

Pharmacologic Treatment for Migraine Prevention in Adults Practice Guideline Recommendations

Report of the AAN Guidelines Subcommittee and the American Headache Society

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Abstract

This practice guideline provides updated evidence-based recommendations regarding the use of pharmacologic migraine prevention in adults. A multidisciplinary panel conducted a systematic review and developed practice recommendations following the process outlined in the 2017 edition of the American Academy of Neurology Clinical Practice Guideline Process Manual. The systematic review includes studies published through June 6, 2024, and is available in a companion publication. Recommendations are supported by structured rationales that integrate evidence from the systematic review, related evidence, principles of care, and inferences from evidence. Recommendations are provided on how to decide when it is appropriate to start a pharmacologic migraine preventive medication and how to decide which migraine preventive medication to start. Recommendations address decision making on appropriate choices of migraine preventive medications in specific situations and populations, including patients with fibromyalgia, obesity, or hypertension; considerations for older adults; treatment during pregnancy and lactation; sex-related factors in choosing medications; and treatment for patients with medication overuse. Recommendations on assessment of treatment efficacy, adverse effects, and discontinuing migraine preventive medications are provided.

Introduction

This practice guideline provides evidence-based recommendations regarding the use of pharmacologic preventive treatments for migraine. The systematic review (SR) of the evidence that informs these recommendations, additional information on the development process, and suggestions for future research are available in a companion publication.¹ This guideline focuses on the following clinical questions:

1. In adults (≥ 18 years) with migraine, which pharmacologic preventive treatments, compared with placebo, reduce headache frequency (change in number of headache days/month, 50% responder rate)?
2. In adults (≥ 18 years) with migraine, which pharmacologic preventive treatments, compared with other active preventive pharmacologic treatments, reduce headache frequency (change in number of headache days/month, 50% responder rate)?

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The American Academy of Neurology Institute and American Headache Society jointly developed the guideline. Approved by the AAN Guidelines Subcommittee on July 19, 2025; by the AAN Quality Committee on October 22, 2025; by the American Headache Society Guidelines Committee on September 29, 2026; by the AAN Institute Board of Directors on April 2, 2026; and by the American Headache Society Board of Directors on November 13, 2025.

Endorsed by the American Academy of Family Physicians.

Glossary

AAN = American Academy of Neurology; AE = adverse effect; AHS = American Headache Society; CrI = credible intervals; CV = curriculum vitae; GS = Guidelines Subcommittee; OR = odds ratio; QOL = quality of life; SMD = standardized mean difference; SR = systematic review.

3. In adults (≥ 18 years) with migraine, which pharmacologic preventive treatments, compared with placebo or other preventive pharmacologic treatments, improve patient-reported quality of life (QOL) on validated instruments?

Analytic Process

In January 2018, the Guidelines Subcommittee (GS) of the American Academy of Neurology (AAN) (eAppendices 1 and 2) convened a panel of experts to develop a guideline on pharmacologic treatments for migraine prevention.² In March 2022, the American Headache Society (AHS) joined the project. The author panel includes content experts (W.J.B., R.C.B., L.C., J.F., A.H., J.L.J., E.L., T.S., S.S.), methodologists (T.P., D.S.), current and former GS members (S.P., M.M., M.O., S.T., G.L.G.P., V.K.R.), an AHS representative (A.H), patient representatives and advocates (S.K., M.M.), and AAN staff (T.F., K.A.B.D., H.M.S.). Each potential author submitted an AAN relationship disclosure form and their curriculum vitae (CV). The panel leadership, consisting of the lead developer (S.P.), the methodologist (T.P.), and GS leadership, reviewed the disclosure forms and CVs for financial and intellectual conflicts of interest (COI). These documents were screened to exclude individuals with a clear financial conflict or professional or intellectual biases that would diminish the credibility of the review. As required by the AAN, at least 51 percent of the panel and the lead developer (S.P.) are free of relevant COI. Six of the 19 developers were determined to have relevant COI judged not significant enough to preclude them from authorship (W.J.B., A.H., S.K., E.L., T.S., S.S.). These developers were not permitted to review or rate evidence but were consulted to help validate the key questions, the scope of the literature search, and the identification of seminal articles to validate the literature search. Because the panel majority is free of COI, the entire panel voted on the recommendations, with panel members free of COI leading recommendation development. This author panel was solely responsible for decisions concerning the design, analysis, and reporting of the SR and practice guideline.

The panel formulated a rationale for recommendations based on the evidence systematically reviewed and stipulated axiomatic principles of care (eAppendix 3). From this rationale, corresponding actionable recommendation statements were inferred. The level of obligation of the recommendations was assigned using a modified Delphi process (an anonymized voting process with multiple

rounds to reach consensus) that considered the confidence in the evidence reviewed, the acceptability of axiomatic principles of care, the strength of indirect evidence, and the relative magnitude of benefit to harm. Additional factors that could modify the level of obligation included judgments regarding the importance of outcomes, cost vs benefit of compliance with the recommendation, the availability of the intervention, and anticipated variations in patients' preferences. Standard modal operators indicate the level of obligation. "Must" corresponds to Level A, very strong recommendations; "should" to Level B, strong recommendations; and "may" to Level C, weak recommendations.

Practice Recommendations

The term chronic migraine refers to headache occurring ≥ 15 days/month for >3 months, which, on at least 8 days/month, has the features of migraine headache.

Deciding to Start a Preventive Medication

Recommendation 1 Rationale

Migraine preventive medications reduce headache days and migraine-associated disability. The decision to use a preventive medication depends on many factors that inform clinician and patient preferences. These include migraine attack factors, such as pain severity, frequency, associated symptoms, and disability, and medication factors, such as cost, adverse effects (AEs), and mode of delivery.³⁻⁶ Many recent clinical trials for migraine preventives require participants to experience ≥ 4 migraine days/month for inclusion. Two studies have identified monthly headache day frequency as a predictor of transformation to chronic migraine.^{7,8} Preventive treatments may prevent the transition of episodic to chronic migraine.

Patients with migraine want⁹ to be involved in the choice to use preventive medication. In a cross-sectional study, 80% of people with ≥ 5 migraine attacks/month expressed an interest in pharmacologic preventive treatment, compared with 20% of patients with <2 attacks/month.³

Recommendation 1 Statements

1A. Clinicians should inform all patients with migraine that effective preventive treatments exist for frequent migraine attacks (Level B).

1B. Clinicians should offer preventive treatments to patients with migraine who experience ≥ 4 migraine days per month, or ≥ 4 moderate to severe headache days per month, to reduce headache frequency (Level B).

1C. Clinicians should offer preventive treatments to patients with substantial disability from migraine to reduce migraine-associated disability (Level B).

Shared and Informed Decision Making

Recommendation 2 Rationale

Our SR of the evidence for medication use for migraine prevention found several medications that are superior to placebo in decreasing headache attack frequency and improving patient-reported QOL.¹ The magnitude of the effect size and confidence in the evidence varies by medication, dosage, and diagnosis of episodic or chronic migraine. Head-to-head trials of medications have generally not provided evidence of sufficient quality to establish superiority of one medication over another. Once the decision to start a preventive medication is made, choosing which medication to start is a collaborative decision between patient and clinician based on the principles of shared and informed decision making.

Recommendation 2 Statements

To improve shared decision making:

2A. Clinicians should inform patients of appropriate medication choices for migraine prevention, taking into account the patient's medical and psychiatric history, currently prescribed medications, and any contraindications to medications used for migraine prevention (Level B).

2B. Clinicians should discuss and understand the patient's preferences with respect to potential AEs of medications used for migraine prevention (Level B).

2C. Clinicians should discuss and understand the patient's preferences with respect to treatment modality (i.e., oral vs injectable) (Level B).

Treatments for Patients Without Significant Comorbidities or Specific Contraindications

Recommendation 3 Rationale

Many pharmacologic options exist for migraine prevention. No single medication has been shown to be clearly superior for efficacy in reducing the frequency of migraine attacks, although some have greater confidence in evidence of efficacy than others. Preventive options can therefore be compared regarding 4 properties:

- Strength of evidence for efficacy: This is quantified in the SR for this guideline.¹
- Tolerability: Tolerability differs per medication and, although it depends on individual factors and cannot be predicted in any individual patient, clinical trials indicate the general tolerability of a drug.
- Safety: All migraine preventive medications approved for clinical use in the United States are relatively safe, but safety will vary based on individual patient factors (e.g.,

risk of cardiovascular disease, chances of becoming pregnant). As long-term safety cannot be determined from relatively short clinical trials, the safety of newer medications is less certain than the safety of older medications.

- Cost: The cost of each treatment option is known, but the importance of cost will vary per patient and health system.

Recommendation 3 Statements

Patient choice is a crucial consideration when developing treatment plans for patients with no significant comorbidities or specific contraindications. The term *offer* refers to the action of providing guidance to the patient about possible appropriate preventive medication choices.

3A. For patients for whom evidence of efficacy is the priority, clinicians should offer patients preventives with high or moderate confidence in the evidence for efficacy based on the SR (Level B).¹

- Episodic migraine: atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab, propranolol, topiramate, and valproate
- Chronic migraine: atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab, onabotulinumtoxinA, topiramate, and valproate

3B. For patients concerned about tolerability, clinicians should offer migraine preventives with fewer side effects (Level B).

- Episodic migraine: atogepant, eptinezumab, erenumab, fremanezumab, and galcanezumab
- Chronic migraine: atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab, and onabotulinumtoxinA

3C. For patients concerned about possible long-term or unknown harms from medications, clinicians should offer migraine preventives that have been widely used for a long period of time while observing specific contraindications (Level B).

- Episodic migraine: propranolol and topiramate
- Chronic migraine: onabotulinumtoxinA and topiramate

3D. For patients concerned about cost, clinicians should offer less expensive preventive treatment options depending on the patient's specific pharmaceutical formulary plan and health care insurance system (Level B).

3E. For patients not responding to choices with higher confidence in the evidence, clinicians should offer migraine preventives with low confidence in the evidence for efficacy (Level B).

- Episodic migraine: amitriptyline, flunarizine, metoprolol, pizotifen, rimegepant, and telmisartan

Treatment During Pregnancy and for Patients Planning Pregnancy

Recommendation 4 Rationale

Drugs taken during pregnancy have the potential to harm the fetus. As randomized controlled trials (RCTs) of drug safety during pregnancy are not ethically possible, no drug can be declared completely safe when taken during pregnancy. Some preventive medications have prolonged half-lives and, therefore, need to be stopped early in female patients planning a pregnancy. Finally, many pregnancies are unplanned, and unexpected fetal drug exposure may occur.

Pregnant women with migraine have a higher risk of pre-eclampsia and preterm birth¹⁰ and a higher risk of cerebrovascular and cardiovascular events during pregnancy. It is unknown whether migraine prevention during pregnancy decreases these risks. Severe migraine attacks can cause significant morbidity during pregnancy (e.g., severe nausea and vomiting),¹¹ and it may be advantageous for selected patients to continue migraine preventive therapy during pregnancy. In these situations, a collaborative decision between patient and clinician based on the principles of shared and informed decision making is required, with risks and benefits considered. The discussion should consider that migraine often improves during pregnancy, especially after the first trimester.¹²

The American College of Obstetricians and Gynecologists (ACOG) developed a clinical practice guideline on headaches in pregnancy and postpartum based on an SR of the literature and following a similar process to the AAN's guideline development process.¹³ Regarding the use of medication for prevention of primary headaches, ACOG recommends that obstetricians review the medications a patient is using for headache prevention and consider continuing, decreasing, changing, or stopping them owing to the likely decrease in headache symptoms during pregnancy (strong recommendation, very low quality evidence). The guideline includes a table of possible therapies (table 2¹³) listed by recommendation, from "recommended," to "balance risks and benefits," to "not recommended," and "insufficient evidence." Medications included in the ACOG guideline as "recommended" or "balance risks and benefits" that were also found to be possibly or probably effective in our AAN SR¹ include: nifedipine (AAN low confidence, ACOG consider as first line use for prevention), amitriptyline (AAN low confidence, ACOG balance risks and benefits), metoprolol (AAN low confidence, ACOG balance risks and benefits), propranolol (AAN moderate confidence, ACOG balance risks and benefits), and onabotulinumtoxinA (chronic migraine only, AAN high confidence, ACOG balance risks and benefits).

The potential associated risks of using these medications in pregnancy according to ACOG are:

- Nifedipine: none.
- Amitriptyline: small for gestational age births, major congenital anomalies, neonatal convulsions, and neonatal respiratory distress.
- Propranolol and metoprolol: cardiovascular abnormalities, cleft lip or palate, neural tube defects, and fetal growth restriction.

The review does not provide statements on the frequency of these outcomes. Despite the inclusion of amitriptyline in table 2 of the ACOG guideline, the text of the guideline states that the use of tricyclic antidepressants is not recommended in pregnancy. ACOG states that there are limited data on the potential associated risks of onabotulinumtoxinA in pregnancy. A Class III study published after the ACOG guideline analyzed pregnancy outcomes in 397 women after onabotulinumtoxinA exposure based on data collected in the Allergan Global Safety Database from 1990 to 2018. The timing of exposure was before conception or during the first trimester in 95% of cases. The prevalence of overall fetal defects was 2.6%, consistent with rates reported in the general population.¹⁴

Recommendation 4 Statements

4A. People with migraine of childbearing potential who require migraine preventive therapy must be made aware of the potential risks to the fetus in the event of an unplanned pregnancy, and agents with known teratogenic effects (e.g., divalproex sodium, topiramate) should be avoided if possible (Level A).

4B. In people who are pregnant or planning a pregnancy, nonpharmacologic approaches that have the potential to reduce migraine attack frequency (e.g., behavioral interventions, acupuncture, exercise, trigger management) must be maximized (Level A).

4C. If pharmacologic migraine prevention is considered potentially necessary during pregnancy, it must be used only after a thorough discussion with the patient of the risks and alternatives, with joint decision making (Level A).

4D. If pharmacologic migraine prevention is necessary during pregnancy, clinicians must develop a strategy with the patient that limits overall pharmacologic exposures while maintaining the best possible migraine control (Level A).

4E. If a migraine preventive medication is considered necessary during pregnancy, clinicians should review the ACOG guideline medication recommendations and potential associated risks determined from their SR (Level B).

4F. If a migraine preventive drug is considered necessary during pregnancy, clinicians may offer nifedipine (Level C).

4G. If a migraine preventive drug is considered necessary during pregnancy and nifedipine is not an option or is ineffective, clinicians may offer metoprolol or propranolol, but

the risks (i.e., cardiovascular abnormalities, cleft lip or palate, neural tube defects, and fetal growth retardation) must be balanced with the potential benefits (Level C).

4H. If a migraine preventive medication is considered necessary during pregnancy for chronic migraine, clinicians may offer onabotulinumtoxinA, but the risks must be balanced with the potential benefits. Extremely limited outcome data are available, and available data mainly pertain to pre-conception and first trimester exposures (Level C).

Treatment During Lactation

Recommendation 5 Rationale

Migraine preventive drugs are present in the breast milk of lactating people (eAppendix 4). The availability of information on the passage of migraine preventives into breast milk varies between drugs and is scarce for newer treatments.¹⁵

Recommendation 5 Statement

5. To improve shared and informed decision making, clinicians must counsel patients who are lactating that migraine preventives pass into breast milk in varying amounts and can impact the health of breastfed infants, including counseling on the risks of specific medications based on evidence-based sources such as reference databases (e.g., LactMed) (Level A).

Treatment Over the Adult Lifespan

Recommendation 6 Rationale

Changes related to aging, particularly in older adults, need to be considered when prescribing migraine preventive medications. With increasing age, there is a greater risk of vascular disease, including coronary and cerebrovascular disease. Older adults are more likely to have reduced renal and hepatic function and are more likely to be taking medications for other health conditions that can lead to drug interactions. They are more prone to experience sedation and/or confusion from medications with sedative potential and have greater risk from falls due to sedation or syncope. Preventive drugs that are more likely to cause sedation include amitriptyline, valproate, topiramate, and pizotifen.¹⁶ RCTs of telmisartan,¹⁷ propranolol,¹⁸ and metoprolol¹⁹ for migraine prevention have demonstrated significant decreases in blood pressure with treatment.

Recommendation 6 Statements

6A. When prescribing a migraine preventive medication for older adults, depending on the drug being considered, the clinician should carefully assess for the presence of vascular disease, potential drug interactions, and reduced renal and/or hepatic function (Level B).

6B. Clinicians prescribing a migraine preventive medication with sedative potential for an older adult should discuss the possibility of side effects such as sedation and confusion and, if appropriate, initiate therapy with lower-than-usual doses (Level B).

6C. When choosing a preventive drug for an older adult, the clinician must discuss the possibility of hypotension or postural hypotension and, if appropriate, avoid drugs that significantly lower blood pressure or start therapy with lower-than-usual doses (Level A).

Recommendation 7 Rationale

A patient's sex may influence choice of a preventive medication. Issues related to pregnancy and lactation are discussed in recommendations 4 and 5. Other considerations when prescribing a migraine preventive drug for a female patient include whether the drug predisposes to polycystic ovary syndrome (PCOS) and whether it may reduce the effectiveness of hormonal contraceptives. In a meta-analysis of studies of women with epilepsy taking valproate, the incidence of PCOS in women treated with valproate was higher (OR 3.04, 95% confidence interval [CI] 2.09–4.43) than in women not treated with valproate.²⁰ Topiramate in doses >200 mg/d reduces estrogen levels in women taking combined oral contraceptives, but doses of ≤200 mg/d result in minimal or no reductions in estrogen and norethindrone levels. There is evidence that low-dose topiramate as used in migraine prevention does not increase the incidence of unintended pregnancy in those on oral contraceptives as compared with patients using propranolol, amitriptyline, or other oral migraine preventives.^{21–23} Similarly, topiramate in doses >200 mg/d causes potentially clinically important reductions in serum etonogestrel concentrations among etonogestrel implant users, while doses of 100 mg/d cause minor decreases.²⁴ Considerations when prescribing a migraine preventive drug for older adult male patients include whether the drug predisposes to urinary retention. In an SR and meta-analysis of the effect of psychotropic drugs on urinary function, tricyclic antidepressants were significantly more likely to cause urinary retention than placebo (odds ratio [OR] 2.52, 95% CI 1.29–4.90).²⁵

Recommendation 7 Statements

7A. Clinicians prescribing valproic acid for migraine prevention must notify female patients that it can increase the risk of PCOS (Level A).

7B. Clinicians prescribing topiramate for migraine prevention must notify female patients of childbearing potential that it can make hormonal contraception less effective at doses above 200 mg/d (Level A).

7C. Clinicians prescribing a migraine preventive for older adult male patients should evaluate whether there is risk of urinary retention and either avoid drugs with anticholinergic effects (e.g., amitriptyline) or discuss this possibility with the patient (Level B).

Treatments for Patients With Comorbid Medical and Psychiatric Conditions

Recommendation 8 Rationale

People with migraine may have additional medical and psychiatric conditions. Where it is possible to treat both migraine

and the coexisting condition with the same medication, this is a viable option as it may reduce the number of medications the patient is required to take and thereby improve treatment adherence and reduce costs. However, if one or both conditions does not respond to this approach, it is important to abandon it and treat each condition independently. With this approach, each condition should be treated with the best treatment option possible, while remaining vigilant for drug interactions and side effects.

Recommendation 8 Statements

8A. Clinicians should discuss with the patient with migraine who has a medical or psychiatric comorbidity whether it is preferable to treat both conditions with a single medication (combined approach) or to treat them both independently (independent approach) (Level B).

8B. If a combined approach is chosen, efficacy and side effects should be closely monitored to determine whether the therapeutic approach should be switched to treating both conditions independently (Level B).

Treatments for Patients With Hypertension

Recommendation 9 Rationale

As several antihypertensives are also used for migraine prevention, these medications can be used to treat both hypertension and migraine with a single agent. This should encourage treatment compliance and reduce the probability of drug interactions. The American College of Cardiology guideline on the treatment of hypertension recommends thiazide diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers as first-line agents for initiation of antihypertensive drug therapy, while initial use of beta blockers for hypertension is only recommended in patients with specific cardiovascular comorbidities.²⁶ First-line agents for hypertension that have been assessed as possibly effective in migraine prevention include telmisartan (low confidence), nifedipine (low confidence), and enalapril (low confidence). Candesartan is widely used in migraine prevention, but there is insufficient evidence to support its use.

Recommendation 9 Statement

9. Clinicians may inform people with migraine and comorbid untreated hypertension that monotherapy options are available to treat both conditions, including enalapril, nifedipine, and telmisartan (Level C).

Treatments for Patients With Fibromyalgia

Recommendation 10 Rationale

Amitriptyline is used for migraine prevention and has also shown efficacy in the treatment of fibromyalgia. In an SR and meta-analysis of RCTs of amitriptyline in patients with fibromyalgia, compared with placebo, amitriptyline (10–50 mg/d) was associated with reduced sleep disturbances (standardized mean difference [SMD] –0.97, 95%

credible intervals [CrI] –1.10 to –0.83), fatigue (SMD –0.64, 95% CrI –0.75 to –0.53), and improved QOL (SMD –0.80, 95% CrI –0.94 to –0.65).²⁷ The use of amitriptyline for migraine prevention in patients with fibromyalgia, especially if they have insomnia, has the potential to be helpful for both disorders.

Recommendation 10 Statement

10. Clinicians should offer amitriptyline for migraine prevention in patients with comorbid fibromyalgia (Level B).

Treatments for Patients With Increased Body Mass

Recommendation 11 Rationale

Many migraine preventive medications (e.g., amitriptyline,¹⁶ propranolol,²⁸ pizotifen,¹⁶ and flunarizine²⁹) promote weight gain in some patients as a side effect. Cross-sectional studies suggest that obesity is a risk factor for chronification of migraine.³⁰ In several RCTs of topiramate for migraine prevention, treatment with topiramate resulted in statistically significant decreases in weight compared with placebo at all dosages (50–200 mg).^{28,31,32}

Recommendation 11 Statement

11. When an oral migraine preventive drug is being considered in a patient with increased body mass index, clinicians should offer topiramate (Level B).

Treatments for Patients With Medication Overuse

Recommendation 12 Rationale

The use of medications to treat acute migraine attacks too frequently is termed “medication overuse.” It is presumed that medication overuse can cause a secondary headache called “medication-overuse headache,” although causality is generally difficult to demonstrate. Medication overuse is defined as the regular use of acute and/or symptomatic migraine drugs, with intake of >9 days/month for prescription migraine pain relieving medication or >14 days/month for nonspecific pain medications.³³ Reduction in headache frequency that occurs in some individuals after discontinuing the overused medication suggests a causal relationship.^{34,35} The frequent use of medications to treat acute migraine attacks is one indication that preventive treatment should be offered or optimized. Although there is a lack of comparative effectiveness data on migraine preventive medications for the treatment of patients who have medication overuse, several medications have demonstrated efficacy in small studies and/or post hoc subgroup analyses of larger clinical trials. From large phase 3 clinical trials, subgroup analyses of participants with migraine and medication overuse have been conducted for onabotulinumtoxinA, eptinezumab, erenumab, fremanezumab, galcanezumab, and atogepant. These analyses have concluded that participants with medication overuse either have superior benefit from the preventive medication compared with a placebo control and/or that those with medication overuse respond similarly to the preventive medication

compared with those without medication overuse.³⁶⁻⁴⁰ Smaller analyses of topiramate amongst those with migraine and medication overuse suggest that topiramate is likely effective in this population.⁴¹⁻⁴⁴ Available evidence suggests that simply starting a preventive medication is equally effective to starting a preventive medication and implementing acute medication withdrawal.^{34,45} However, these studies included only small numbers of participants who had overuse of opioids or barbiturate-containing medications, and thus, there is insufficient evidence to draw a similar conclusion for these scenarios.

Recommendation 12 Statements

12A. Preventive medication should be offered to those with migraine who meet criteria for medication overuse (Level B).

12B. Preventive medication should be offered to those who have medication-overuse headache (Level B).

12C. Preventive medications that have evidence for efficacy in individuals with medication overuse or medication-overuse headache (e.g., CGRP [calcitonin gene-related peptide] monoclonal antibodies [mAbs], atogepant, onabotulinumtoxinA, and topiramate) should be considered before medications that lack such evidence (Level B).

Current Use of Acute Treatments

Recommendation 13 Rationale

Nearly all individuals with migraine use acute treatments to treat migraine attack symptoms. Thus, most patients being prescribed migraine preventive medication are also taking acute migraine medication. There is a lack of data comparing the benefits and risks of combining specific migraine preventive medications with specific acute medications. The potential for medication interactions, side effects, and overlap in mechanisms of action are considerations when recommending a migraine preventive medication to a patient already taking an acute migraine medication.^{46,47}

Recommendation 13 Statements

13A. When prescribing a migraine preventive medication, clinicians must evaluate the risk of drug interactions with a patient's migraine acute medications (Level A).

13B. When prescribing a migraine preventive medication, the clinician must evaluate the risk of side effects based on combining that preventive medication with the patient's migraine acute medications (Level A).

When to Assess Treatment Efficacy

Recommendation 14 Rationale

In the SR of the evidence on the use of medication for migraine prevention, superiority to placebo was typically demonstrated between 8 and 12 weeks for oral medications, with the most common timepoint across these studies being 12 weeks. Studies of onabotulinumtoxinA evaluated response at 24 weeks, while studies of CGRP mAbs evaluated response at

both 12 and 24 weeks. Although medications have varying mechanisms of action, expected final pathophysiologic changes driving improvement in migraine take weeks to months to occur, although initial changes may occur sooner. Some medications demonstrate a dose-response relationship with a minimal effective dose and a higher response with increasing doses. Adverse events were reported within days to weeks of initiating treatment, some leading to treatment discontinuation before attaining therapeutic response. Individuals have the autonomy to decide if side effects are tolerable. Lifestyle and trigger management is an essential aspect of migraine treatment. Patient preference should be paramount in decision making and may enhance the efficacy-expectation response.

Recommendation 14 Statements

14A. Clinicians should wait at least 8–12 weeks at the recommended tolerated dose of most medications for migraine prevention before assessing efficacy (Level B).

14B. Clinicians should wait 24 weeks at the recommended dose before assessing efficacy of onabotulinumtoxinA injections for migraine prevention before assessing efficacy (Level B).

14C. If suboptimal treatment response is observed by 8 weeks, physicians should optimize the dose of the medication for migraine prevention to the maximum tolerated dose or predetermined maximum based on efficacy studies (Level B).

14D. If no efficacy is observed after 8–12 weeks of treatment and other contributing factors are identified (e.g., inconsistent treatment adherence, frequent exposure to known triggers), physicians should engage in shared decision making with patients to continue an additional observation period (Level B).

14E. Clinicians should encourage continued lifestyle and trigger management in patients who take a medication for migraine prevention (Level B).

14F. If side effects are not tolerable, clinicians should consider a dose reduction (Level B).

14G. If side effects are not tolerable, clinicians should offer an alternative treatment option (Level B).

14H. If suboptimal response is observed after 12–24 weeks (see 14A and 14B), and other options are available and not contraindicated, clinicians should engage in shared decision making with the patient to initiate an alternate medication for migraine prevention (Level B).

Assessment of Treatment Efficacy

Recommendation 15 Rationale

In our SR of evidence on the use of medication for migraine prevention, effectiveness was measured by assessing the

change in the number of days with migraine, the proportion of individuals with a $\geq 50\%$ decrease in migraine attack days, and migraine-specific QOL measures. The migraine-specific QOL measures used in randomized clinical trials of migraine treatments that were sensitive to improvement in outcomes included the Migraine Disability Assessment Scale (MIDAS), Headache Impact Test (HIT-6), Migraine Specific Quality of Life Questionnaire (MSQ), and Migraine Physical Function Impact Diary (MPFID). Shared decision making between clinicians and patients forms a basis for establishing an effective migraine treatment regimen. Medication adherence is critical for optimal treatment outcomes and emphasizing the importance of adherence can lead to better patient outcomes.⁴⁸

Recommendation 15 Statements

15A. Clinicians should document the frequency of migraine attacks to optimize assessment of treatment efficacy (Level B).

15B. Clinicians may use a measurement tool (e.g., headache diary, HIT-6, or MIDAS) consistently across patient visits to monitor efficacy and treatment response (Level C).

15C. Clinicians' assessment of treatment efficacy must be patient-centric and based on individual goals (Level A).

15D. Clinicians should utilize frequency, severity, migraine-associated symptoms, QOL, and use of acute therapy when assessing efficacy of treatment (Level B).

Counseling and Assessment of AEs

Recommendation 16 Rationale

AEs are a common reason for treatment noncompliance or discontinuation and are treatment specific. Clinicians prescribing medications for migraine prevention require adequate knowledge of AEs that are common, bothersome, or serious. Educating and counseling patients about the possible AEs associated with the use of medications for migraine allows patients to make informed decisions about their treatment options. Patient education and counseling on potential AEs resulting from migraine medication use should be based on the most common and most serious AEs cited in the drug label/product monograph or within drug databases (e.g., Lexicomp) that contain evidence-based information about adverse reactions, warnings and precautions, and other information regarding drug effects.

Recommendation 16 Statements

16A. Clinicians must provide counseling on common and serious or life-threatening AEs based on product monographs and drug information databases before prescribing migraine preventive medications (Level A).

16B. Clinicians must monitor patients for common and serious or life-threatening AEs as part of routine follow-up (Level A).

Stopping Preventive Therapy

Recommendation 17 Rationale

Migraine is a lifelong disorder with fluctuations in frequency, severity, and duration. Patients require knowledge about the needed duration of treatment to inform decision making. Patients vary in their desire to taper an effective treatment. There are only 2 studies of migraine preventive cessation of sufficient design to inform recommendations. After 6 months of use of topiramate (50–200 mg) for migraine prevention, randomized discontinuation (by 100 mg/wk) resulted in a slight increase in migraine attack days (1.19 days in 4 weeks, 95% CI 0.71–1.66; $p < 0.0001$), a greater number of days on acute medication, and a decrease in migraine-related QOL on the MIDAS.⁴⁹ Similarly, after 6 months of galcanezumab treatment for migraine prevention, discontinuation of galcanezumab was associated with $>50\%$ of month 6 responders (defined as a decrease in monthly migraine headache day frequency by $\geq 50\%$) losing their response 5 months after discontinuation.⁵⁰

Recommendation 17 Statements

17A. Clinicians should counsel patients that there is limited evidence that suggests a risk of increased headache days and decreased headache-related QOL after discontinuing a preventive medication (Level B).

17B. Clinicians should discuss the potential benefits and risks of tapering a migraine preventive medication after 6 months of treatment (Level B).

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Conflict of Interest

The American Academy of Neurology (AAN) is committed to producing independent, critical, and trustworthy clinical practice guidelines (CPGs) and evidence-based documents. Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this evidence-based document. Management and disclosure of document developer relationships is conducted in compliance with the 2017 AAN process manual section titled, "Implementing the AAN Conflict of Interest Policy for Guidelines and Case Definitions," which can be viewed at aan.com.

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