



Headaches

Streamlining the Treatment of a Common Complaint

VA



U.S. Department of Veterans Affairs

Veterans Health Administration
PBM Academic Detailing Service

Headaches

Streamlining the Treatment of a Common Complaint

A VA Clinician's Guide



VA PBM Academic Detailing Service

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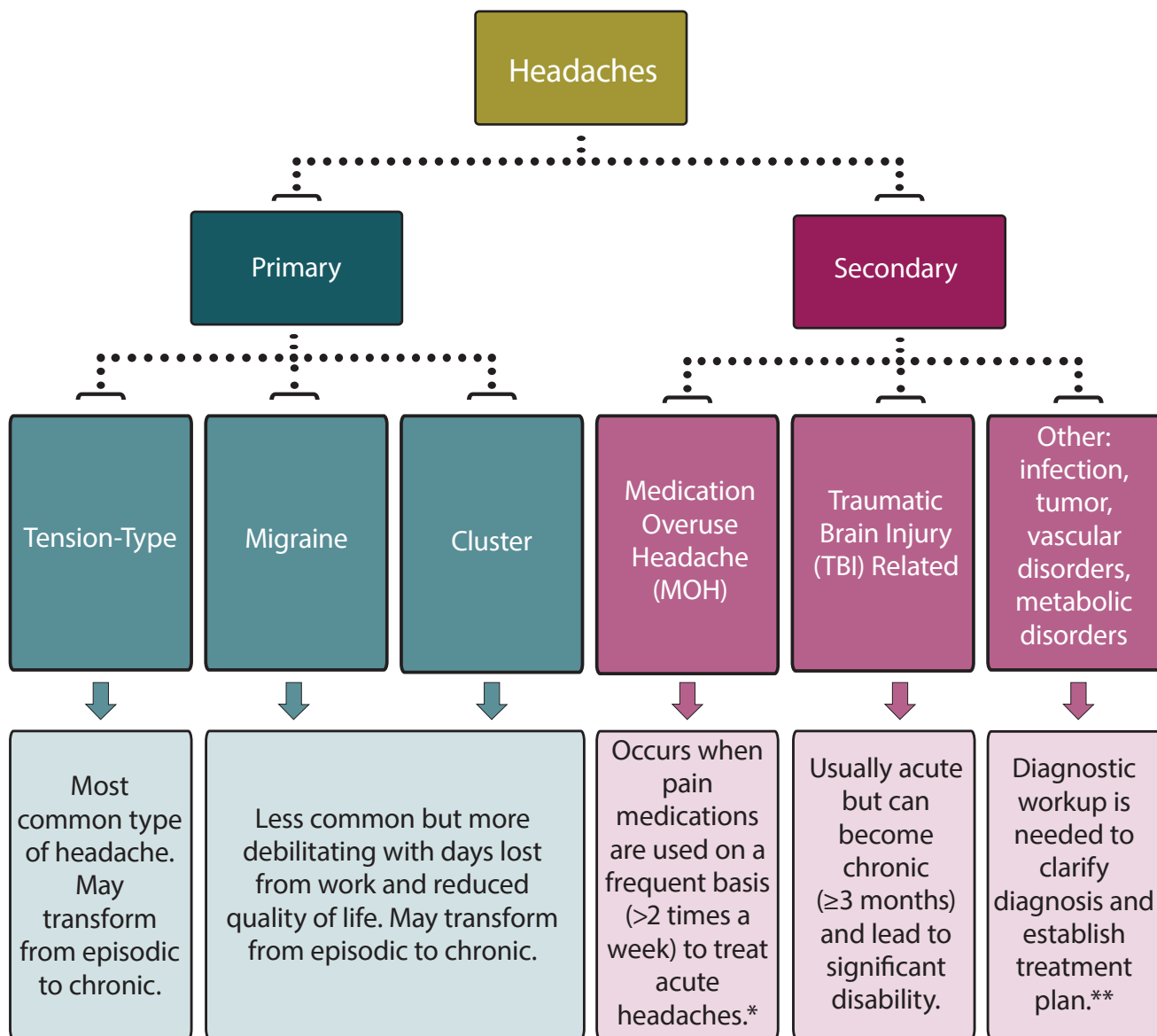
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Headaches are a common complaint of patients and can cause significant disability. Over 50% of Americans have had a headache at least once in the past year and over 90% have suffered from a headache in their lifetime.^{1,2}

Headaches can be classified as primary or secondary based on the cause of the headache and further sub-classified based on symptoms.³

Figure 1. Types of Headaches¹⁻⁴



*Common medications causing MOH include: barbiturates > opioids > serotonin 5HT agonists (triptans) > NSAIDs.
 **Red Flags which include sudden onset of headache, fundamental change in headache pattern or character, onset of headache after 50 years of age, increased frequency or severity of headache, new onset of headache with an underlying medical condition, headache with concomitant systemic illness, focal neurologic signs and symptoms, papilledema, history of seizure, and headache subsequent to head trauma should prompt provider to perform diagnostic workup. NSAID = Nonsteroidal anti-inflammatory drug.

Primary Headaches

What Type of Headache is it? Tension-Type — Migraine — Cluster Headache?

Determining what type of headache and the most appropriate treatment can take time. Consideration of lifestyle changes and nonpharmacologic options, as well as pharmacologic options for acute and preventive treatment, are necessary to locate the optimal treatment.

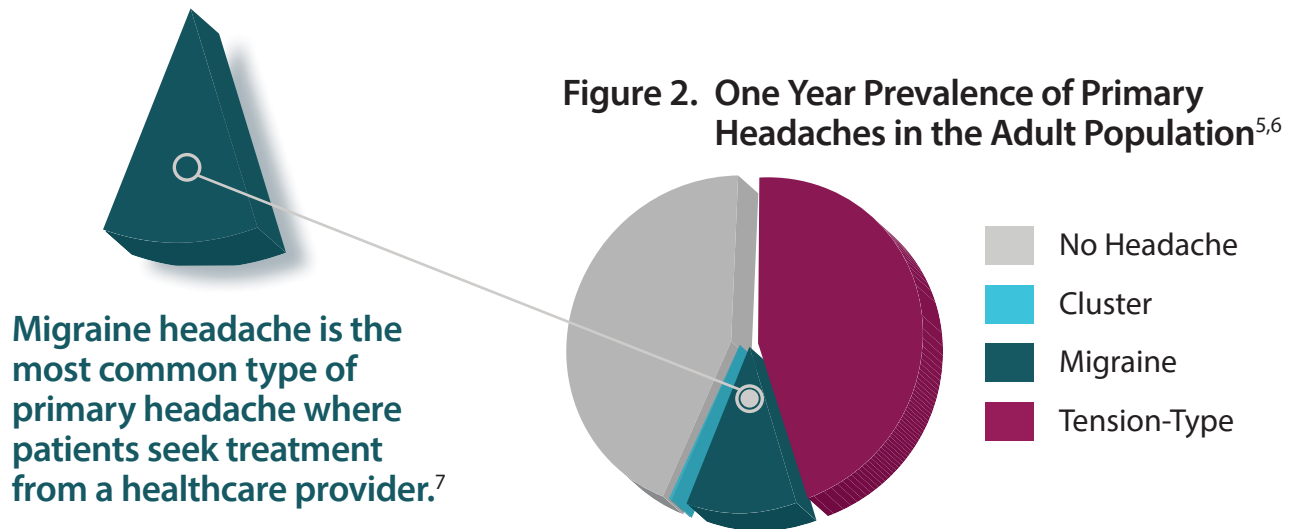










Table 1. Characteristics of Primary Headaches^{2,4,7,8}

Tension-Type	Migraine	Cluster
<ul style="list-style-type: none"> • Location: bilateral • Severity: mild to moderately severe • Duration: 30 minute to 7 days • May have light or sound sensitivity • No aura • No nausea/vomiting • Near equal gender prevalence 	<ul style="list-style-type: none"> • Location: unilateral • Severity: moderate to severe • Duration: over 4 hours if untreated • Light and sound sensitivity • Nausea/vomiting • Aura common • Patient’s usual response: minimizing movement and exertion • More common in females 	<ul style="list-style-type: none"> • Location: unilateral orbital or retroorbital • Severity: severe to extremely severe • Duration: less than 3 hours if untreated • Rarely light sensitivity • Rarely has aura • Rarely has nausea/vomiting • Patient’s usual response: agitation and pacing • More common in males

Nonpharmacologic Approaches to Improve Symptoms in Patients with Headaches

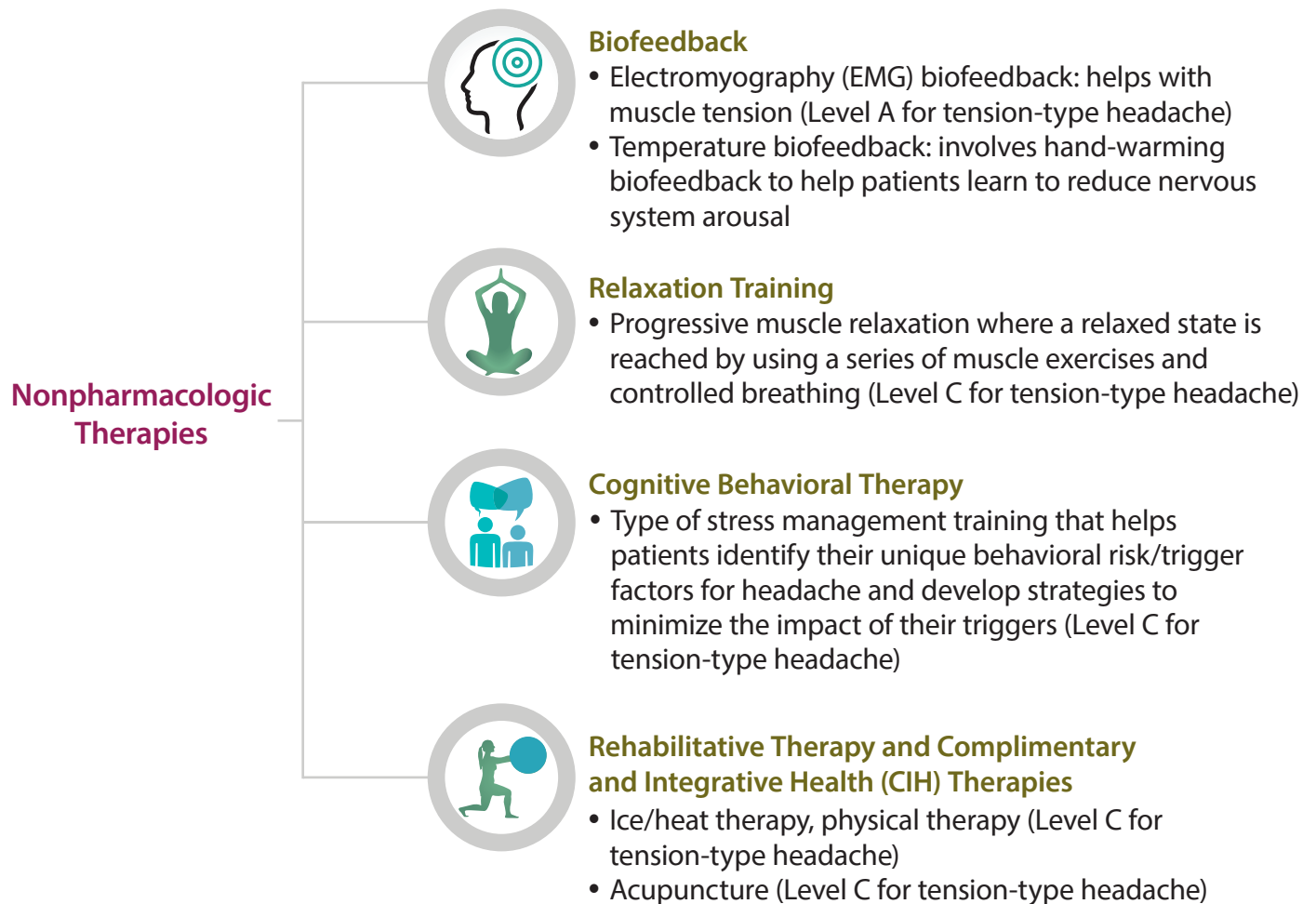
Consider using nonpharmacologic approaches alone or in combination with medications to reduce the frequency and intensity of chronic headaches.⁹ Nonpharmacologic approaches can be beneficial for any patient with headaches.

Figure 3. Address Lifestyle Triggers and other Common Factors that Exacerbate Headaches^{9,10}

	Stress	Reduce it by deep breathing, relaxation, meditation, yoga, exercise
	Mood Disorders	Address with counseling and/or medications, exercise
	Sleep Patterns	Evaluate restless sleep, snoring, sleep apnea
	Inactivity	Increase activity/exercise to at least 30 minutes a day
	Pain Medications	Keep use to less than 2 times a week for any reason
	Blood Pressure and Pulse	Monitor at least every 6 months and if hypertensive, treat to recommended goal range, encourage exercise
	Caffeine Consumption	Keep use to 1 cup of coffee a day or less
	Diet	Avoid skipping meals, eating aged cheeses, processed meats or red wine high in tannins, artificial sweeteners* and adding MSG** to foods; drink plenty of water daily to avoid dehydration

*Aspartame and saccharin have been associated with triggering migraine headaches. **Monosodium glutamate.

Figure 4. Common Nonpharmacologic Therapies with Evidence to Support Use in Headaches^{9,20}



Level of Evidence: A = established as effective; B = probably effective; C = possibly effective.

Some groups may experience greater benefit from these approaches including the following:

- Patients with mood and/or anxiety disorders
- Patients with difficulty coping with headache or significant disability from headaches
- Patients with high perceived stress level or significant problems with managing stress
- Medication overuse
- History of trauma
- Patients wanting to use nonpharmacologic therapy

Address lifestyle triggers and other common factors which can worsen headache symptoms.

Nutraceuticals with Evidence to Support Use in Headaches^{11-13,15}

Many patients with headaches use complementary and alternative medicine (CAM) for headache relief at different points in their headache history. Some begin these in order to avoid using medications, while others may turn to these options after a lack of effect, cost concerns, and/or side effects from prescribed medications. Providers should ask about the use of CAM and consider potential drug-nutraceutical interactions when medications are started or doses are adjusted.

49.5% of patients with migraine/severe headache reported using complementary and alternative medicine (CAM)

Table 2. Nutraceuticals with Evidence for Use in Primary Headaches¹¹⁻¹⁸

Nutraceutical*	Type of Headache	Level of Evidence**	Considerations
Petasites (Butterbur)***	Prevention of migraine	A/B	Caution some preparations may contain plant carcinogens and hepatotoxic pyrrolizidine alkaloids; consider products where these have been completely removed.****
Magnesium	Treatment and prevention of migraine	B/C	May be more effective in patients who are deficient in magnesium.
Riboflavin***	Prevention of migraine	B/C	Low risk of side effects.
Coenzyme Q10 (CoQ10)***	Prevention of migraine	C	May work better in patients who are deficient in CoQ10.
Melatonin	Prevention of cluster headache	C	Low risk of side effects, more research needed.

***Federal law does not require dietary supplements (nutraceuticals) to be proven safe or effective to FDA standards before being sold to consumers.** **Based on American Academy of Neurology/American Headache Society and European Federation of Neurological Sciences Ratings. ***Not available from VA Pharmacy.

****Butterbur has clinical evidence to support use for headache, however, many preparations have pyrrolizidine alkaloids (PA) which can be carcinogenic, hepatotoxic and cause bleeding problems. Petadolex® brand is PA-free. Level of evidence: A = established as effective; B = probably effective; C = possibly effective.

Acute Treatment of Primary Headaches

Figure 5. Goals of Therapy for Acute Headache Treatment^{7,12,19,20}



Table 3. Medications Used for Treatment of Acute Headaches^{7,12,20–32}

Acute Treatment	Tension-Type	Migraine	Cluster
First Line	Acetaminophen (APAP) Aspirin, NSAIDs	NSAIDs, aspirin or APAP Oral triptan, injectable sumatriptan, intranasal triptan or intranasal DHE ^{NF*} Combination of oral triptan and NSAID ^{**}	Injectable sumatriptan Oxygen 100% at 6–12 L/minute for 15 minutes Intranasal triptan (patient resisting injection)
Second Line	Acetaminophen/caffeine ^{NF} Aspirin/caffeine ^{NF} Acetaminophen/aspirin/caffeine ^{NF}	Injectable DHE May add prochlorperazine or promethazine, or chlorpromazine ^{***} for nausea/vomiting	Oral triptan

*Dihydroergotamine. **If monotherapy with triptan is not effective, consider adding an NSAID (caution in elderly, renal impairment and history of GI bleed). ***Avoid metoclopramide due to risk of tardive dyskinesia, which involves involuntary movement of the body that can continue after the drug is discontinued. If patient cannot take triptan or DHE due to contraindication (e.g., heart disease) and are having nausea/vomiting, consider using combination of acetaminophen, aspirin and antiemetic (prochlorperazine, promethazine, chlorpromazine). **NF = Not currently on VA National Formulary**; MOH = medication overuse headache; OUD = opioid use disorder.

Table 3. Medications Used for Treatment of Acute Headaches^{7,12,20-32} (Cont.)

Acute Treatment	Tension-Type	Migraine	Cluster
Recommend Against	Triptans due to lack of effect Muscle relaxants due to lack of effect		
	Opioids and butalbital due to risk of MOH, OUD and possible overdose due to taking repetitive doses during acute headache		

*Dihydroergotamine. **If monotherapy with triptan is not effective, consider adding an NSAID (caution in elderly, renal impairment and history of GI bleed). ***Avoid metoclopramide due to risk of tardive dyskinesia, which involves involuntary movement of the body that can continue after the drug is discontinued. If patient cannot take triptan or DHE due to contraindication (e.g., heart disease) and are having nausea/vomiting, consider using combination of acetaminophen, aspirin and antiemetic (prochlorperazine, promethazine, chlorpromazine). **NF = Not currently on VA National Formulary**; MOH = medication overuse headache; OUD = opioid use disorder.

Use first line and second line treatment options, when possible, for acute headache treatment.

Preventive Treatment for Primary Headaches

Medication for prophylaxis of headaches should be considered for any patient who has headaches more than 2 days a week or who experiences headaches that interfere with work or other activities.^{19,20,33-36}

Encourage patients to continue to work on lifestyle changes and non-pharmacologic therapies when preventive treatments are started.

Most medications for headache prophylaxis require dose titration and the onset can take four to six weeks or longer.³⁴

- ✓ Titrate at a slower rate for patients who are sensitive to medication adverse effects.
- ✓ Clearly explain to patients the expectations of the medication.
- ✓ Try to use preventive medications that may also help other comorbidities in the patient.

Are Patients Receiving Migraine Preventive Treatments?³⁴

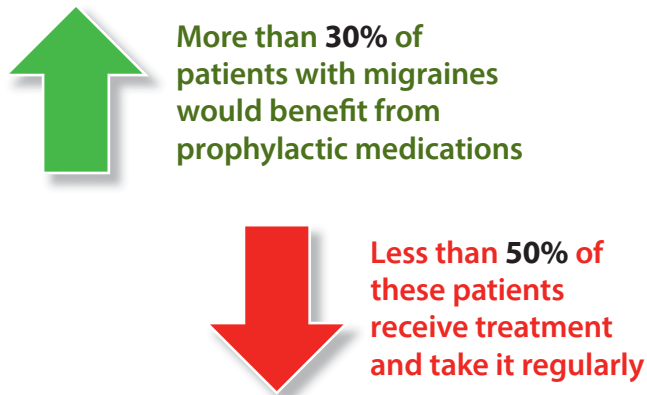
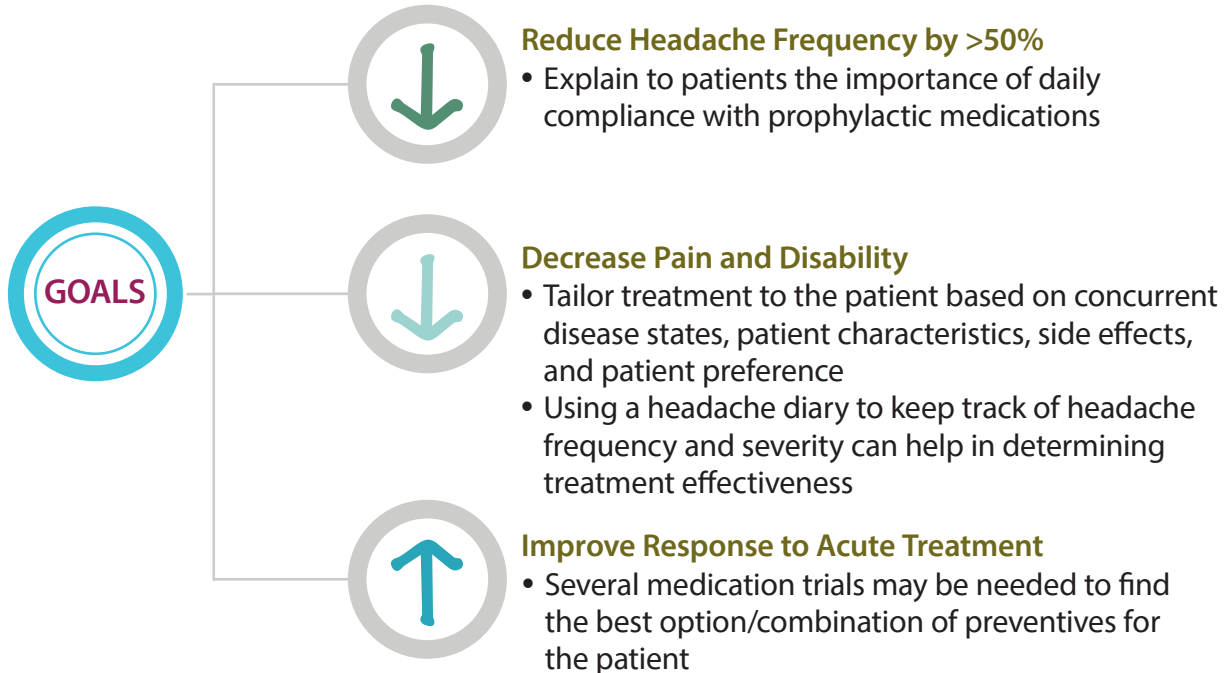


Figure 6. Goals of Medication Therapy for Headache Prevention^{19,20,33,34}



Choose preventive medication(s) based on co-morbidities, to reduce total number of medications prescribed. Use medication that is dosed once or twice daily if possible to improve medication adherence.

Table 4. Medications Used for the Prevention of Headaches^{19,20–23,26,27,29,32–36}

Preventive Treatment	Tension-Type	Migraine	Cluster*
First Line	Antidepressants: Amitriptyline Imipramine Nortriptyline** Desipramine**	Antiepileptics: Topiramate, Divalproex, Sodium Valproate Beta Blockers: Metoprolol Propranolol, Timolol ^{NF}	Verapamil***
Second Line	Antidepressants: Mirtazapine Venlafaxine	Antidepressants: Amitriptyline Imipramine Nortriptyline** Desipramine** Venlafaxine Beta Blockers: Atenolol, Nadolol ^{NF}	Mood stabilizer: Lithium**** Antiepileptic: Topiramate****
Third Line	Antidepressants: Clomipramine	Antihypertensives: Lisinopril Clonidine Guanfacine Candesartan ^{NF} Antiepileptics: Carbamazepine Other: Cyproheptadine Botulinum Toxin [†]	Antiepileptic: Divalproex, Sodium Valproate**** Antispasmodic: Baclofen****
Recommend Against	Triptans and botulinum due to lack of effect Muscle relaxants due to lack of effect Opioids and butalbital due to risk of MOH, OUD and possible overdose due to taking repetitive doses		

*Recommendations for treatment are based primarily on the American Academy of Neurology (AAN) endorsed systematic review for Migraine, on European Federation of Neurologic Societies Guidelines for Tension and Cluster Headache, and on a new AHS guideline for Cluster Headache. Much less clinical trial information is available for cluster headache, so the cluster recommendations were modified to incorporate both clinical experience and available trial evidence. **Consider nortriptyline or desipramine if needing less anticholinergic effects and less sedation, but amitriptyline has the best level of evidence. ***Use single suboccipital injection of short and long-acting betamethasone as transitional therapy while starting verapamil. ****Use for episodic and chronic cluster headache. All other preventatives were evaluated only for episodic cluster headache. †See VA PBM Criteria for Use for Botulinum Toxin at www.cmopnational.va.gov/cmop/PBM/default.aspx for patients with migraines on 15 or more days a month. **NF = Not currently on VA National Formulary.**

Provide preventive treatment for patients experiencing frequent headaches, typically more than 2 headaches a week or based on disability from the headache.

Opioid Analgesics for Headaches?

Opioid analgesics are often prescribed for headaches, despite not being recommended as first line therapy by consensus guidelines.^{19,37} The first prescription of an opioid can lead to chronic use in some patients. A common place where patients receive opioids for headaches is the emergency room (ER) with one review showing opioid use for headaches increasing from 20.6% to 35% in the time period of 2001 to 2010.³⁷

Figure 7. Weighing the Benefits and Risks of Using Opioids for Headaches

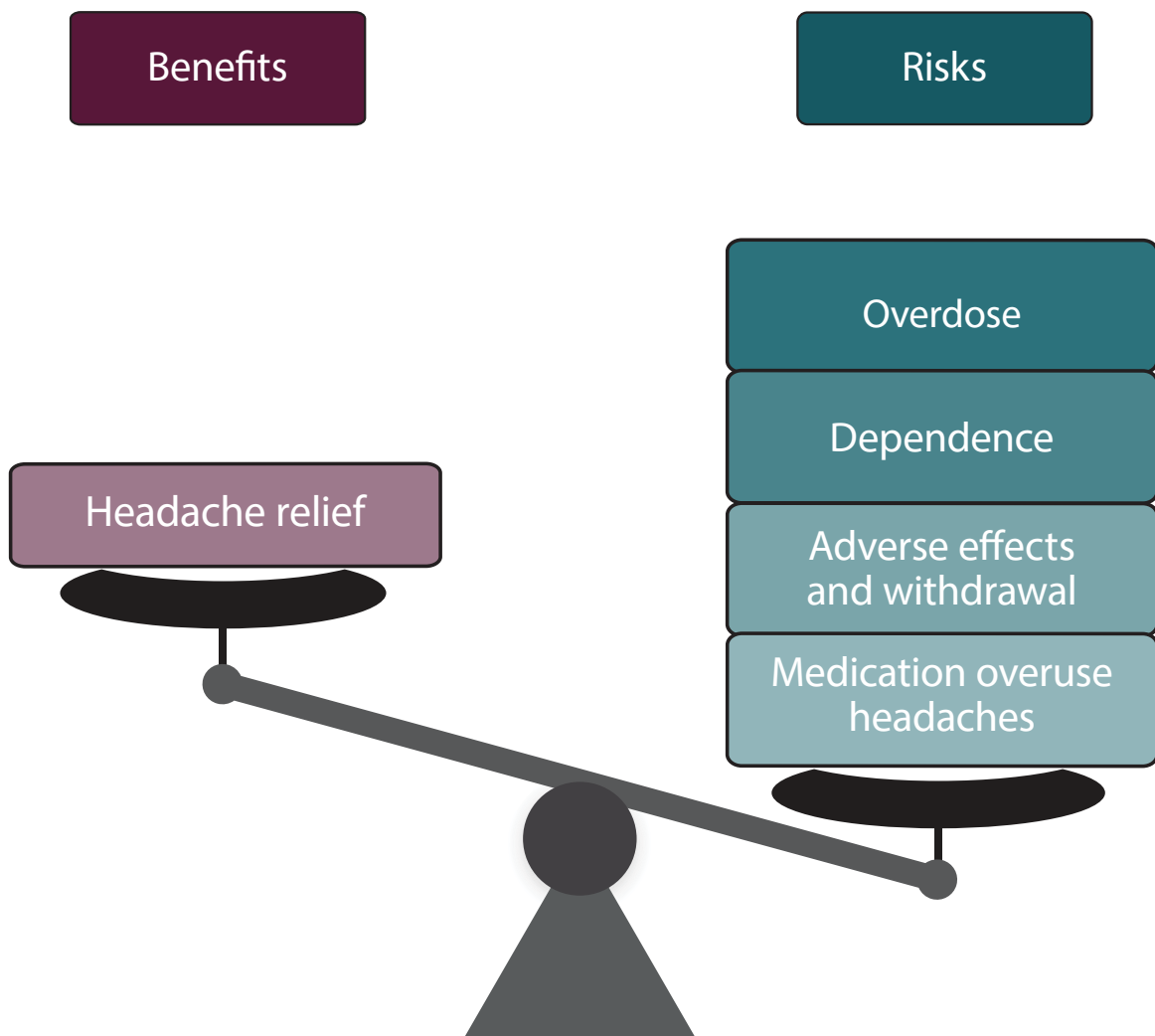
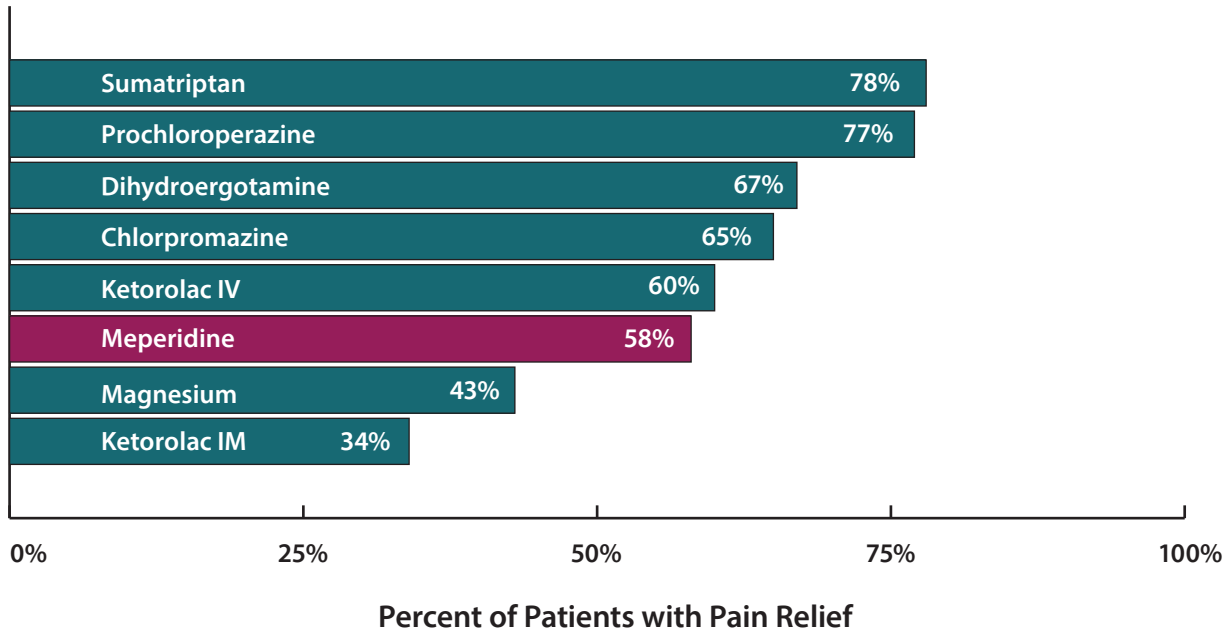


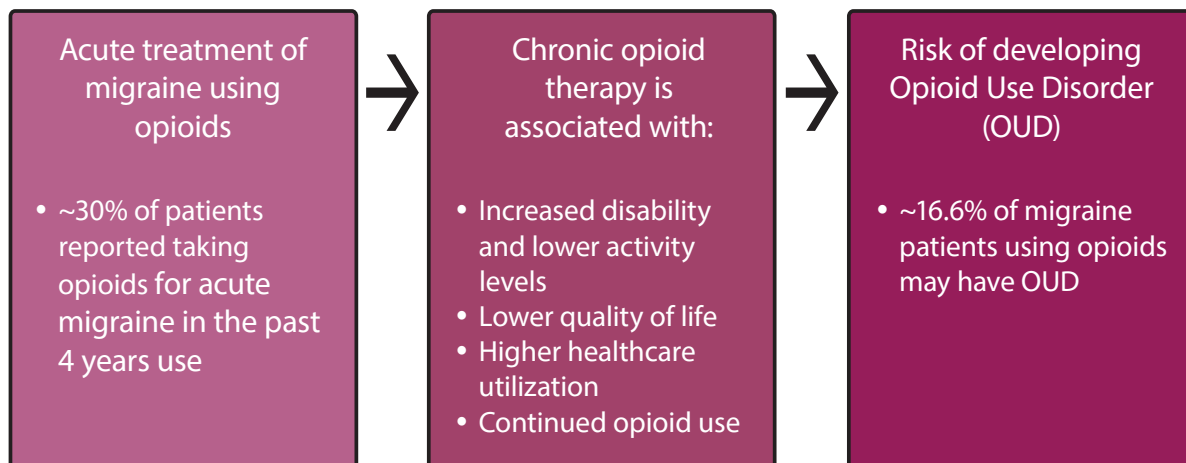
Figure 8. Opioids are not Superior in Reducing Migraine Headache Pain to First and Second Line Acute Headache Treatments³⁸



Weighted averages of the percentages of pain relief from migraine headache for all medications for which there were >2 randomized trials with the medication used as a single agent. IM = intramuscular; IV = intravenous.

Opioids are not recommended for acute or preventive headache treatment.

Figure 9. Using Opioids for Acute Headache Treatment Can Lead to Chronic Use of Opioids^{30,39-41}



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Avoid prescribing opioid or butalbital-containing medications for headaches due to the risk of medication overuse headache (MOH), opioid use disorder (OUD), and possible overdose.

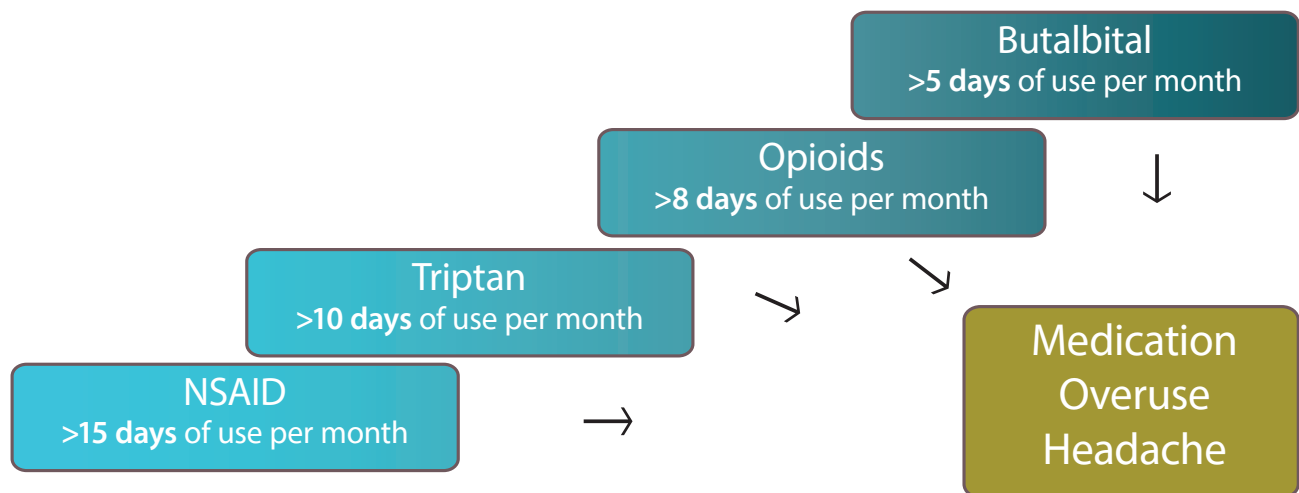
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Secondary Headaches

Medication Overuse Headaches (MOH)^{3,42}

Medication Overuse Headache (MOH) is a headache that develops secondary to the use of medications for the acute treatment of headaches. Most medications that are used for acute treatment of headaches can cause MOH, but the frequency of use which results in MOH can vary between different medications. MOH are more commonly seen in patients with migraine, but can occur in patients with tension and cluster type headaches.

Figure 10. Acute Headache Treatments can Cause Medication Overuse Headaches. The Risk is Highest with Butalbital and Opioids^{3,42,43}

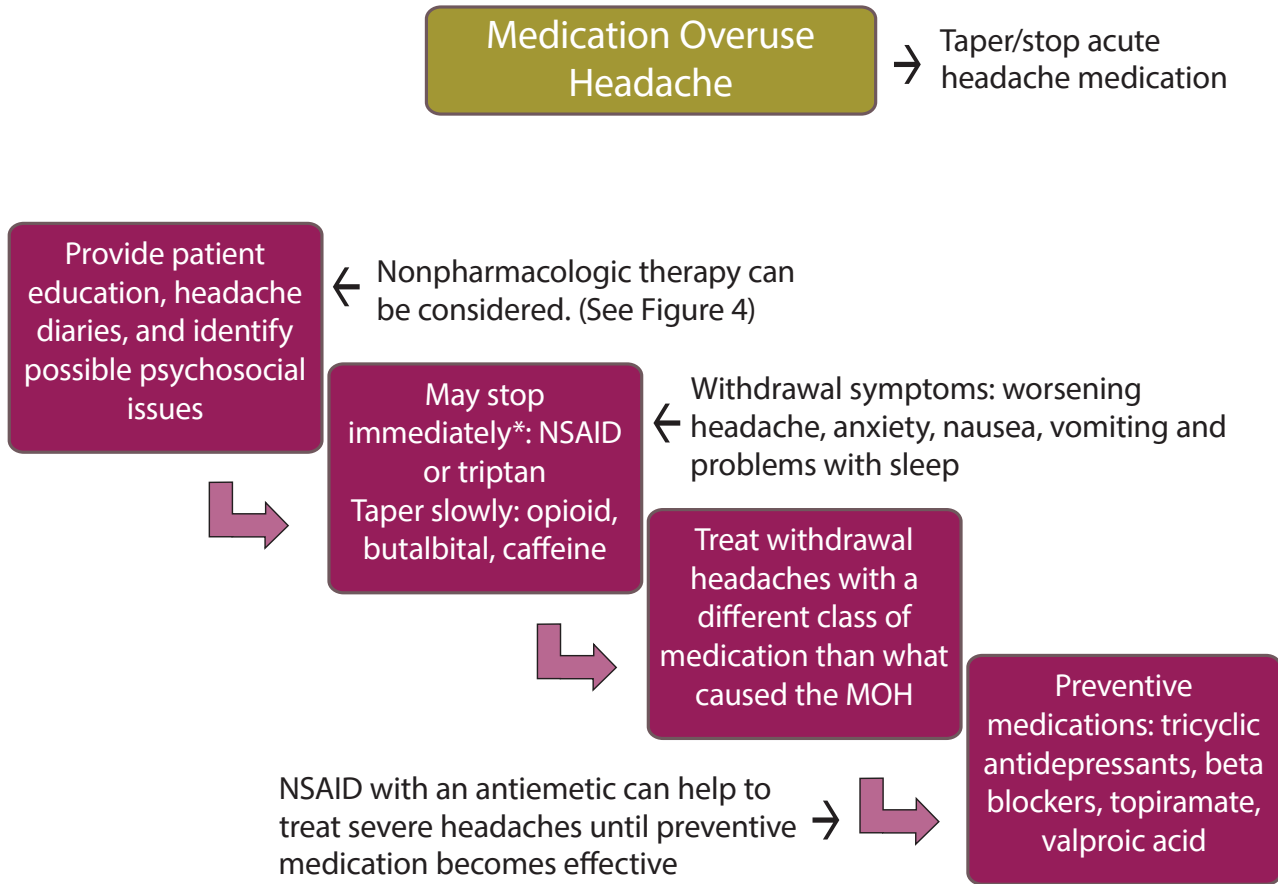


STOP

Using opioids for nonheadache purposes, like low back pain, can cause MOH in patients with a history of migraine headaches.

If the patient is experiencing MOH, consider starting a prophylactic medication and, depending on the type of medication, stop or begin tapering the medication causing the overuse headache. Provide close follow up for 8–12 weeks.

Figure 11. Treatment of Medication Overuse Headaches^{43–46}



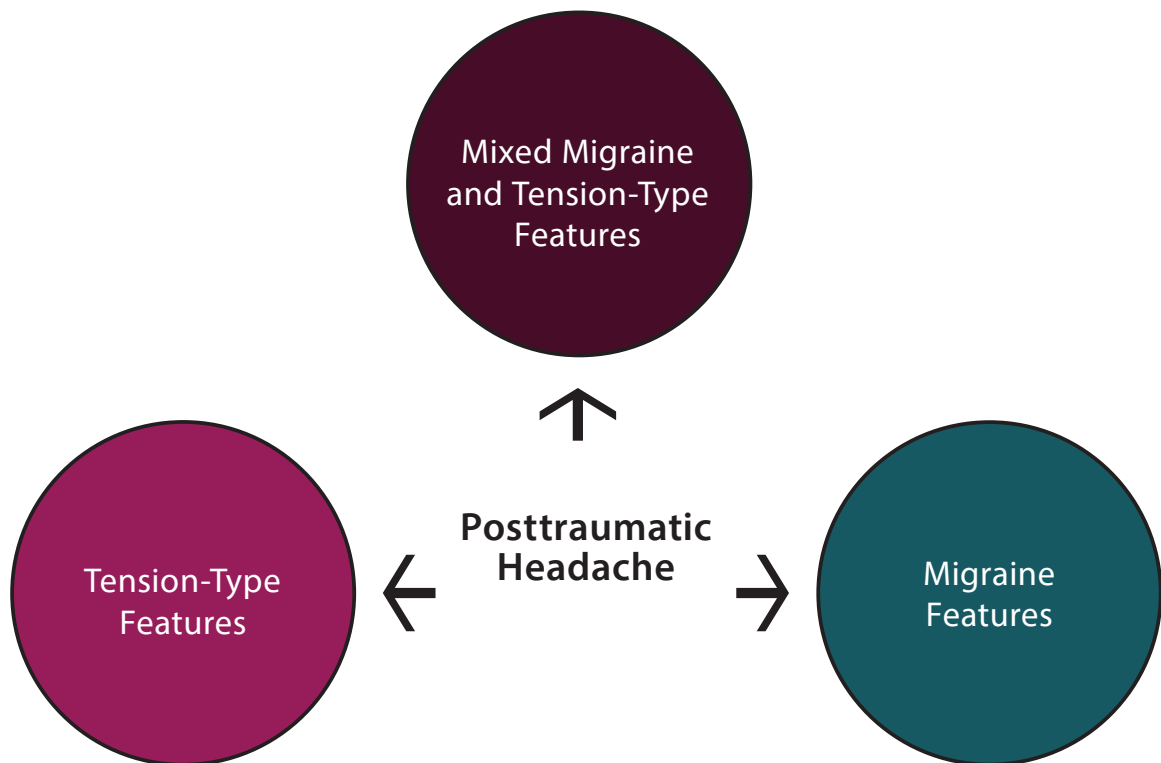
*Stopping NSAID or triptan abruptly can cause worsening headache symptoms. Consider a slow taper over four to six weeks of any/all abortive medications to usage no more than two times weekly. Initiating nonpharmacologic therapies with or without pharmacologic preventives can help manage pain and improve the success of the taper.

In patients with headaches, do not use pain medications more than 2 times a week (**for any reason!**) to avoid medication overuse headaches (MOH).

Headaches from Traumatic Brain Injury (TBI)^{47,48}

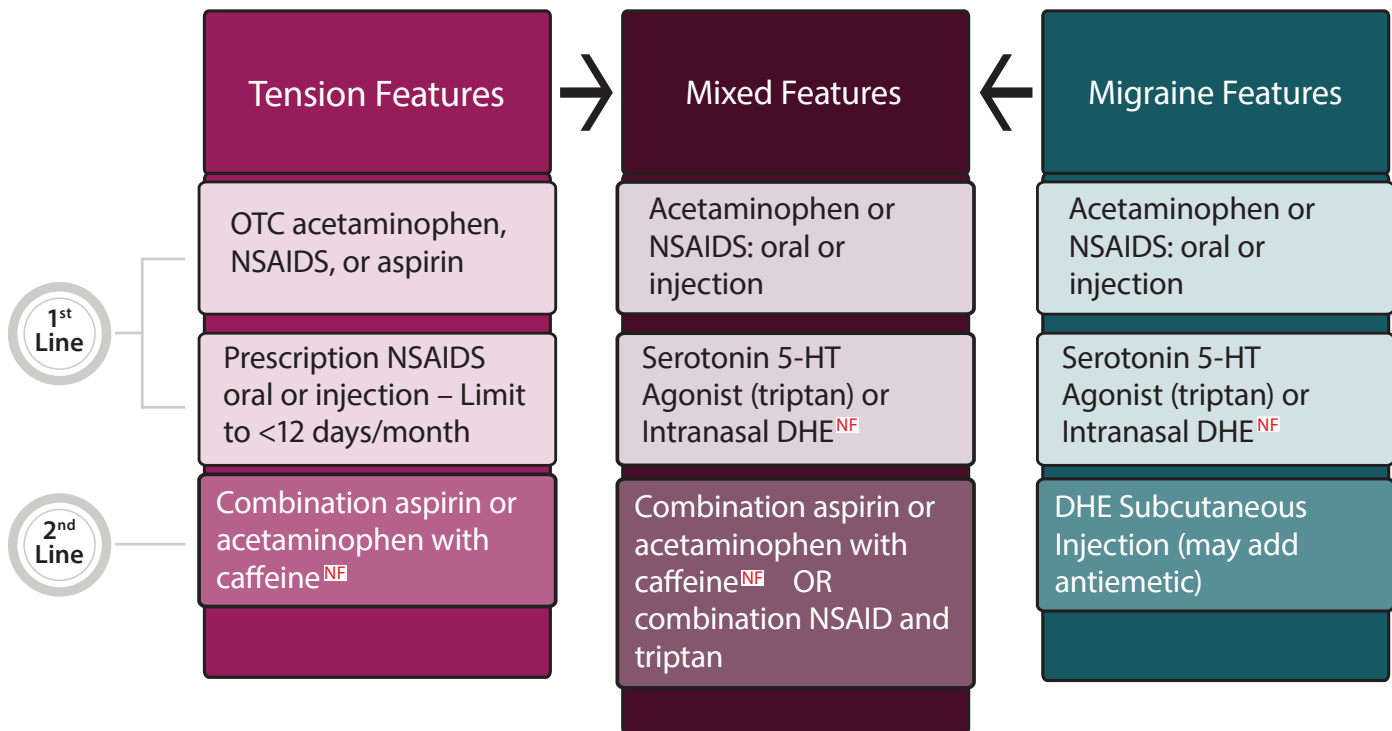
Headache is one of the most common persisting complaints in Veterans after experiencing a TBI. After a TBI, posttraumatic headaches can be classified as acute or chronic. Acute posttraumatic headaches resolve within three months, while chronic posttraumatic headaches continue for longer than three months. Neck and spine trauma also needs to be evaluated as a cause of posttraumatic headaches. Rule out medication overuse headaches in patients with posttraumatic headaches.

Figure 12. Presentation of TBI Related Headaches⁴⁷



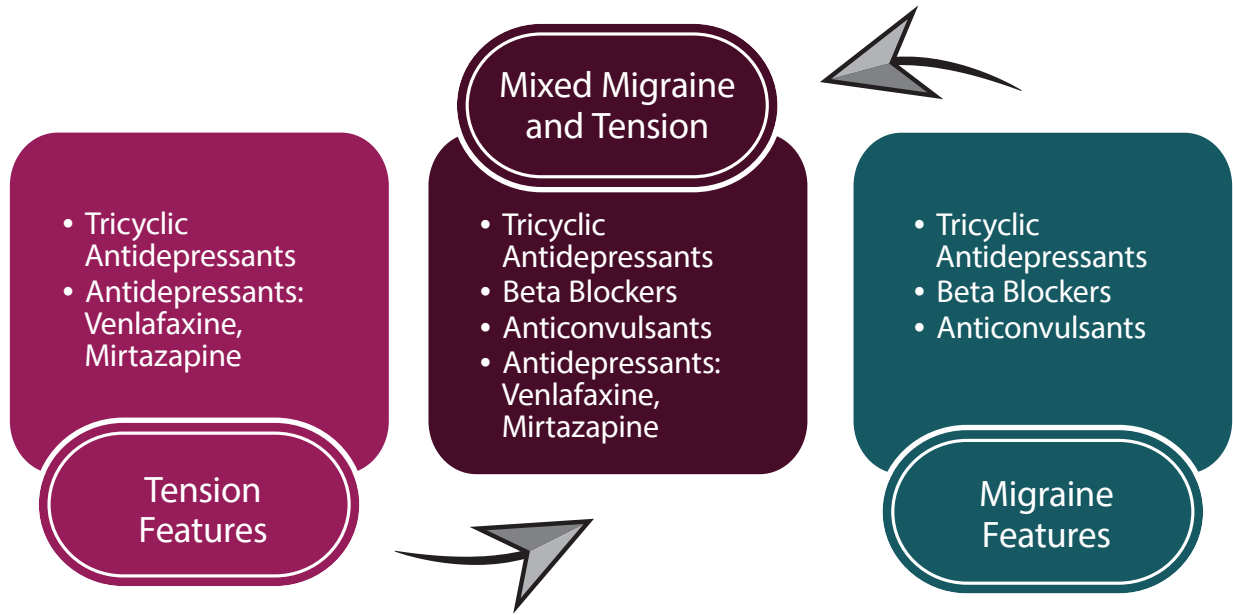
Treatment of the headache should be based on the character of the headache. In Veterans with mixed migraine and tension-type headaches, treatment of both types of headache may be necessary.⁴⁷ To identify migrainous features ask if they have photophobia, phonophobia, or nausea with their most severe headache. Other comorbidities like sleep disorders (sleep apnea), anxiety disorders, PTSD, and depression should also be addressed since headaches may improve once these are addressed. If necessary, try to use preventive medications that address associated co-morbidities as well as headache type. If headaches do not respond to the treatments below, consider referring patients to headache specialists or pain specialists.

Figure 13. Acute Treatment for Chronic TBI Headache by Predominant Feature^{*19,20,24,25,36,47}



*In general avoid using acute pain medications more than 2 times a week to reduce risk of MOH.
NF = Not currently on VA National Formulary. For mild to moderate symptoms, start with the first box of the first line therapy. For moderate to severe symptoms, consider starting with the second box of the first line therapy.

Figure 14. Preventive Treatment for TBI Related Headache^{19,20,33-36,47}



Depending on the predominance of headache features in Veterans with TBI related headaches, use the corresponding recommended preventive and abortive therapies for a primary migraine or tension-type headache.

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This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing Service SharePoint.

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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