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DRUGS FOR MIGRAINE

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▶ Treatment of Migraine

An oral nonopioid analgesic may be sufficient for treatment of mild to moderate migraine without severe nausea or vomiting. A triptan is the drug of choice for treatment of moderate to severe migraine.^{1,2} Use of a triptan early in an attack when pain is still mild to moderate in intensity improves headache response and reduces recurrence rates.

ANALGESICS – Aspirin and acetaminophen, used alone or together in combination with caffeine (*Excedrin Migraine*, and others), and **nonsteroidal anti-inflammatory drugs (NSAIDs)** such as naproxen sodium (*Aleve*, and others) and ibuprofen (*Advil*, *Motrin*, and generics) are effective in relieving mild to moderate migraine pain.³⁻⁵ The NSAID diclofenac is FDA-approved as a powder for oral solution (*Cambia*) for treatment of migraine; it has a rapid onset of action (about 15 minutes).⁶ Some patients may respond better to one NSAID than to another.

Products that combine **butalbital** and caffeine with aspirin (*Fiorinal*, and others) or acetaminophen (*Fioricet*, and others) are used for treatment of migraine despite evidence that butalbital is not effective in relieving migraine pain. Their frequent use can lead to tolerance, addiction, and medication overuse headache. Oral combinations of aspirin or acetaminophen with an **opioid** can be effective for relief of migraine pain, but they cause the usual opioid adverse effects (e.g., nausea, drowsiness, and constipation), and regular use can lead to dependence and addiction.

Pregnancy – Occasional use of acetaminophen for treatment of mild to moderate migraine during pregnancy is generally considered safe.

TRIPTANS – The short-acting oral serotonin (5-HT_{1B/1D}) receptor agonists (triptans) **sumatriptan** (*Imitrex*, and others), **almotriptan** (*Axert*, and generics), **eletriptan**

Recommendations for Treatment and Prevention of Migraine

Treatment

- ▶ A nonopioid analgesic may be effective for mild to moderate migraine.
- ▶ A triptan is the drug of choice for moderate to severe migraine.
- ▶ The short-acting oral triptans sumatriptan, almotriptan, eletriptan, rizatriptan, and zolmitriptan are similar in efficacy and speed of onset.
- ▶ Intranasal triptan formulations have a faster onset of action than oral triptans.
- ▶ Subcutaneous sumatriptan is the fastest-acting and most effective triptan formulation.
- ▶ Patients who do not respond to one triptan may respond to another.
- ▶ Use of opioids and butalbital for migraine treatment is discouraged.

Prevention

- ▶ Topiramate, valproate, and the beta blockers propranolol, timolol, and metoprolol are effective for prevention of migraine.

(*Relpax*), **rizatriptan** (*Maxalt*, and generics), and **zolmitriptan** (*Zomig*, and generics) are similar in efficacy.⁷ 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.⁸ Patients with migraine who have nausea or vomiting may not be able to take an oral triptan.

An oral fixed-dose combination of sumatriptan and naproxen (*Treximet*) is more effective in relieving moderate or severe migraine pain than either of its components alone.⁹

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

Comparison Chart of Triptans (online only)

www.medicalletter.org/downloads/triptans.pdf

Table 1. Triptans

	Onset of action	Elimination half-life
Almotriptan	30-60 min	3-4 hrs
Eletriptan	30-60 min	~4 hrs
Frovatriptan	~2 hrs	~25 hrs
Naratriptan	1-3 hrs	~6 hrs
Rizatriptan	30-60 min	2-3 hrs
Sumatriptan tablets	30-60 min	~2 hrs
nasal spray and powder	10-15 min	
SC injection	~10 min	
Zolmitriptan tablets	30-60 min	2-3 hrs
nasal spray	10-15 min	

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.¹⁰

Subcutaneously administered sumatriptan relieves pain faster (in about 10 minutes) and more effectively than other triptan formulations, but it causes more adverse effects.

Recurrence – In patients with moderate to severe migraine, the rate of recurrence within 24 hours after treatment with a triptan is generally 20-40%. Early treatment of an attack reduces recurrence rates. Recurrences may respond to a second dose of the triptan.

Adverse Effects – Tingling, flushing, dizziness, drowsiness, fatigue, and a feeling of heaviness, tightness, or pressure in the chest can occur with all triptans, but most commonly with SC sumatriptan. A burning sensation at the injection site is also common with SC sumatriptan. Intranasal formulations of sumatriptan and zolmitriptan can have an unpleasant taste. CNS symptoms such as somnolence and asthenia following triptan therapy may be part of the migraine attack, unmasked by the successful treatment of pain, rather than adverse effects of the drugs. Sumatriptan is contraindicated for use in patients with severe hepatic impairment. Naratriptan is contraindicated in patients with severe renal or hepatic impairment.

Angina, myocardial infarction, cardiac arrhythmia, stroke, seizure, and death have occurred rarely with triptans.¹¹ All triptans are contraindicated for use in patients with ischemic or vasospastic coronary artery disease, Wolff-Parkinson-White syndrome, peripheral vascular disease, ischemic bowel disease, uncontrolled hypertension, or a history of stroke, transient ischemic attack, hemiplegic migraine, or migraine with brainstem aura. Triptans should be used with caution in patients with other significant risk factors for vascular disease, particularly diabetes.

Drug Interactions – The labels of all triptans state that a triptan should not be taken within 24 hours of another triptan or an ergot because vasoconstriction could be additive. MAO inhibitors increase serum concentrations of rizatriptan, sumatriptan, and zolmitriptan; they should not be used within 2 weeks of each other. Propranolol increases serum concentrations of eletriptan, frovatriptan, rizatriptan, and zolmitriptan. Cimetidine increases serum concentrations of zolmitriptan. Inhibitors of CYP3A4 can increase serum concentrations of almotriptan and eletriptan.¹² Cases of serotonin syndrome have been reported with concurrent use of triptans and selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs), but data from large observational databases suggest that the risk is low.^{13,14}

Pregnancy and Lactation – Based on available evidence, use of sumatriptan, or possibly rizatriptan, eletriptan, or zolmitriptan during pregnancy does not appear to be associated with an increased risk of birth defects.^{15,16} Levels of sumatriptan and eletriptan in breast milk are low and these drugs would not be expected to cause adverse effects in most breastfed infants¹⁷; avoiding breastfeeding for 8-12 hours after taking a short-acting triptan would reduce the infant's risk of exposure to the drug.

ERGOTS – A fixed-dose combination of **ergotamine tartrate**, a nonspecific serotonin agonist and vasoconstrictor, and caffeine is available as tablets (*Cafergot*) and suppositories (*Migergot*) for treatment of moderate to severe migraine. The combination is less effective than a triptan for acute treatment of migraine.¹⁸

Dihydroergotamine, which can be administered subcutaneously, intramuscularly, intravenously (*D.H.E.*, and generics), or intranasally (*Migranal*), is effective for acute treatment of migraine. Dihydroergotamine nasal spray relieves migraine after 2 hours in about 50% of patients, with a 15% incidence of recurrence within 24 hours. It can be effective in some patients who do not respond to triptans.

Adverse Effects – Dihydroergotamine is a weaker arterial vasoconstrictor than ergotamine and causes fewer serious adverse effects. Nausea and vomiting are fairly common with ergotamine, but pretreatment with or concurrent use of an antiemetic such as metoclopramide (*Reglan*, and generics) can reduce GI effects. Serious adverse effects, such as vascular (including coronary) occlusion and gangrene, are rare and are usually associated with overdosage (>6 mg in 24 hours or >10 mg per week). Hepatic impairment

Table 2. Some Drugs for Treatment of Migraine

Drug	Formulations	Usual Adult Dosage ¹	Cost ²
Triptans			
Almotriptan ³ – generic <i>Axert</i> (Janssen)	6.25, 12.5 mg tabs	6.25 or 12.5 mg PO; can be repeated after 2 hrs (max 25 mg/d)	\$33.00 42.70
Eletriptan – <i>Relpax</i> (Pfizer)	20, 40 mg tabs	20 or 40 mg PO; can be repeated after 2 hrs (max 80 mg/d)	52.00
Frovatriptan – generic <i>Frova</i> (Endo)	2.5 mg tabs	2.5 mg PO; can be repeated after 2 hrs (max 7.5 mg/d)	53.60 73.60
Naratriptan – generic <i>Amerge</i> (GSK)	1, 2.5 mg tabs	2.5 mg PO; can be repeated after 4 hrs (max 5 mg/d)	11.00 56.60
Rizatriptan ⁴ – generic	5, 10 mg tabs	5 or 10 mg PO; can be repeated after 2 hrs (max 30 mg/d) ^{5,6}	1.60
<i>Maxalt</i> (Merck)	5, 10 mg orally disintegrating tabs		3.20
<i>Maxalt-MLT</i>	5, 10 mg tabs		36.60
	5, 10 mg orally disintegrating tabs		36.60
Sumatriptan – generic <i>Imitrex</i> (GSK)	25, 50, 100 mg tabs	50 or 100 mg PO; can be repeated after 2 hrs (max 200 mg/d)	2.00 60.40
	6 mg/0.5 mL, vials; 4, 6 mg/0.5 mL auto-injector pen and refill cartridge ⁷	6 mg SC; can be repeated after 1 hr (max 12 mg/d)	45.10 176.10
	5, 20 mg/0.1 mL nasal spray	5, 10, or 20 mg intranasally; can be repeated after 2 hrs (max 40 mg/d)	49.20 75.40
<i>Onzetra Xsail</i> (Avanir)	11 mg nasal powder capsules	22 mg intranasally; can be repeated after 2 hrs (max 44 mg/d)	65.00
<i>Sumavel DosePro</i> (Endo)	6 mg/0.5 mL needle-free delivery system	6 mg SC; can be repeated after 1 hr (max 12 mg/d)	169.20
<i>Zembrace SymTouch</i> (Promius)	3 mg/0.5 mL auto-injector	3 mg SC; can be repeated after 1 hr (max 12 mg/d)	149.80
Zolmitriptan – generic	2.5, 5 mg tabs	2.5 or 5 mg PO; can be repeated after 2 hrs (max 10 mg/d) ⁸	26.20 27.70
<i>Zomig</i> (Impax)	2.5, 5 mg orally disintegrating tabs		89.40
<i>Zomig-ZMT</i>	2.5, 5 mg tabs		89.40
<i>Zomig</i> nasal spray ³	2.5, 5 mg orally disintegrating tabs		89.40
	2.5, 5 mg/0.1 mL nasal spray	2.5 or 5 mg intranasally; can be repeated after 2 hrs (max 10 mg/d)	61.50
Triptan/NSAID Combination			
Sumatriptan/naproxen ³ – <i>Treximet</i> (Pernix)	10/60, 85/500 mg tabs	85/500 mg PO; can be repeated after 2 hrs (max 170/1000 mg/d) ⁹	81.00
Ergots			
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/d, 6 mg/wk)	124.80 1176.80
<i>Migranal</i> nasal spray (Valeant)	4 mg/mL nasal spray	1 spray (0.5 mg) into each nostril, repeated 15 min later (2 mg/dose; max 3 mg/d)	421.40
Ergotamine/caffeine – generic <i>Cafergot</i> (Sandoz)	1/100 mg tabs	2 tabs PO at attack onset, then 1 tab q30 min PRN (max 6 tabs/attack)	11.10 12.40
<i>Migergot</i> (Horizon)	2/100 mg rectal suppository	1 supp at attack onset, repeat in 1 hr if needed (max 2 supp/attack)	63.90

1. Dosage may need to be adjusted for renal or hepatic impairment or for drug interactions.

2. Approximate WAC for one dose at the lowest usual dosage. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. January 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.

3. Also approved for use in patients 12-17 years old.

4. Also approved for use in patients 6-17 years old.

5. Dose for pediatric patients is 5 mg (<40 kg) or 10 mg (≥40 kg). In pediatric patients, the efficacy and safety of redosing within 24 hours have not been established.

6. Adults and children (≥40 kg) also taking propranolol should only use a 5-mg dose (max 15 mg/d for adults and 5 mg/d for children). Combined use not recommended for children weighing <40 kg.

7. Generic also available as a 6-mg syringe.

8. Patients also taking cimetidine should only use a 2.5-mg dose (max 5 mg/d).

9. Dosage for adolescents 12-17 years old is 10/60 mg (max 85/500 mg/d).

or fever can accelerate development of severe vasoconstriction. Ergots are contraindicated in patients with arterial disease or uncontrolled hypertension.

Drug Interactions – The effects of ergots can be potentiated by triptans, beta blockers, dopamine, nicotine, or CYP3A4 inhibitors. Use of ergots is contraindicated with strong CYP3A4 inhibitors such as

clarithromycin (*Biaxin*, and generics) or itraconazole (*Sporanox*, and generics).¹² Ergots and triptans should not be taken within 24 hours of each other.

Pregnancy and Lactation – Ergots can reduce placental blood flow and are contraindicated for use during pregnancy. Ergotamine is excreted in human breast milk; women who take an ergot should avoid breastfeeding.

TRANSCRANIAL MAGNETIC STIMULATION – The FDA has approved the use of a transcranial magnetic stimulation device (*SpringTMS* – eNeura) for self-treatment of migraine with aura. In one trial, the pain-free response rate 2 hours after treatment of the first migraine attack was significantly higher with use of transcranial magnetic stimulation at the onset of aura than with sham stimulation (39% vs 22%).¹⁹

MEDICATION OVERUSE HEADACHE – Overuse of drugs for headache, particularly butalbital and opioids, can lead to chronic headache with structural and functional changes in the brain. Treatment of medication overuse headache involves withdrawing the overused drug(s); abrupt withdrawal may require hospitalization and bridge therapy with other drugs. Preventive treatment for migraine should be considered. Future use of acute migraine treatments should be limited to ≤ 2 days per week.^{20,21}

▶ Prevention of Migraine

Patients with frequent or severe migraine headaches and those who cannot take vasoconstrictors or are refractory to acute treatment should receive preventive treatment.^{22,23} Menstrual migraine attacks may sometimes be prevented by a brief course of an NSAID or triptan, particularly frovatriptan or naratriptan, taken for several days before and after the onset of menstruation.^{24,25} Preventive therapy is generally not recommended during pregnancy.

BETA BLOCKERS – Beta blockers are commonly used for prevention of migraine. Propranolol (*Inderal LA*, and others) and timolol are the only beta blockers approved by the FDA for this indication, but metoprolol (*Lopressor*, and others), nadolol (*Corgard*, and generics), and atenolol (*Tenormin*, and generics) are also effective in preventing migraine.²³ All beta blockers can cause fatigue, exercise intolerance, and orthostatic hypotension, and should not be used in patients with decompensated heart failure. All are relatively contraindicated in patients with asthma. Patients with migraine often have comorbid depression, which may be aggravated by beta blockers.

Pregnancy – Intrauterine growth retardation, small placentas, and congenital abnormalities have been reported with use of propranolol during pregnancy. Atenolol has been associated with the birth of small for gestational age infants and, at high doses, with embryofetal resorptions in animals.

ANTIEPILEPTIC DRUGS – Valproate (*Depakote*, and others) and topiramate (*Topamax*, and generics) are similarly effective in decreasing migraine frequency and are FDA-approved for migraine prevention. About 50% of patients achieve a $\geq 50\%$ reduction in headache frequency with these drugs.²⁶ In randomized, double-blind trials, topiramate was at least as effective as propranolol for migraine prevention.^{27,28} Topiramate has reduced the number of migraine headache days per month and improved associated symptoms in patients with chronic migraine (≥ 15 headache days/month for ≥ 3 months) and medication overuse headache.^{29,30} In a trial in pediatric patients, however, topiramate was no better than placebo in preventing migraine.³¹

Adverse Effects – 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. Other adverse effects include polycystic ovary syndrome, hyperinsulinemia, lipid abnormalities, hirsutism, and menstrual disturbances. Topiramate commonly causes paresthesias; fatigue, language and cognitive impairment, taste perversion, weight loss, and nephrolithiasis can also occur. Topiramate can rarely cause secondary narrow-angle glaucoma, oligohydrosis, and symptomatic metabolic acidosis.

Pregnancy – Use of topiramate or valproate during pregnancy has been associated with congenital malformations^{32,33}; neither drug should be used for migraine prevention in pregnant women.

Antidepressants – Amitriptyline is the only **tricyclic** antidepressant shown to be effective for migraine prevention in clinical trials,³⁴ but it often causes sedation, dry mouth, and weight gain. Other tricyclics such as nortriptyline, which may have fewer adverse effects than amitriptyline, are frequently used for migraine prevention in adults. In a trial in pediatric patients, amitriptyline was no better than placebo in preventing migraine.³¹

The **SNRIs** venlafaxine (*Effexor*, and others) and duloxetine (*Cymbalta*, and generics) may also be effective in preventing migraine.^{22,35,36} They can cause nausea, vomiting, sweating, tachycardia, urinary retention, and increased blood pressure.

Pregnancy – Tricyclic antidepressant use during pregnancy has been associated with jitteriness and seizures in newborns. Fetal malformations are uncommon with SNRIs, but increased risks of neonatal behavioral syndrome and perinatal complications have been reported with use of SNRIs during pregnancy.³⁷

Table 3. Some Drugs for Prevention of Migraine in Adults

Drug	Some Available Formulations	Usual Adult Dosage ¹	Cost ²
Beta Blockers			
Metoprolol ³ – generic	25, 50, 100 mg tabs	50-100 mg bid	\$1.80
<i>Lopressor</i> (Validus)	50, 100 mg tabs		57.60
extended-release – generic	25, 50, 100, 200 mg ER tabs	100-200 mg once/d	36.30
<i>Toprol-XL</i> (AstraZeneca)			53.90
Propranolol – generic	10, 20, 40, 60, 80 mg tabs	40-160 mg divided bid	20.40
extended-release – generic	60, 80, 120, 160 mg ER caps	60-160 mg once/d	50.10
<i>Inderal LA</i> (Akrimax)			530.40
Timolol – generic	5, 10, 20 mg tabs	10-15 mg bid or 20 mg once/d	75.30
Antiepileptic Drugs			
Valproate ⁴ – generic	125, 250, 500 mg delayed-release tabs;	250-500 mg bid	17.80
<i>Depakote</i> (Abbvie)	125 mg sprinkle caps		195.80
extended-release – generic	250, 500 mg ER tabs	500-1000 mg once/d	87.60
<i>Depakote ER</i>			156.60
Topiramate ⁵ – generic	25, 50, 100, 200 mg tabs;	50 mg bid ⁶	13.50
<i>Topamax</i> (Janssen)	15, 25 mg sprinkle caps		574.60
Tricyclic Antidepressants³			
Amitriptyline – generic	10, 25, 50, 75, 100, 150 mg tabs	25-150 mg once/d	9.50
Nortriptyline – generic	10, 25, 50, 75 mg caps	25-150 mg once/d	8.00
SNRI³			
Venlafaxine – generic	25, 37.5, 50, 75, 100 mg tabs	25-50 mg tid	47.70
extended-release – generic	37.5, 75, 150 mg caps;	75-150 mg once/d	11.70
<i>Effexor XR</i> (Pfizer)	37.5, 75, 150, 225 mg tabs		352.50
<i>37.5, 75, 150 mg caps</i>			
Botulinum Toxin Type A			
OnabotulinumtoxinA – <i>Botox</i> (Allergan) ⁷	100, 200 unit vials	155 units IM every 12 weeks ⁸	1158.00 ⁹

ER = extended-release

- Dosage adjustments may be required for renal or hepatic impairment.
- Approximate WAC for 30 days' treatment at the lowest usual dosage. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. January 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.
- Not FDA-approved for this indication.
- Oral formulations marketed as divalproex sodium (*Depakote*, and others) and valproic acid (*Depakene*, and others). Only divalproex sodium is FDA-approved for prevention of migraine.
- Extended-release formulations of topiramate (*Trokendi XR*; *Qudexy XR*, and generic) are not FDA-approved for migraine prevention.
- Dosage should be titrated to 100 mg/day over 4 wks: wk 1: 25 mg in the evening; wk 2: 25 mg morning and evening; wk 3: 25 mg morning and 50 mg evening; wk 4: 50 mg morning and evening.
- Botox* is FDA-approved for prevention of headaches in adult patients with chronic migraine. *Botox Cosmetic* is not FDA-approved for migraine prevention.
- Total dosage of 155 units is divided over 7 specific head/neck muscle areas (detailed information provided in package insert).
- Cost of one 200-unit vial.

OTHER PREVENTIVE TREATMENTS – NSAIDs, such as naproxen and ibuprofen, have been used for prevention of migraine and for aborting acute attacks.³⁸

The **angiotensin-converting enzyme (ACE) inhibitor** lisinopril (*Prinivil*, and others) and the **angiotensin receptor blocker (ARB)** candesartan (*Atacand*, and generics) have reduced migraine frequency by about 30-35% in small, double-blind trials.³⁹ In a randomized, placebo-controlled, crossover trial, candesartan was noninferior to propranolol for prevention of migraine.⁴⁰

The **calcium channel blocker** verapamil (*Calan*, and others) was somewhat more effective than placebo in some small studies.⁴¹

The combination of **simvastatin** (*Zocor*, and others) and **vitamin D** was effective for migraine prevention in one small, randomized, placebo-controlled trial.⁴²

The **dietary supplement** petasites (butterbur; *Petadolex*) 100-150 mg daily reduced migraine attack frequency by 36-60% in two randomized, placebo-controlled trials in about 300 patients,³⁸ but it has been associated with hepatic toxicity.⁴³ Melatonin, riboflavin, magnesium citrate, coenzyme Q10, and feverfew have also been effective in preventing migraine in small, randomized, placebo-controlled trials.^{38,43,44}

Pericranial intramuscular injections of **onabotulinum-toxinA** (*Botox*) are FDA-approved for prevention of headaches in adults with chronic migraine (≥ 15 headaches/month).⁴⁵ Botulinum toxin is not recommended for prevention of episodic migraine.

A **transcutaneous electrical nerve stimulation device** (*Cefaly*) that is worn on the forehead has been approved by the FDA for prevention of episodic migraine in adults. In one small study, daily 20-minute treatments for 3 months were modestly effective in reducing the number of migraine days per month.⁴⁶ ■

Comparison Chart of Drugs for Migraine Prevention (online only)

www.medicalletter.org/downloads/migraine-prevention.pdf

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The mission of The Medical Letter's Continuing Medical Education Program is to support the professional development of healthcare providers 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 to increase the participant's ability to know, or apply knowledge into practice after assimilating, information presented in materials contained in *The Medical Letter*.

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 healthcare providers through Core Competencies by providing continuing medical education that is unbiased and free of industry influence. The Medical Letter does not sell advertising or receive any commercial support.

GOAL:

Through this program, The Medical Letter expects to provide the healthcare community with unbiased, reliable, and timely educational content that they will use to make independent and informed therapeutic choices in their practice.

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 *The Medical Letter* with specific attention to clinical trials, pathophysiology, dosage and administration, drug metabolism and interactions, and patient management. Activity participants will make independent and informed therapeutic choices in their practice.

Upon completion of this program, the participant will be able to:

1. Explain the current approach to the management of migraine.
2. Discuss the pharmacologic options available for treatment and prevention of migraine and compare them based on their efficacy, dosage and administration, potential adverse effects, and drug interactions.
3. Determine the most appropriate therapy given the clinical presentation of an individual patient with migraine.

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Issue 1514 Questions

(Correspond to questions #31-40 in Comprehensive Exam #76, available July 2017)

Drugs for Migraine

- Which of the following would be a reasonable choice for initial treatment of a mild migraine attack without nausea or vomiting in a 28-year-old nonpregnant woman?
 - acetaminophen
 - butalbital/acetaminophen/caffeine
 - oxycodone/acetaminophen
 - ergotamine
- Orally administered short-acting triptans have an onset of action of about:
 - 5-10 minutes
 - 15-30 minutes
 - 30-60 minutes
 - 60-90 minutes
- Which of the following triptan formulations has the fastest onset of action?
 - almotriptan tablets
 - naratriptan tablets
 - zolmitriptan nasal spray
 - frovatriptan tablets
- Compared to oral sumatriptan, the subcutaneous formulations:
 - relieve pain faster
 - are more effective in relieving pain
 - cause more adverse effects
 - all of the above
- A 35-year-old woman with severe episodic migraine attacks with nausea and vomiting asks about switching from sumatriptan oral tablets to the nasal spray formulation. You should tell her that:
 - intranasal sumatriptan generally starts relieving pain in about 10-15 minutes
 - intranasal sumatriptan can have an unpleasant taste
 - sumatriptan nasal spray is partially absorbed in the GI tract, and absorption of the drug could be reduced in patients with vomiting
 - all of the above
- Which of the following statements is true?
 - The combination of ergotamine and caffeine is safer and more effective than a triptan for acute treatment of migraine
 - Patients who do not respond to a triptan alone should take both a triptan and an ergot
 - Dihydroergotamine may be effective in some patients who do not respond to a triptan
 - all of the above
- The drug of choice for treatment of moderate to severe migraine is:
 - aspirin
 - a triptan
 - an ergot
 - onabotulinumtoxinA
- For migraine prevention, beta blockers should be used with caution or not be used at all in patients who have:
 - asthma
 - depression
 - decompensated heart failure
 - all of the above
- About what percentage of patients achieve a $\geq 50\%$ reduction in migraine headache frequency when taking topiramate or valproate for migraine prevention?
 - 20%
 - 50%
 - 75%
 - 90%
- A 31-year-old woman with a history of frequent severe migraine attacks has been taking topiramate for 3 years for migraine prevention. She tells you that she is planning to become pregnant in the near future. You should:
 - increase her dose of topiramate because serum concentrations of the drug decrease significantly during pregnancy
 - switch her to valproate because it is safer for use during pregnancy
 - switch her to dihydroergotamine nasal spray taken once weekly during pregnancy
 - discontinue topiramate because it can cause congenital malformations

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