AAN Summary of Evidence-based Guideline for CLINICIANS

UPDATE: PHARMACOLOGIC TREATMENT FOR EPISODIC MIGRAINE PREVENTION IN ADULTS

This is a summary of the American Academy of Neurology (AAN) and American Headache Society guideline update regarding use of pharmacologic treatment for episodic migraine prevention.

Please refer to the full guideline at* www.aan.com *for more information, including definitions of the classifications of evidence and recommendations and the complete clinical context section.

DRUG WARNINGS

The following treatments have associated US Food and Drug Administration warnings:
Divalproex sodium: *www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/ucm153869.htm*
Topiramate: *www.fda.gov/Drugs/DrugSafety/ucm245085.htm*
Valproate: *www.fda.gov/Drugs/DrugSafety/ucm261543.htm*

For patients with migraine, which pharmacologic therapies are proven effective for prevention, as measured by reduced migraine attack frequency, reduced number of migraine days, and/or reduced attack severity?	
Angiotensin Receptor Blockers	
Weak evidence	Candesartan is possibly effective and may be considered for migraine prevention (**Level C**).
	Telmisartan is possibly ineffective and may not be considered for migraine prevention (**Level C negative**).
ACE Inhibitors	
Weak evidence	Lisinopril is possibly effective and may be considered for migraine prevention (**Level C**).
Alpha Agonists	
Weak evidence	Clonidine and guanfacine are possibly effective and may be considered for migraine prevention (**Level C**).
Antithrombotics	
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of acenocoumarol or Coumadin for migraine prevention (**Level U**).
Antidepressants	
Moderate evidence	Amitriptyline and venlafaxine are probably effective and should be considered for migraine prevention (**Level B**).
	Clomipramine is probably ineffective and should not be considered for migraine prevention (**Level B negative**).
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of fluoxetine, fluvoxamine, or protriptyline for migraine prevention (**Level U**).
Antiepileptic Drugs	
Strong evidence	Divalproex sodium, sodium valproate, and topiramate are established as effective and should be offered for migraine prevention (**Level A**).
	Lamotrigine is established as ineffective and should not be offered for migraine prevention (**Level A negative**).
Weak evidence	Carbamazepine is possibly effective and may be considered for migraine prevention (**Level C**).
	Oxcarbazepine is possibly ineffective and may not be considered for migraine prevention (**Level C negative**).
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of gabapentin for migraine prevention (**Level U**).
Clinical context	In most headache trials, patients taking divalproex sodium or sodium valproate reported no more adverse events (AEs) than those on placebo. However, weight gain has been clinically observed with divalproex sodium long-term use. Treatment with these agents requires careful follow-up and testing because of pancreatitis, liver failure, and teratogenicity risks.
Beta-blockers	
Strong evidence	Metoprolol, propranolol, and timolol are established as effective and should be offered for migraine prevention (**Level A**).
Moderate evidence	Atenolol and nadolol are probably effective and should be considered for migraine prevention (**Level B**).
Weak evidence	Nebivolol and pindolol are possibly effective and may be considered for migraine prevention (**Level C**).
	Acebutolol is possibly ineffective and may not be considered for migraine prevention (**Level C negative**).
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of bisoprolol for migraine prevention (**Level U**).

Calcium-channel Blockers	
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of nicardipine, nifedipine, nimodipine, or verapamil for migraine prevention (**Level U**).
Triptans	
Strong evidence	Frovatriptan is established as effective and should be offered for short-term menstrually associated migraine (MAMs) prevention (**Level A**).
Moderate evidence	Naratriptan and zolmitriptan are probably effective and should be considered for short-term MAMs prevention (**Level B**).
Other Agents	
Weak evidence	Clonazepam and nabumetone are possibly ineffective and may not be considered for migraine prevention (**Level C negative**).
Insufficient evidence	Evidence is conflicting or inadequate to support or refute the use of acetazolamide, cyclandelate, or picotamide for migraine prevention (**Level U**).

CLINICAL CONTEXT*

Evidence to support pharmacologic treatment strategies for migraine prevention indicates which treatments might be effective but is insufficient to establish how to choose an optimal therapy. Consequently, although Level A recommendations can be made for pharmacologic migraine prevention, similar evidence is unavailable to help the practitioner choose one therapy over another. Treatment regimens, therefore, need to be designed case by case. Moreover, decision making must remain with the physician and the patient to determine the optimal therapy. Often trial and error is needed.

Evidence is also unavailable for making broad-range comparisons among multiple agents within a single class; such evidence would provide a more comprehensive understanding of relative efficacy and tolerability profiles across a broader range of therapeutic agents. Studies are needed that specifically evaluate when preventive therapy is warranted and how medications should be titrated. Table e-1 of the published guideline lists some specific consensus-based clinical circumstances wherein considering preventive therapy would be reasonable. A shortcoming of migraine prevention clinical studies is the relatively brief treatment duration. Long-term assessment of the efficacy and safety of migraine preventive treatments is needed. Additionally, overall cost is a consideration when prescribing medications; cost may influence compliance, especially long-term.

It seems reasonable that a clinician be mindful of comorbid and coexistent conditions in patients with migraine, to maximize potential treatment efficacy and minimize AE risk. Table e-2 of the published guideline identifies which therapies to consider or avoid when common migraine coexisting conditions are present. Because migraine is frequent in women of childbearing age, the potential for fetal AEs related to migraine prevention strategies is particularly concerning.

Evidence from the two Class I frovatriptan studies meets the AAN threshold for a Level A recommendation for short-term use to prevent menstrual migraine (reduction in MAM headache incidence by 26% on 2.5 mg bid). However, the FDA questions whether the benefit demonstrated is clinically meaningful and has not approved frovatriptan for this indication.

This AAN and AHS guideline was endorsed by the American Osteopathic Association.

**See the published guideline for the complete clinical context section.*

AMERICAN HEADACHE SOCIETY

Copies of this summary and additional companion tools are available at *www.aan.com* or through AAN Member Services at (800) 879-1960.

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