

# Migraine and Tension Headache Guideline

Major Changes as of May 2021 .....	2
Medications <b>Not</b> Recommended for Headache Treatment .....	2
Background .....	2
Diagnosis	
Red flag warning signs .....	3
Differential diagnosis .....	3
Imaging .....	3
Migraine versus tension headache .....	4
Medication overuse headache .....	4
Menstruation-related migraine .....	4
Tension Headache	
Acute treatment .....	5
Prophylaxis .....	5
Migraine Headache	
Acute treatment .....	7
Treatment of refractory migraine .....	8
Prophylaxis: overview, guiding principles .....	9
Prophylaxis options: self-care, monitoring .....	9
Prophylaxis options: complementary/alternative medicine .....	10
Prophylaxis options: supplements .....	11
Prophylaxis options: medications and procedures .....	12
Menstruation-related migraine prophylaxis .....	15
Medication Overuse Headache Treatment .....	16
Evidence Summary .....	17
References .....	21
Clinician Lead and Guideline Development .....	22

## Last guideline approval: May 2021

**Guidelines** are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

This evidence-based guideline was developed by **Kaiser Permanente Washington (KPWA)**.

# Major Changes as of May 2021

- **Melatonin, zinc, and vitamin D** may be considered for migraine prophylaxis.
- **Butterbur and coenzyme Q10** are no longer recommended for migraine prophylaxis.
- Additional **complementary and alternative therapies** may be considered for preventing both tension and migraine headaches, including biofeedback, cognitive behavioral therapy, relaxation training, mindfulness, and yoga.
- **Occipital nerve block** may be used as an adjunct treatment to reduce the frequency and intensity of migraine headaches.
- **Botulinum toxin or anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies** may be given to reduce the frequency and intensity of migraine headaches. Administration of these treatments is limited to Neurology providers. Adequate trial of at least three other formulary preferred prophylactic migraine medications and documentation of no medication overuse headache may be required for health plan coverage.

## Medications That Are *Not* Recommended

- KP Washington and national headache guidelines advise **against** the use of **opioids and butalbital-containing medications** (e.g., Fiorinal, Fioricet) for treatment of headaches. Print out and share or encourage your patients to view the Choosing Wisely guide on the low value and risks of using opiates for headache: <https://www.choosingwisely.org/wp-content/uploads/2018/02/Treating-Migraine-Headaches-AAN.pdf>
- KPWA advises **against** the use of **estrogen-containing oral contraceptive pills for migraine with aura** due to increased risk for stroke.
- There is insufficient evidence to support the use of **SSRIs, venlafaxine, gabapentin, or coenzyme Q10** for migraine prophylaxis.
- **Butterbur** is no longer recommended for migraine prophylaxis because it may contain a compound that is hepatotoxic and carcinogenic.

## Background

This guideline includes diagnosis and treatment of the most common headache types that are managed in Primary Care:

- Tension headache
- Migraine headache, including menstrual migraine
- Medication overuse headache (also known as rebound headache)

Cluster headaches are excluded from this guideline because of their low prevalence in the general population and the severity of the symptoms. For patients with suspected cluster headaches, consider consulting with Neurology for evaluation and treatment.

Populations excluded from this guideline include pregnant individuals and children aged 13 years and younger.

**Note:** KPWA and national guidelines advise **against** the use of **opioids and butalbital-containing medications** (e.g., Fiorinal, Fioricet) for treatment of headaches.

# Diagnosis

## Red flag warning signs

*For patients with a rapidly accelerating course, a recent history of head injury, or focal neurologic findings, consult with a neurologist or neurosurgeon.*

Use the **SNOOP** mnemonic to identify red flag warning signs requiring immediate or urgent evaluation:

### Systemic

- Conditions: malignancy, HIV, pregnancy
- Signs: fevers, sweats, rash, weight loss

### Neurologic

- Symptoms: any neurologic symptoms other than classic aura (such as confusion or double vision)
- Signs: optic nerve edema, abnormal neurologic exam

### Onset sudden (< 5 minutes)

### Older than 50 years

### Pattern change

- Change in type or quality of headache
- More than 50% increase in frequency or severity

Consider using the Patient Questionnaire for Headaches to evaluate patients for red flags.

**When patients have no red flags or indications for imaging**, ask them to gather more data on their headaches and schedule follow-up in Primary Care in 1 to 2 weeks to assess their response to empiric treatment. The SmartPhrase **.AVSHEADACHEDIARY** and the handout Your Headache Log provide patients instructions for keeping a headache log and advice about when to seek immediate medical attention.

## Differential diagnosis

Consider the following “can’t miss” headache causes at least once in your evaluation of a new-onset headache or a change in an existing headache pattern.

Create a concrete differential diagnosis to rule out “can’t miss” causes of headache using the **DATA C<sup>2</sup>A<sup>2</sup>N** save lives mnemonic from David Newman-Toker, MD:

**D**issection (carotid or vertebral)

**A**rteritis (giant cell)

**T**hrombosis (dural venous)

**A**neurysm (leak, expansion, or subarachnoid hemorrhage)

**C**arbon monoxide, **C**olloid cyst

**A**ngle closure glaucoma, **A**ngina

**N**orepi neoplasm (pheochromocytoma)

## Imaging

Order imaging only when your differential diagnosis supports it. Imaging should not be done solely for reassurance. High-end imaging (CT or MRI) for uncomplicated headache increases costs, radiation (CT), and anxiety for patients without improving quality of care.

Most urgent causes of headache are **not** ruled out with a non-contrast head CT and need to be excluded with specific imaging, exam, or serologic testing. **A head CT does not “clear” a patient with headache.**

# Migraine versus tension headache

Source: International Headache Society 2018

<b>Table 1. Distinguishing between migraine and tension-type headache</b>	
<b>Migraine headache</b>	<b>Tension headache</b>
4–72 hours' duration. Aura may be present.  <i>At least two</i> of the following bullets are true: <ul style="list-style-type: none"> <li>• Unilateral location.</li> <li>• Moderate to severe pain intensity. <sup>1</sup></li> <li>• Pain described as pulsating.</li> <li>• Aggravated by routine activity.</li> </ul> <i>At least one</i> of the following two bullets is true: <ul style="list-style-type: none"> <li>• Sensitivity to light and/or sound is present.</li> <li>• Nausea and/or vomiting is present.</li> </ul>	30 minutes' to 7 days' duration. No aura.  <i>At least two</i> of the following bullets are true: <ul style="list-style-type: none"> <li>• Bilateral location.</li> <li>• Mild to moderate pain intensity. <sup>1</sup></li> <li>• Pain described as pressing or tightening (not pulsating).</li> <li>• Not aggravated by routine activity.</li> </ul> <i>Both</i> of the following bullets are true: <ul style="list-style-type: none"> <li>• No sensitivity to light or sound, <b>or</b> sensitivity to only one of the two.</li> <li>• Neither nausea nor vomiting is present.</li> </ul>
<sup>1</sup> Pain intensity <ul style="list-style-type: none"> <li>• Mild: Patient is aware of headache, but able to continue daily routine with minimum alterations.</li> <li>• Moderate: Headache inhibits daily activities, but is not incapacitating.</li> <li>• Severe: Headache is incapacitating.</li> </ul>	

## Medication overuse headache (MOH)

Source: International Headache Society 2018

Medication overuse headache (MOH; also known as *rebound headache*) is headache occurring at least 15 days per month in patients with pre-existing primary headache who have regularly overused acute or symptomatic headache medication for 3 months or longer. ("Overuse" is defined as > 10 days or > 15 days per month, depending on the medication.) It usually, but not invariably, resolves after the overuse is stopped. A common culprit is over-the-counter medications, which are not always on the medication list.

It is important to rule out MOH prior to initiating therapy for any acute headache. See MOH Treatment, p. 16.

## Menstruation-related migraine

Source: International Headache Society 2018

Episodes of migraine without aura (as defined in Table 1) occurring in the window of 2 days before to 3 days after menstruation, in at least two out of three menstrual cycles.

# Tension Headache

## Acute treatment of tension headache

**Note:** It is important to rule out medication overuse headache (MOH) prior to initiating therapy for any acute headache. See MOH Treatment, p. 16.

Table 2. Pharmacologic options for acute treatment of tension headache				
<b>NOT RECOMMENDED</b>				
KPWA and national headache guidelines advise <b>against</b> the use of <b>opioids and butalbital-containing medications</b> (e.g., Fiorinal, Fioricet) for treatment of headaches.				
<b>ASPIRIN/NSAIDS (contraindicated if history of GI bleeding)</b>				
Medication	Initial dose	Max dose/day	Relative <i>contraindications</i>	Special considerations
Aspirin	500 mg x1, may repeat in 4–6 hours	4000 mg	Age < 19 years Post–Roux-en-Y gastric bariatric surgery	OTC Possible side effects: GI
Ibuprofen	400 mg x1, may repeat in 4–6 hours	1200 mg	Post–Roux-en-Y gastric bariatric surgery	OTC Possible side effects: GI, cardiovascular, and renal
Acetaminophen/aspirin/caffeine	500 mg (aspirin component), may repeat in 6 hours	4000 mg (acetaminophen component)	Age < 19 years Post–Roux-en-Y gastric bariatric surgery	OTC Ask about acetaminophen from other sources. Lower max dose in severe liver disease.
Naproxen	500 mg x1, may repeat in 6–8 hours	1250 mg	Post–Roux-en-Y gastric bariatric surgery	OTC Possible side effects: GI, cardiovascular, and renal
Diclofenac	50 mg x1, may repeat in 8–12 hours	150 mg	Safety/efficacy not established in pediatrics Post–Roux-en-Y gastric bariatric surgery	Possible side effects: GI, cardiovascular, and renal

## Prophylaxis of tension headache

### Self-care

Advise the patient about the following self-care strategies:

- Keeping a regular schedule of sleep, exercise, and good nutrition. Poor sleeping and eating patterns are triggers for headaches.
- Rearranging work or study areas to avoid physical strain. For example, moving computer screens to eye level, lowering chair so that thighs are parallel to the floor, using a lumbar roll to maintain a good sitting posture, and using a phone headset instead of cradling phone on the neck.
- Gentle stretching exercises and relaxation techniques to prevent neck pain. Heat and ice to relieve neck pain and gentle stretches to help loosen tension in the neck. Robin McKenzie’s book *Treat Your Own Neck* is a good source for effective self-care exercises to lower neck muscle tension naturally. Consider effects of depression and anxiety in neck tension.
- KPWA offers free apps such as the Calm app to help patients incorporate self-care into their daily lives. Despite the lack of strong evidence, mindfulness and good self-care are important ways to promote wellness.
- Limiting caffeine intake to no more than 2 cups a day to help avoid caffeine withdrawal headaches.
- Limiting use of over-the-counter pain medicines (such as Tylenol, Excedrin, aspirin, or ibuprofen) or decongestants (such as Sudafed or pseudoephedrine) to no more than 3 days a week for headaches, to avoid medication overuse headaches.

## Monitoring and prophylaxis planning

- Advise the patient to keep and review a headache diary to monitor the effects of treatment on severity, frequency, and disability. Use the .AVSHEADACHEDIARY SmartPhrase. Patients may opt to use a smartphone app, such as Migraine Buddy, an electronic headache diary.
- Work with the patient to establish an individualized goal of prophylaxis, noting that reducing the frequency and/or severity of headaches—rather than eliminating them completely—is a realistic target.
- Consider follow-up by phone visit in 4–6 weeks to check and adjust treatment options.

## Complementary/alternative medicine

See Options for migraine prophylaxis: Complementary/alternative medicine (CAM), p. 10.

## Medication

While no well-designed randomized controlled trials have shown clear benefit of using SSRIs in prophylaxis of tension headache, this could be considered but may not be effective until at least one month at the maximally tolerated or recommended dose of the SSRI (expert opinion). If there is a concern about concurrent migraine, consider migraine prophylaxis (see p. 9).

# Migraine Headache

## Acute treatment of migraine in Primary Care

The choice of acute migraine treatments should be dictated by the rapidity of onset, headache severity, associated symptoms (e.g., nausea/vomiting), and patient preference. If a patient doesn't respond to 1–2 adequate doses of a given medication during a migraine episode, it is appropriate to try another medication. Use the .MIGRAINEAVS SmartPhrase in KP HealthConnect.

**Note:** It is important to rule out medication overuse headache (MOH) prior to initiating therapy for any acute headache. See MOH Treatment, p. 16.

<b>Table 3. Pharmacologic options for acute treatment of migraine in Primary Care</b>					
<b>NOT RECOMMENDED</b>					
KPWA and national headache guidelines advise <b>against</b> the use of <b>opioids and butalbital-containing medications</b> (e.g., Fiorinal, Fioricet) for treatment of headaches.					
<b>TRIPTANS</b>					
<ul style="list-style-type: none"> <li>• Triptans are first-line treatment for severe migraines as they are generally highly effective, with a low risk of side effects.</li> <li>• Failure of one triptan does not indicate failure of the entire class of medication. Consider trying a second triptan medication if the first one does not improve symptoms.</li> <li>• A combination of triptan and NSAID may be more effective than either medication alone.</li> </ul>					
Medication	Initial dose	Max dose/day	Relative indications	Relative contraindications	Special considerations
Sumatriptan - oral	25–100 mg x1, may repeat in 2 hours	200 mg	Relatively safe in pregnancy	Concomitant ergot or MAOI use	Good choice for most people, most of the time
Rizatriptan - oral	5–10 mg x1, may repeat in 2 hours	30 mg		Cerebrovascular syndrome Significant cardiovascular disease	Prescribe 5 mg dose with concomitant propranolol
Naratriptan - oral	1–2.5 mg x1, may repeat in 4 hours	5 mg	People with ≥ 3-day headaches (long half-life)	Hemiplegic or basilar migraine	Complement to NSAIDs for perimenopausal patients Prescribe 1 mg dose in mild to moderate renal or hepatic disease
Zolmitriptan - oral	1.25–2.5 mg x 1, may repeat in 2 hours	10 mg			
Sumatriptan – nasal solution (e.g., Imitrex)	5–20 mg x1, may repeat in 2 hours	40 mg	Nausea/vomiting or rapid peak in migraine intensity		Taste not acceptable to some patients High cost
Sumatriptan – SQ	6 mg x1, may repeat in 1 hour	12 mg	Nausea/vomiting or rapid peak in migraine intensity		High cost
<b>ASPIRIN &amp; NSAIDs (contraindicated if history of GI bleeding)</b>					
Medication	Initial dose	Max dose	Relative indications	Relative contraindications	Special considerations
Aspirin + acetaminophen + caffeine (Excedrin Migraine or similar)	500 mg (aspirin component), may repeat in 6 hours	4000 mg (acetaminophen component)		Age < 19 years Post-Roux-en-Y gastric bariatric surgery	OTC Ask about acetaminophen from other sources Lower max dose in severe liver disease
Naproxen	500 mg x1, may repeat in 6–8 hours	1250 mg		Post-Roux-en-Y gastric bariatric surgery	OTC Possible side effects: GI
Ibuprofen	400 mg x1, may repeat in 4–6 hours	1200 mg		Post-Roux-en-Y gastric bariatric surgery	OTC Possible side effects: GI
Diclofenac	50 mg x1, may repeat in 8–12 hours	150 mg		Safety/efficacy not established in pediatrics Post-Roux-en-Y gastric bariatric surgery	Possible side effects: cardiovascular, GI

Table 3 continues...

**Table 3. Pharmacologic options for acute treatment of migraine in Primary Care, continued**

ANTIEMETICS					
Medication	Initial dose	Max dose	Relative indications	Relative contraindications	Special considerations
Metoclopramide (Reglan)	5 mg x1, may repeat with adjunctive medication	20 mg	Nausea/vomiting	People at risk for extrapyramidal syndromes (EPS)	Adjunct only, not standalone Caution with long-term use
ERGOTS					
Medication	Initial dose	Max doses	Relative indications	Relative contraindications	Special considerations
Dihydroergotamine - nasal	0.5 mg x1, may repeat in 15 minutes	2 mg daily 4 mg weekly	More severe headache	Safety/efficacy not established in pediatrics	After failure of preferred treatment
Dihydroergotamine - SQ/IM	1 mg x1, may repeat in 1 hour	3 mg daily 6 mg weekly	Nausea/vomiting	Pregnancy Hemiplegic or basilar migraine Ischemic heart disease Severe hepatic or renal impairment	High cost Possible side effects: ergotism (peripheral vascular ischemia, headache, vomiting, diarrhea, gangrene of the fingers and toes)

## Treatment of refractory migraine

For patients with migraines that are not relieved by home care, consider treatment with **fluids, an antiemetic, and an NSAID**.

The choice of medication should be directed by the severity of the attack, the type of symptoms present, patient preference, and patient-specific factors. Two possible starting points are:

- A “cocktail” of IV fluids, IV or IM ondansetron, and IM ketorolac
- A “cocktail” of medications that has worked for the patient before and does **not** include opioids

Sumatriptan SQ may be a useful adjunct if indicated. For other IV or IM options, consult with Urgent Care or Neurology.

For patients who have repeated refractory migraines, consider medication overuse as an underlying cause.



# Migraine prophylaxis

## Overview

There are no clear evidence-based recommendations for when to start preventive therapy for migraine.

The choice of migraine prevention medication should be made based on comorbid conditions (e.g., consider tricyclics for patients with depression and/or neuropathic pain syndromes, valproic acid/divalproex for persons with seizure disorders) and the relative value the patient places on efficacy versus avoidance of side effects.

Develop a **written headache treatment plan** for prevention and management of acute migraine to:

- Decrease headache frequency. (Aim for fewer than 5 headache days per month.)
- Decrease headache severity. (Headaches will respond quickly to an abortive therapy.)
- Avoid medication/caffeine overuse headache. (See MOH Treatment, p. 16.)

## Guiding principles of migraine prophylaxis

- Each medication dose change may take 2–4 weeks to reach maximal effectiveness.
- Using fewer than 5 headache days per month as a goal, the initial dose of each medication should be fairly low, and gradually increased to the maximal tolerated or maximal safe dose. Keep medication at that dose for 1 month before making modifications to therapy.
- Ideally, an adequate trial of a prophylactic medication is 4 weeks at the maximum recommended or tolerated dose before considering an alternative medication.
- When headache days remain fewer than 5 per month for 1 to 2 months, start tapering therapy of the least well-tolerated medication to find the lowest effective dose.
- **Note:** It is important to address medication overuse headache (MOH) prior to initiating headache prophylaxis. See MOH Treatment, p. 16. Patients not responding to combinations of two or three prophylactic medications should be reassessed for MOH, an alternative diagnosis, or confounding psychiatric or social stresses. Drug therapy alone may not be sufficient.

## Options for migraine prophylaxis

### Self-care

Advise the patient about the following self-care strategies:

- Paying attention to food and beverages consumed, as they can trigger migraine attacks. Possible triggers include red wine (sulfites), aged cheeses, and chocolate.
- Keeping a regular schedule of sleep, exercise, and good nutrition. Poor sleeping and eating patterns are triggers for headaches.
- Rearranging work or study areas to avoid physical strain. For example, moving computer screens to eye level, lowering chair so that thighs are parallel to the floor, using a lumbar roll to maintain a good sitting posture, and using a phone headset instead of cradling phone on the neck.
- Gentle stretching exercises and relaxation techniques to prevent neck pain. Heat and ice to relieve neck pain and gentle stretches to help loosen tension in the neck. Robin McKenzie's book *Treat Your Own Neck* is a good source for effective self-care exercises to lower neck muscle tension naturally. Consider effects of depression and anxiety in neck tension.
- KPWA offers free apps such as the Calm app to help patients incorporate self-care into their daily lives. Despite the lack of strong evidence, mindfulness and good self-care are important ways to promote wellness.
- Limiting caffeine intake to no more than 2 cups a day to help avoid caffeine withdrawal headaches.
- Limiting use of over-the-counter pain medicines (such as Tylenol, Excedrin, aspirin, or ibuprofen) or decongestants (such as Sudafed or pseudoephedrine) to no more than 3 days a week for headaches, to avoid medication overuse headaches.

### Monitoring and prophylaxis planning

- Advise the patient to keep and review a headache diary to monitor the effects of treatment on severity, frequency, and disability. Use the **.AVSHEADACHEDIARY** SmartPhrase in KP HealthConnect. Patients may opt to use a smartphone app such as Migraine Buddy, an electronic headache diary.
- Work with the patient to establish an individualized goal of prophylaxis, noting that reducing the frequency and/or severity of headaches—rather than eliminating them completely—is a realistic target.

- Work with the patient to establish an individualized goal of prophylaxis, noting that reducing the frequency and/or severity of headaches—rather than eliminating them completely—is a realistic target.
- Consider follow-up by phone visit in 4–6 weeks to check and adjust treatment options.

## **Complementary/alternative medicine (CAM)**

Note: Patients may incur out of pocket costs for these CAM treatments. For questions about coverage, patients can contact Member Services. A list of preferred CAM providers can be found on the KPWA member website at <https://wa-member.kaiserpermanente.org/html/public/services/alternative> (log-in required).

### **Acupuncture**

- Moderate evidence supports the effectiveness of acupuncture in reducing migraine frequency and medication use in adult patients who have not responded to prophylactic medications.
- There is no evidence on the impact of acupuncture on migraine severity.
- There is no evidence on the effectiveness of acupuncture in teens.

### **Biofeedback**

- Biofeedback is a relaxation technique that uses special equipment to teach the patient how to monitor and control certain physical responses. The most common types of biofeedback are thermal (hand-warming) and electromyographic (EMG).
- Low-strength evidence suggest that biofeedback may help decrease the frequency, duration, and intensity of both migraine and tension-type headaches.
- Biofeedback may also improve secondary outcomes of headache, such as medication use, muscle tension, anxiety, and depression.

### **Cognitive behavioral therapy (CBT)**

- CBT teaches patients strategies on how to cope with everyday stressors that may bring on, worsen, or prolong headaches.
- Low-strength evidence suggests that including a CBT component in self-management interventions may double the effect size on mood but has no significant effect on headache-related disability or pain intensity, so will be most helpful for patients who are also experiencing depression or anxiety.

### **Mindfulness**

- Mindfulness is a mental state achieved by focusing one's awareness on the present moment, while calmly acknowledging and accepting one's feelings, thoughts, and bodily sensations.
- The evidence on use of mindfulness as a therapeutic intervention for migraine or tension-type headache is conflicting.
- Due to lack of harms, mindfulness may be considered for patients who are interested in alternative treatments.
- Mindfulness may be most helpful for patients who are also experiencing depression or anxiety.

### **Yoga**

- Low-strength evidence suggests that yoga may reduce headache frequency, duration, and pain intensity in patients with chronic or episodic tension-type headache.
- When used as an adjunct to medication treatment, yoga + medications may be more effective than medication alone.

### **Relaxation training**

- Relaxation techniques include deep breathing exercises, progressive muscle relaxation, mental imagery relaxation, and relaxation to music.
- There is insufficient published evidence to recommend relaxation training for the treatment of adults with migraine or tension headache.

### **Cefaly device**

- One high-quality randomized controlled trial indicates that transcutaneous supraorbital stimulation using the Cefaly device may be more effective than sham procedure in the short term as prevention therapy.
- The long-term effect of using a Cefaly device is not known.
- It is not likely to be covered. Patients can purchase personal device, returnable after a 90-day trial.

## Supplements

For more information on over-the-counter supplements, see [Consumer Reports](#) or [ConsumerLab.com](#).

### **Riboflavin (B2)**

- Moderate-strength evidence supports the effectiveness of riboflavin in reducing migraine frequency, duration, and disability in the short term (3 months).
- The recommended dose of riboflavin is 400 mg daily.
- The most common side effects are polyuria and diarrhea.
- Consider in combination with magnesium.
- The onset of therapeutic action is 1 to 3 months.

### **Magnesium**

- Low-strength evidence supports the use of magnesium in migraine prophylaxis.
- The recommended dose is 600 mg of elemental magnesium daily.
- Possible side effects include stomach upset and diarrhea.

### **Vitamin D**

- Vitamin D may be beneficial in reducing the frequency of migraine headache days in patients with migraines **and** a known history of vitamin D deficiency. However, vitamin D screening is not routinely recommended.
- Vitamin D does not reduce the severity, duration, or associated symptoms of migraines.
- The dose of vitamin D used in a single randomized controlled trial was 4000 IU/day (Gazerani 2019). No clinical trials have examined the influence of vitamin D supplementation on tension type headaches.

### **Zinc**

- Use of zinc may be superior to placebo in decreasing the frequency of migraine attacks.
- Zinc does not reduce the severity, duration, or associated symptoms of migraines.
- The dose of zinc sulfate used in a single RCT was 220 mg/day (Ahmadi 2020).

### **Melatonin**

- Melatonin may be more effective than placebo in preventing migraines.
- The recommended dose of melatonin is 3 mg.
- Is it difficult to separate the confounding role of melatonin in mood disorders and sleep problems from its impact on migraines.
- There is insufficient evidence to determine the comparative effectiveness of melatonin versus other therapies for preventing migraines in adults.

## Medications and procedures

Table 4 – Medication options for migraine prophylaxis (pp. 12–13)

Table 5 – Additional procedure and medication options for migraine prophylaxis: *Neurology consultation required* (p. 14)

<b>Table 4. Medication options for migraine prophylaxis</b>					
<b>NOT RECOMMENDED</b>					
<p>KPWA and national headache guidelines advise <b>against</b> the use of <b>opioids and butalbital-containing medications</b> (e.g., Fiorinal, Fioricet) for treatment of headaches.</p> <p>There is <b>insufficient evidence to support</b> the use of SSRIs, venlafaxine, gabapentin, or coenzyme Q10 as prophylactic treatment for migraine. Butterbur is no longer recommended because it may contain a compound that is hepatotoxic and carcinogenic.</p>					
<b>BETA BLOCKERS</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Propranolol IR Propranolol ER	40 mg b.i.d. (IR) 80 mg daily (ER)	240 mg (divided t.i.d.) (IR) 240 mg daily (ER)	Hypertension Angina Essential tremor Stress-related migraine Tachycardia	Asthma Depression CHF Raynaud's disease Diabetes Bradycardia	
<b>CALCIUM CHANNEL BLOCKERS</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Verapamil	80 mg daily	240 mg (divided t.i.d.)	Hypertension Arrhythmia Angina Aura Asthma Cluster headache	Constipation Hypotension Sick sinus syndrome Second- or third-degree AV block without pacemaker Severe left ventricular dysfunction	
<b>ACE INHIBITORS</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Enalapril	5 mg	40 mg	Intolerance to other migraine meds Hypertension ASCVD	Pregnancy Hereditary or idiopathic angioedema	Possible side effects: cough
Lisinopril	5 mg	40 mg	Intolerance to other migraine meds Hypertension ASCVD	Pregnancy Hereditary or idiopathic angioedema	Possible side effects: cough
<i>Table 4 continues...</i>					

**Table 4. Medication options for migraine prophylaxis, *continued***

<b>ANTIEPILEPTICS</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Topiramate	25 mg daily	100 mg (divided b.i.d.)	Seizure disorder Bipolar disorder Obesity	Pregnancy Kidney stones Weight loss concerns Cognitive impairment Glaucoma	Titrate by 25 mg weekly Monitor serum bicarbonate, BUN, Cr while titrating Consider in obese patients Possible side effects: "Brain fog" Weight loss Metabolic acidosis
Divalproex DR	125 mg b.i.d.	2000 mg (divided b.i.d.)	Seizure disorder Bipolar disorder Mania	Pregnancy Liver disease Bleeding disorder Obesity	Titrate by 125 mg weekly Monitor ALT, AST, CBC while titrating Possible side effects: Weight gain/loss Hair loss
<b>ANTIDEPRESSANTS</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Nortriptyline – TCA	10–25 mg q.h.s.	150 mg	Neuropathic pain Depression Anxiety Insomnia	Mania Urinary retention Heart block High risk in elderly	Take at bedtime May be helpful for neck tightness, occipital myalgia, insomnia  Better tolerated than amitriptyline
Amitriptyline – TCA	25 mg q.h.s.	150 mg	Depression Anxiety Insomnia Neuropathic pain	Mania Urinary retention Heart block High risk in elderly	Effective combined w/topiramate

**Table 5. Additional options for migraine prophylaxis: *Neurology consultation required***

<b>PROCEDURES</b>					
<b>Procedure</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Occipital nerve block	NA	NA	May reduce the frequency and intensity of migraine headache  Can be used as an adjunct treatment		Administered by Neurology
Botulinum toxin (onabotulinumtoxinA)	NA		Limited benefit, reduces chronic migraine frequency by around 2 days/month and improves patient quality of life when compared to placebo		Adequate trial of at least 3 formulary preferred prophylactic migraine medications may be required for health plan coverage  Administered by Neurology Should be given every 3 months
<b>MEDICATIONS (anti-CGRP monoclonal antibodies)</b>					
<b>Medication</b>	<b>Initial dose</b>	<b>Max dose</b>	<b>Relative indications</b>	<b>Relative contraindications</b>	<b>Special considerations</b>
Erenumab-aooe (SQ)	70 mg monthly	140 mg monthly	More effective than placebo in preventing episodic and chronic migraine headaches	Avoid in pregnancy and in adults with cardiovascular risks or vascular malformations  Constipation with serious complications and hypertension have been reported with erenumab-aooe	Long-term side effects are unknown  Adequate trial of at least 3 formulary preferred prophylactic migraine medications may be required for health plan coverage  Prescribed in Neurology
Fremanezumab-vfrm (SQ)	225 mg monthly <b>or</b> 675 mg every 3 months	225 mg monthly <b>or</b> 675 mg every 3 months			
Galcanezumab-gnlm (SQ)	Loading dose: 240 mg x 1  Maintenance dose: 120 mg monthly	120 mg monthly			
Eptinezumab-jjmr (IV)	100 mg every 3 months	300 mg every 3 months			

# Menstruation-related migraine prophylaxis

**Note:** For acute treatment of menstruation-related migraine, see “Acute treatment of migraine in Primary Care” on p. 7.

## Monitoring and prophylaxis planning

- Advise an individual with suspected menstrual migraine to keep a headache diary for at least 2 months to determine if they are having regular and predictable menses and if these correlate with headache onset. Some patients experience migraines around the time of ovulation (either alone or in addition to during menses).
- Use the **.AVSHEADACHEDIARY** SmartPhrase in KP HealthConnect. Patients may opt to use a smartphone app, such as Migraine Buddy, an electronic headache diary.
- Work with the patient to establish an individualized goal of prophylaxis, noting that reducing the frequency and/or severity of headaches—rather than eliminating them completely—is a realistic target.
- Consider follow-up by phone visit in 4–6 weeks to check and adjust treatment options.

## Medication options

Table 6. Medication options for menstruation-related migraine prophylaxis					
<b>NOT RECOMMENDED</b>					
KPWA advises <b>against</b> the use of estrogen-containing <b>oral contraceptive pills</b> for menstrual migraine <b>with aura</b> due to increased risk for stroke. KPWA and national headache guidelines advise <b>against</b> the use of <b>opioids and butalbital-containing medications</b> (e.g., Fiorinal, Fioricet) for treatment of headaches.					
<b>ORAL CONTRACEPTIVES</b>					
Oral contraceptives are first-line treatment for patients with irregular menses and premenstrual migraines <b>without aura</b> . Aura is defined as non-headache symptoms (e.g., tingling in limbs, visual disturbances) that precede the onset of a migraine headache.					
Medication	Initial dose	Max dose	Relative indications	Relative contraindications	Special considerations
Use shared decision-making to choose appropriate option for the individual				Migraine with aura	
<b>NSAIDS</b>					
Consider a short course of prophylaxis with naproxen or a triptan twice a day starting 2–3 days before the anticipated onset of the headache and continuing for 5 days through the at-risk period.					
Medication	Initial dose	Max dose	Relative indications	Relative contraindications	Special considerations
Naproxen	500 mg x1, may repeat in 6–8 hours	1250 mg		Post-Roux-en-Y gastric bariatric surgery	OTC Possible GI side effects
<b>TRIPTANS</b>					
Long-acting forms are recommended. Consider a short course of prophylaxis with naproxen or a triptan twice a day starting 2–3 days before the anticipated onset of the headache and continuing for 5 days through the at-risk period.					
Medication	Initial dose	Max dose	Relative indications	Relative contraindications	Special considerations
Naratriptan	1–2.5 mg x1, may repeat in 4 hours	5 mg	Patients with ≥ 3-day headaches (long half-life)	Concomitant ergot or MAOI use Cerebrovascular syndrome Significant cardiovascular disease	Complement to NSAIDs for perimenopausal individuals Prescribe 1 mg dose in mild to moderate renal or hepatic disease
Zolmitriptan	1.25–2.5 mg x1, may repeat in 2 hours	5 mg	Patients with ≥ 3-day headaches (long half-life)	Hemiplegic or basilar migraine	

# Medication Overuse Headache Treatment

Medication overuse headache (MOH) is a state of daily or near-daily refractory headaches. Also known as *rebound headache*, MOH occurs at least 15 days per month in patients with pre-existing headache disorder who have regularly overused acute or symptomatic headache medication for 3 months or longer. (“Overuse” is defined as > 10 days or > 15 days per month, depending on the medication.)

**Rule out medication overuse headache prior to initiating therapy for any acute headache.** If MOH is present, prevention and acute headache medications may not be effective. Overuse is a concern with all headache medications, including over-the-counter medications (all NSAIDs, analgesics, or decongestants) and caffeine in more than moderate amounts. Overuse of prescription acute migraine remedies (e.g., sumatriptan, rizatriptan) can also cause medication overuse headaches.

For patients found to have MOH,

1. Advise that it will take 2–6 weeks to resolve the MOH after withdrawing all acute headache medications that the patient has been taking.
2. Stop all acute headache medications. Tapering may be required.
3. Start a prophylactic medication at the same time or, ideally, prior to stopping acute headache medications. See “Options for migraine prophylaxis—medications and procedures,” p. 12.
4. Treat symptoms during withdrawal of acute headache medications.
5. Use the SmartPhrase **.AVSHEADACHEMEDOVERUSE** to develop a written headache treatment plan that includes acute and prophylactic treatment as well as a plan for close follow-up and relapse prevention.



# Evidence Summary

The Migraine and Tension Headache Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

## External guidelines eligible for adapting

- 2018 Scottish Intercollegiate Guidelines Network (SIGN). [Pharmacological Management of Migraine](#). (SIGN publication no. 155)
- 2019 The Global Campaign against Headache on behalf of the European Headache Federation and Lifting the Burden: [Aids to management of headache disorders in primary care \(2nd edition\)](#)
- 2018 The American Headache Society [Position Statement on Integrating New Migraine Treatments into Clinical Practice](#)
- 2018 Kaiser Permanente Southern California Clinical Reference: Migraines: Approach to the Management of the Adult Patient

## Key questions

1. What is the safety and effectiveness of **calcitonin gene-related peptide (CGRP) receptor antagonists (CGRP-RAs)** compared to standard/routine drugs used for the preventive management of episodic and chronic migraine in adults?
2. What is the comparative safety and effectiveness of **occipital nerve block** versus other pharmacological or nonpharmacological therapies used to reduce pain in adult patients with chronic migraine headache?
3. What is the comparative safety and effectiveness of **botulinum toxin** versus other pharmacological or nonpharmacological therapies used for the prophylactic management of chronic migraine headache in adults?
4. What is the safety and effectiveness of vitamins and supplements for migraine prevention and/or relief of symptoms in adolescents and adults with frequent episodes of headache: **vitamin D, coenzyme Q10, zinc, melatonin**?
5. What is the evidence on the harms associated with **butterbur** used for the prevention of migraine or tension headache?
6. What is the safety and effectiveness of biobehavioral/psychological therapies for the treatment and /or prophylactic management of migraine or tension headache in adults and adolescents: **biofeedback, cognitive behavioral therapy, relaxation training, mindfulness**?
7. What is the efficacy of **yoga** when used as an adjuvant therapy in reducing the frequency and intensity of migraine headache in adults?

**1. What is the safety and effectiveness of calcitonin gene-related peptide (CGRP) monoclonal antibodies compared to standard/routine drugs used for the preventive management of episodic and chronic migraine in adults?**

The published randomized controlled trials (RCTs) CONQUER (Mulleners 2020), FOCUS (Ferrari 2019), and LIBERTY (Reuter 2018) and meta-analyses of phase II and phase III RCTs (Deng 2020, Han 2019) show that the three monoclonal antibodies targeting the CGRP—fremanezumab, galcanezumab, and erenumab—are superior to placebo in reducing monthly migraine headache days and are well tolerated for up to 12 weeks (the durations of the trials) in adult non-pregnant patients who had previously not responded to up to four classes of migraine-preventive medications. These results, however, may not be generalized to pregnant or breastfeeding patients, adolescents, or younger children, as these patient groups were excluded from the published trials.

The three trials had valid methodology with very low risk of bias. However, all comparisons were made versus placebo and not to an active comparator; the follow-up duration was only 12 weeks; and the trials were funded by pharmaceutical companies.

In conclusion, there is insufficient published evidence to date to determine:

- The comparative safety and effectiveness of CGRP mAbs versus other therapies used for the prophylaxis of episodic or chronic migraine headache.
- The long-term safety and effectiveness of CGRP mAbs compared to placebo.
- The gender or ethnic subgroups of patients who may respond better to the therapy, as the majority of study participants were white women.
- The most efficacious regimen and/or dose for the CGRP mAbs evaluated and approved by the FDA.

**2. What is the comparative safety and effectiveness of occipital nerve block (also known as greater occipital nerve block or GONB) versus other pharmacological or non-pharmacological therapies used to reduce pain in adult patients with chronic migraine headache?**

Low-strength evidence from two recent systematic reviews with meta-analyses (Shauly 2019, Zhang 2018) of small RCTs evaluating the efficacy of GONB for the treatment of migraine headache suggests that GONB may reduce the frequency and intensity of migraine headache and the use of analgesic medication over the short duration of the studies. The meta-analyses had generally valid methodology; however, both had the limitations of including relatively small studies, short follow-up duration, lack of details on migraine frequency, variations between trials in the types and dosages of local anesthetics given with or without steroids, and the time and techniques of applying GONB.

**3. What is the comparative safety and effectiveness of botulinum toxin (BTX) versus other pharmacological or nonpharmacological therapies used for the prophylactic management of chronic migraine headache in adults?**

There is low-strength evidence from two recent meta-analyses of RCTs (Bruloy 2018, Herd 2019) suggesting that:

- Botulinum toxin may reduce the frequency of chronic migraine episodes by around 2 days/month and improve patient quality of life when compared to placebo.
- There was no significant difference in the frequency of chronic migraines when BTX was compared to active preventive therapies (topiramate or sodium valproate).
- No significant improvement was observed for patients with episodic migraine.
- The rate of adverse events associated with BTX was twice that of placebo, but slightly lower when compared to active prophylactic treatments used in the trials.

**4. What is the safety and effectiveness of vitamins and supplements for migraine prevention and/or relief of symptoms in adolescents and adults with frequent episodes of headache: vitamin D, coenzyme Q10, zinc, melatonin?**

*Vitamin D*

The more recent published systematic reviews (SRs) and RCTs on the effect of vitamin D supplementation in patients with migraine headache consists of two qualitative SRs (Nowaczewska 2020, Ghorbani 2019) and three RCTs (Gazerani 2019, Mottaghi 2015, Buettner 2015).

These provide low-strength evidence suggesting that vitamin D supplementation may be beneficial in reducing the frequency of migraine headache days but not the severity, duration, or associated symptoms in patients with migraine, especially those with vitamin D deficiency.

*Coenzyme Q10*

There is insufficient published evidence to date to determine the safety or efficacy of coenzyme Q10 for the prevention of migraine headache.

*Zinc*

Low-strength evidence from one relatively small recent RCT (Ahmadi 2020) suggests that zinc supplementation is superior to placebo in decreasing the frequency of migraine attacks, but not in reducing the severity and duration of the attacks. No adverse events were reported by the participants.

*Melatonin*

The literature search on the use of melatonin for prophylaxis and/or treatment of acute headache identified three systematic reviews without or with meta-analysis when feasible (Liampas 2020, Long 2019, Leite Pacheco 2018), a small recent pilot study on the use of melatonin for the acute treatment of migraine in children and adolescents, and earlier published small RCTs, case control studies, and observational studies included in the Liampas systematic review.

Low-strength evidence suggests that melatonin may be more efficacious than placebo in the preventive treatment of migraine. As noted by Liampas and colleagues, "The complex relationship of migraine with mood disorders, as well as sleep problems, does not allow determining the effect of these confounding factors on the outcomes of the studies."

In conclusion, there is insufficient evidence overall to determine the comparative effectiveness and safety of any of these supplements versus other active preventive therapies used in adult patients with migraine headache.

**5. What is the evidence on the harms associated with butterbur used for the prevention of migraine or tension headache?**

Very low-strength evidence suggests that butterbur may be effective in the prophylactic treatment of migraine headaches; however, there is insufficient evidence to determine its long-term efficacy or safety, and there are concerns regarding the association between butterbur and liver toxicity. According to the literature, it is unclear if hepatotoxicity is due to alkaloids in the formulation or in the butterbur itself.

**6. What is the safety and effectiveness of biobehavioral/psychological therapies for the treatment and/or prophylactic management of migraine or tension headache in adults and adolescents: biofeedback, cognitive behavioral therapy, relaxation training, mindfulness?**

The literature search for meta-analyses and RCTs published in the last 5 years on psychological treatment for headache identified two systematic reviews with meta-analyses (Lee 2019, Probyn 2017), two meta-analyses on mindfulness meditation (Anheyer 2019, Gu 2018), and a literature review conducted by Veterans Affairs researchers (Kondo 2019) on the efficacy of biofeedback for different health conditions, including migraine. The results of the published literature on each of these interventions are as follows:

*Biofeedback*

Low-strength evidence suggests that biofeedback may help decrease the frequency, duration, and intensity of both migraine and tension-type headaches.

*Cognitive behavioral therapy*

There is low-strength evidence from one meta-analysis (Probyn 2017) suggesting that including a CBT component in self-management interventions may double the effect size on mood but with no significant effect on headache-related disability or pain intensity. An earlier meta-analysis (Harris 2015) could not draw a conclusion on the effect of CBT on migraine due to mixed findings.

*Mindfulness*

The published evidence on mindfulness-based stress reduction (MBSR), and mindfulness-based cognitive therapy (MBCT) interventions for migraine or tension-type headache is conflicting and insufficient to make any recommendations on the use of the interventions for the treatment of adult patients with primary headache.

*Relaxation training*

There is insufficient published evidence to recommend relaxation training for the treatment of adults with migraine or tension headache.

**7. What is the efficacy of yoga as an adjuvant therapy in reducing the frequency and intensity of migraine headache in adults?**

The more recent published literature on the effects of yoga on headache includes a systematic review with meta-analysis (Anheyer 2019) that investigated the effect of yoga on headache disorders, and an RCT (Kumar 2020) that evaluated the effectiveness of yoga as an adjuvant to conventional medical management on clinical outcomes in patients with migraine.

The Anheyer meta-analysis provides low-quality evidence suggesting that yoga may reduce headache frequency, duration, and pain intensity in patients with chronic or episodic tension-type headache, but not in those with migraine headache. These results should be interpreted with caution, as all the trials included were small, had poor methodological quality, and had variations in the intensity, duration, and frequency of the interventions. In addition, four of the five trials were conducted in India, where yoga is a common practice and its interventions may be much more intense than those in the Western world.

The Kumar RCT shows that yoga used as an add-on therapy may be superior to medical therapy alone in patients with migraine headache. The authors did not perform any sub-analyses to determine whether the positive effect of adding yoga to medical therapy was related to the type of yoga regimen used, its duration, or the timing of practice in relation to the stage of migraine.

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## Guideline Development Process and Team

### Development process

To develop the Migraine and Tension Headache Guideline, the guideline team adapted recommendations from external developed evidence-based guidelines and/or recommendations organizations that establish community standards. The guideline team reviewed additional evidence in several areas. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in May 2021.

### Team

The Headache Guideline development team included representatives from the following specialties: Adolescent Medicine, Family Practice, Neurology, Obstetrics/Gynecology, Pharmacy, Residency, and Urgent Care.

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