrari et al. Oral triptans (serotonin 5-HT_{1B/1D} agonists) in acute migraine treatment: a meta-analysis of 53 trials. *Lancet* 2001; 358:1668.
10. Zolmitriptan (*Zomig*) nasal spray for migraine. *Med Lett Drugs Ther* 2004; 46:7.
11. FG Freitag et al. Effect of pain intensity and time to administration on responsiveness to almotriptan: results from AXERT 12.5 mg Time Versus Intensity Migraine Study (AIMS). *Headache* 2007; 47:519.
12. PJ Goadsby et al. Treatment-emergent CNS symptoms following triptan therapy are part of the attack. *Cephalalgia* 2007; 27:254.
13. The Medical Letter Adverse Drug Interactions Program.
14. CYP3A and drug interactions. *Med Lett Drugs Ther* 2005; 47:54.
15. FDA Public Health Advisory. Combined use of 5-hydroxytryptamine receptor agonists (triptans), selective serotonin reuptake inhibitors (SSRIs) or selective serotonin/norepinephrine reuptake inhibitors (SNRIs) may result in life-threatening serotonin syndrome. Updated November 24, 2006. Available at www.fda.gov/cder/drug/advisory/SSRI_SS200607.htm.
16. MJ Láinez et al. Crossover, double-blind clinical trial comparing almotriptan and ergotamine plus caffeine for acute migraine therapy. *Eur J Neurol* 2007; 14:269.
17. EA Wammes-van der Heijden et al. Risk of ischemic complications related to the intensity of triptan and ergotamine use. *Neurology* 2006; 67:1128.
18. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24 suppl 1:9.
19. Z Katsarava and R Jensen. Medication-overuse headache: where are we now? *Curr Opin Neurol* 2007; 20:326.
20. LK Mannix et al. Efficacy and tolerability of naratriptan for short-term prevention of menstrually related migraine: data from two randomized, double-blind, placebo-controlled studies. *Headache* 2007; 47:1037.

Drugs for Migraine

21. SD Silberstein et al. A randomized trial of frovatriptan for the intermittent prevention of menstrual migraine. *Neurology* 2004; 63:261.
22. V Limmroth and MC Michel. The prevention of migraine: a critical review with special emphasis on beta-adrenoceptor blockers. *Br J Clin Pharmacol* 2001; 52:237.
23. V Shaygannejad et al. Comparison of the effect of topiramate and sodium valproate in migraine prevention: a randomized blinded crossover study. *Headache* 2006; 46:642.
24. E Chronicle and W Mulleners. Anticonvulsant drugs for migraine prophylaxis. *Cochrane Database Syst Rev* 2004; (3):CD003226.
25. Topiramate (*Topamax*) for prevention of migraine. *Med Lett Drugs Ther* 2005; 47:9.
26. Gabapentin (*Neurontin*) for chronic pain. *Med Lett Drugs Ther* 2004; 46:29.
27. HC Diener et al. Topiramate in migraine prophylaxis--results from a placebo-controlled trial with propranolol as an active control. *J Neurol* 2004; 251:943.
28. SD Silberstein et al. Efficacy and safety of topiramate for the treatment of chronic migraine: a randomized, double-blind, placebo-controlled trial. *Headache* 2007; 47:170.
29. HC Diener et al. Topiramate reduces headache days in chronic migraine: a randomized, double-blind, placebo-controlled study. *Cephalalgia* 2007; 27:814.
30. MJ Láinez et al. Time course of adverse events most commonly associated with topiramate for migraine prevention. *Eur J Neurol* 2007; 14:900.
31. Information for Healthcare Professionals: Suicidalilty and antiepileptic drugs. FDA Alert. January 31, 2008. Available at: www.fda.gov/cder/drug/InfoSheets/HCP/antiepilepticsHCP.htm.
32. DK Ziegler et al. Propranolol and amitriptyline in prophylaxis of migraine. Pharmacokinetic and therapeutic effects. *Arch Neurol* 1993; 50:825.
33. H Schrader et al. Prophylactic treatment of migraine with angiotensin converting enzyme inhibitor (lisinopril): randomised, placebo controlled, crossover study. *BMJ* 2001; 322:19.
34. E Tronvik et al. Prophylactic treatment of migraine with an angiotensin II receptor blocker: a randomized controlled trial. *JAMA* 2003; 289:65.
35. RB Lipton et al. Petasites *hybridus* root (butterbur) is an effective preventive treatment for migraine. *Neurology* 2004; 63:2240.
36. J Schoenen et al. Effectiveness of high-dose riboflavin in migraine prophylaxis. a randomized controlled trial. *Neurology* 1998; 50:466.
37. A Peikert et al. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. *Cephalalgia* 1996; 16:257.
38. PS Sandor et al. Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial. *Neurology* 2005; 64:713.
39. HC Diener et al. Efficacy and safety of 6.25 mg t.i.d. feverfew CO₂-extract (MIG-99) in migraine prevention—a randomized, double-blind, multicentre, placebo-controlled study. *Cephalalgia* 2005; 25:1031.
40. S Evers and J Olesen. Botulinum toxin in headache treatment: the end of the road? *Cephalalgia* 2006; 26:769.
41. SK Aurora et al. Botulinum toxin type A prophylactic treatment of episodic migraine: a randomized, double-blind, placebo-controlled exploratory study. *Headache* 2007; 47:486.
42. AH Elkind et al. A series of three sequential, randomized, controlled studies of repeated treatments with botulinum toxin type A for migraine prophylaxis. *J Pain* 2006; 7:688.
43. JP Gladstone et al. Migraine in special populations. Treatment strategies for children and adolescents, pregnant women, and the elderly. *Postgrad Med* 2004; 115:39.
44. ML Hilaire et al. Treatment of migraine headaches with sumatriptan in pregnancy. *Ann Pharmacother* 2004; 38:1726.

Coming Soon in *Treatment Guidelines*:

Diet, Drugs and Surgery for Weight Loss – April 2008

Anticoagulants and Antiplatelet Drugs – May 2008

Treatment Guidelines[®]

from The Medical Letter

EDITOR: Mark Abramowicz, M.D.

EXECUTIVE EDITOR: Gianna Zuccotti, M.D., M.P.H., Weill Medical College of Cornell University

DEPUTY EDITOR: Jean-Marie Pflomm, Pharm.D.

ASSISTANT EDITOR, DRUG INFORMATION: Susan Morey, Pharm.D.

CONTRIBUTING EDITOR: Eric J. Epstein, M.D. Albert Einstein College of Medicine

CONTRIBUTING EDITOR, DRUG INTERACTIONS: Philip D. Hansten, Pharm.D., University of Washington

ADVISORY BOARD:

Jules Hirsch, M.D., Rockefeller University

David N. Juurlink, BPhm, M.D., PhD, Sunnybrook Health Sciences Centre

Richard B. Kim, M.D., University of Western Ontario

Gerald L. Mandell, M.D., University of Virginia School of Medicine

Hans Meinertz, M.D., University Hospital, Copenhagen

Dan M. Roden, M.D., Vanderbilt University School of Medicine

F. Estelle R. Simons, M.D., University of Manitoba

Neal H. Steigbigel, M.D., New York University School of Medicine

SENIOR ASSOCIATE EDITORS: Donna Goodstein, Amy Faucard

ASSOCIATE EDITOR: Cynthia Macapagal Covey

EDITORIAL FELLOWS:

Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School

Lauren K. Schwartz, M.D., Mount Sinai School of Medicine

DRUG INTERACTIONS FELLOW: Emily Ung, BScPhm, Children's Hospital of Western Ontario

EDITORIAL ASSISTANT: Liz Donohue

PRODUCTION COORDINATOR: Cheryl Brown

MANAGING EDITOR: Susie Wong

EXECUTIVE DIRECTOR OF SALES: Gene Carbona

FULFILLMENT AND SYSTEMS MANAGER: Cristine Romatowski

DIRECTOR OF MARKETING COMMUNICATIONS: Joanne F. Valentino

VICE PRESIDENT AND PUBLISHER: Yosef Wissner-Levy

Founded in 1959 by

Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer: The Medical Letter is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter is supported solely by subscription fees and accepts no advertising, grants or donations.

No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The editors do not warrant that all the material in this publication is accurate and complete in every respect. The editors shall not be held responsible for any damage resulting from any error, inaccuracy or omission.

Subscription Services

Mailing Address:

The Medical Letter, Inc.
1000 Main Street
New Rochelle, NY 10801-7537

Customer Service:

Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
Web Site: www.medicalletter.org
E-mail: custserv@medicalletter.org

Permissions:

To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org

Subscriptions (US):

1 year - \$98; 2 years - \$167;
3 years - \$235. \$49/yr. for students, interns, residents and fellows in the US and Canada.

E-mail site license inquiries to:

info@medicalletter.org or call 800-211-2769 x315.
Special fees for bulk subscriptions. Special classroom rates are available. Back issues are \$12 each. Major credit cards accepted.

Copyright 2008. ISSN 1541-2792

Introducing

Treatment Guidelines: Online Continuing Medical Education

Up to 24 credits included with your subscription

www.medicalletter.org/tgcm

For over 25 years, The Medical Letter has offered health care professionals continuing medical education (CME) with *The Medical Letter on Drugs and Therapeutics*. We are now offering CME for *Treatment Guidelines from The Medical Letter* in an online format only, called the Online Series. Each Online Series is comprised of 6 monthly exams and eligible for up to 12 credits. For those who just need a few credits, we also offer the Quick Online Credit Exam (earn up to 2 credits/12 questions). For more information, please visit us at www.medicalletter.org/tgcm.

Choose CME from *Treatment Guidelines from The Medical Letter* and earn up to 24 Category 1 AMA PRA Credits per year in the format that's right for you:

Online Series - Answer 12 questions per issue online. Earn up to 2 credits/exam. Take up to 6 short exams per six-month series and earn up to a total of 12 credits. The Online Series is included with a paid subscription to *Treatment Guidelines*.

Quick Online Credit Exam - Access content for any available issue, answer 12 questions online, and earn up to 2 credits for \$12.00 (available to both subscribers and non-subscribers).

ACCREDITATION INFORMATION:

ACCME: The Medical Letter is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Medical Letter designates this educational activity for a maximum of 2 AMA PRA Category 1 Credit(s)[™]. Physicians should only claim credit commensurate with the extent of their participation in this activity. This CME activity was planned and produced in accordance with the ACCME Essentials.

AAFP: The Medical Letter (2008) has been reviewed and is acceptable for up to 15 Prescribed credits by the American Academy of Family Physicians. AAFP accreditation begins 01/01/08. Term of approval is for one year from this date. This exam is approved for 1.25 Prescribed credits. Credits may be claimed for one year from the date of this exam.

ACPE: The Medical Letter is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This issue is acceptable for 2.0 hours of Continuing Education Credit (0.2 CEU).



AANP and AAPA: The **American Academy of Nurse Practitioners (AANP)** and the **American Academy of Physician Assistants (AAPA)** accept *AMA Category 1 Credit* for the Physician's Recognition Award from organizations accredited by the ACCME.

AOA: This activity, being ACCME (AMA) approved, is acceptable for Category 2-B credit by the **American Osteopathic Association**.

MISSION:

The mission of The Medical Letter's Continuing Medical Education Program is to support the professional development of health care professionals including physicians, nurse practitioners, pharmacists and physician assistants by providing independent, unbiased drug information and prescribing recommendations that are free of industry influence. The program content includes current information and unbiased reviews of FDA-approved and off-label uses of drugs, their mechanisms of action, clinical trials, dosage and administration, adverse effects and drug interactions. The Medical Letter delivers educational content in the form of self-study material.

The expected outcome of the CME Program is that knowledge and consideration of the information contained in *The Medical Letter* and *Treatment Guidelines* can affect health care practice and ultimately result in improved patient care and outcomes.

The Medical Letter will strive to continually improve the CME program through periodic assessment of the program and activities. The Medical Letter aims to be a leader in supporting the professional development of health care professionals by providing continuing medical education that is unbiased and free of industry influence.

LEARNING OBJECTIVES:

Activity participants will read and assimilate unbiased reviews of FDA-approved and off-label uses of drugs and other treatment modalities.

Activity participants will be able to select and prescribe, or confirm the appropriateness of the prescribed usage of the drugs and other therapeutic modalities discussed in *Treatment Guidelines* with specific attention to pathophysiology, dosage and administration, drug metabolism and interactions, and patient management.

Activity participants will make independent and informed therapeutic choices in their practice.

DO NOT FAX OR MAIL THIS EXAM

To take this exam, go to:

www.medicalletter.org/tgcm

Issue 67 Questions

1. Metoclopramide taken at the onset of migraine symptoms can:
- increase gastric motility
 - enhance absorption of oral analgesics
 - decrease nausea
 - all of the above

Page: 17

2. The fastest-acting triptan formulations (excluding injections) are:
- sublingual tablets
 - swallowed tablets
 - nasal sprays
 - rectal suppositories

Page: 17

Continues on next page >>

Treatment Guidelines: Online Continuing Medical Education
(www.medicalletter.org/tgcme)

<p>3. The highest response rate within 2 hours has been with: a. sumatriptan tablets b. sumatriptan nasal spray c. sumatriptan subcutaneous injection d. naratriptan Page: 17/18</p>	<p>8. For the first-line treatment of mild migraine, it would be reasonable to use: a. a nonopioid analgesic b. an opioid analgesic c. ergotamine tartrate d. botulinum toxin Page: 21</p>
<p>4. Naratriptan and frovatriptan, compared to sumatriptan, have: a. a faster onset of action b. a higher initial response rate c. a shorter half-life d. a lower rate of recurrences Page: 18/19</p>	<p>9. For continuous prophylaxis of migraine, the drug of choice for most patients would be: a. a triptan b. a beta-blocker c. a tricyclic antidepressant d. an ACE inhibitor Page: 21</p>
<p>5. Triptans can cause adverse reactions if they are taken concurrently with: a. ergotamine tartrate b. an MAO inhibitor c. an SSRI d. all of the above Page: 19</p>	<p>10. The drug of choice for treatment of moderate to severe migraine is: a. naproxen sodium b. a beta-blocker c. a triptan d. dihydroergotamine Page: 21</p>
<p>6. Overuse of ergots or triptans can cause: a. leukopenia b. Lupus c. hair loss d. headache Page: 19</p>	<p>11. Which one of the following statements about triptans is true? a. Patients who do not respond to one may respond to another b. Patients who do not respond to one are unlikely to respond to another c. they all have about the same duration of action d. they all can be given parenterally Page: 21</p>
<p>7. Topiramate is effective for migraine prophylaxis, but it can often cause: a. hyperglycemia b. cognitive impairment c. bronchospasm d. compulsive gambling Page: 20</p>	<p>12. For prevention of migraine attacks, the antiepileptics valproate and topiramate appear to be: a. less effective than beta-blockers b. about as effective as beta-blockers c. more effective than beta-blockers d. ineffective Page: 21</p>

ACPE UPN: 379-000-08-067-H01-P