

While there currently is no cure for migraine, there are multiple treatment options—none of which work for everyone, and many of which need to be tried for a few months or in combination with each other to see if they are effective. This is a long process that requires patience, perseverance, and courage! Often, people who live with migraine experience the most success managing their disease with a toolbox approach that combines different options.



### Prescription Medications

- ✓ Preventive
- ✓ Abortive
- ✓ Rescue
- ✓ Other options currently in the clinical pipeline



### Non-Invasive Medical Devices

- ✓ CEFALY®
- ✓ gammaCore™
- ✓ Nerivio®
- ✓ Relivion® MG
- ✓ SAVI Dual™



### Non-Pharmaceutical Options

- ✓ Lifestyle Modifications
- ✓ Supplements
- ✓ Alternative Treatments
- ✓ Over-the-Counter Tools

## WHAT'S IN YOUR TOOLBOX?

Migraine is a complex, neurological disease which presents itself on a wide spectrum of frequency, severity, symptoms, attack triggers, and responses to treatments. What works for one person may not help another at all. In some cases, what helps one person may even make another worse or directly trigger attacks. Unfortunately, the journey to effective migraine treatment is not a “one size fits all” process. We encourage you to talk with your doctor and partner in your healthcare, learn about all the different options that may be appropriate for you, and come join us online to ask questions, learn about new developments, and connect with other people who live with migraine!

Visit [MIGRAINEMEANDERINGS.COM/MIGRAINE-TOOLBOX](https://MIGRAINEMEANDERINGS.COM/MIGRAINE-TOOLBOX)  
for more information about these treatment options!

PLEASE NOTE: *Nothing in this document should be taken as medical advice, or as either a recommendation or endorsement of the treatments listed. All decisions about migraine treatment should be made in conjunction with your doctor.*

## PREVENTIVE/PROPHYLACTIC MEDICATIONS

According to the current [American Headache Society guidelines](#), preventive medications are used to reduce the severity and frequency of migraine attacks, the number of migraine days, frequency of acute medication use, and disability. They are recommended for people who have 4 or more migraine days per month, whose attacks significantly interfere with daily routine despite acute treatment, where there is contraindication to acute medication, and/or patient preference. For some people it may take more than one preventive medication to get relief, and it is important to work with your doctor to determine what is best for you. While some of these medications are not specifically FDA-approved for migraine, they are often prescribed due to the level of evidence based on the AAN/AHS guidelines.



### FDA APPROVED

- Erenumab-aooe (**Aimovig**<sup>®</sup>) – monoclonal antibody CGRP inhibitor (self-injection)
- Fremanezumab-vfrm (**Ajovy**<sup>®</sup>) – monoclonal antibody CGRP inhibitor (self-injection)
- Galcanezumab-gnlm (**Emgality**<sup>®</sup>) – monoclonal antibody CGRP inhibitor (self-injection)
- Eptinezumab-jjmr (**Vyepti**<sup>®</sup>) – monoclonal antibody CGRP inhibitor (IV infusion)
- Rimegepant (**Nurtec**<sup>®</sup> ODT) – oral tablet CGRP inhibitor
- Atogepant (**Qulipta**<sup>™</sup>) – oral tablet CGRP inhibitor
- Propranolol (**Inderal**<sup>®</sup>)
- Timolol maleate (**Blocadren**<sup>®</sup>)
- Topiramate (**Topamax**<sup>®</sup>, **Trokendi XR**<sup>®</sup>, **Quedexy**<sup>®</sup> XR)
- Divalproex sodium (**Depakote**<sup>®</sup>)



### EVIDENCE-BASED OFF-LABEL

- Alpha-2 Agonists (e.g.: clonidine)
- ACE Inhibitors (e.g.: benazepril, fosinopril sodium)
- Angiotensin II Receptor Blockers (e.g.: candesartan)
- Beta Blockers (e.g.: metoprolol, nadolol)
- Calcium Channel blockers (e.g.: diltiazem, felodipine)
- Antihistamines (e.g.: cyproheptadine)
- Tricyclic Antidepressants (e.g.: nortriptyline, amitriptyline)
- SSRIs, SNRIs & MAOIs (e.g.: escitalopram, venlafaxine)
- Cox-2 Enzyme Inhibitors (e.g.: celecoxib)
- Muscle relaxers (e.g.: carisoprodol, tizanidine)
- Neuronal stabilizing agents, anticonvulsants (e.g.: gabapentin, zonisamide, lamotrigine)
- Leukotriene blockers (e.g.: montelukast, zafirlukast)
- Alzheimers medications (e.g.: memantine)
- Triptans sometimes used as preventives for menstrual migraine (e.g.: frovatriptan, naratriptan)

## ABORTIVE MEDICATIONS

These work to stop the migraine attack itself with all its associated symptoms. Too frequent use of some of these can cause medication overuse headache (MOH), now known as medication adaptation headache, in some people, so it is important to follow your doctor's directions. For some people it may take more than one abortive medication, including non-oral agents, as well as other treatment options, to get relief, and it is important to work with your doctor to determine what is best for you.

### Gepants (CGRP receptor-antagonists)

- Ubrogapant (**Ubrovelvy**<sup>®</sup>)—oral tablet
- Rimegepant (**Nurtec**<sup>®</sup> ODT)—oral dissolving tablet
- Zavegepant (**Zavzpret**<sup>™</sup>)—nasal spray

### Ditans

- Lasmiditan (**Reyvow**<sup>®</sup>)—oral tablet, 5-HT<sub>1F</sub> receptor agonist

### Triptans

- Sumatriptan –available in USA as tablet, nasal spray, injection (Imitrex<sup>®</sup>, **Zembrace**<sup>®</sup>, **Onzetra**<sup>®</sup>)
- Rizatriptan (**Maxalt**<sup>®</sup>)—available in USA as oral tablet, oral dissolving tablet
- Zolmitriptan (**Zomig**<sup>®</sup>)—available in USA as oral tablet, oral dissolving tablet, nasal spray
- Naratriptan (**Amerge**<sup>®</sup>)
- Eletriptan (**Relpax**<sup>®</sup>)
- Almotriptan (**Axert**<sup>®</sup>)
- Frovatriptan (**Frova**<sup>®</sup>)
- Sumatriptan with naproxen sodium (**Treximet**<sup>®</sup>)

### Ergotamines:

- Dihydroergotamine nasal spray (**Migranal**<sup>®</sup>, **Trudhesa**<sup>™</sup>)
- Dihydroergotamine subcutaneous injection (**DHE-45**<sup>®</sup>)

### Butalbital compounds

- Butalbital, aspirin & caffeine (**Fiorinal**<sup>®</sup>)
- Butalbital, acetaminophen & caffeine (**Fioricet**<sup>®</sup>)

### Anti-Emetics (anti-nausea)

- Prochlorperazine (**Compazine**<sup>®</sup>)
- Promethazine (**Phenergan**<sup>®</sup>)
- Ondansetron (**Zofran**<sup>®</sup>)
- Metoclopramide (**Reglan**<sup>®</sup>)

### Muscle Relaxants

- Carisoprodol (**Soma**<sup>®</sup>)
- Tizanidine (**Zanaflex**<sup>®</sup>)
- Cyclobenzaprine (**Flexeril**<sup>®</sup>)

### Prescription Strength NSAIDs

- Indomethacin (**Indocin**<sup>®</sup>)
- Diclofenac potassium (**Cambia**<sup>®</sup>)
- Ketorolac tromethamine – options include tablet, nasal spray, injection, IV (**Toradol**<sup>®</sup>, **Sprix**<sup>®</sup>).
- Celecoxib (**Elyxyb**<sup>™</sup>)



## RESCUE MEDICATIONS

These may be taken *if abortives fail to stop an attack OR you can't take abortives*. Some rescue medications may only temporarily "mask" migraine symptoms. In addition, use of opioids and/or barbiturates can increase the risk of episodic migraine progressing to chronic migraine and/or triggering medication adaptation headache in some people.

### Corticosteroids

- Methylprednisolone (Depo-Medrol<sup>®</sup>, Medrol<sup>®</sup>, Solu-Medrol<sup>®</sup>) prednisone (Deltasone<sup>®</sup>, Prednisone Intenol<sup>®</sup>), dexamethasone

### Ketamine

- IV infusion or nasal spray

### Nerve Blocks

- May be used to abort an intractable migraine, or as a chronic migraine preventive. Nerves targeted include the auriculotemporal, occipital, supraorbital, trigeminal, and sphenopalatine ganglion

### IV "Cocktails"

- Various combinations of medications may be given "in-office" or in the ER

# UNDERSTANDING NON-INVASIVE MEDICAL DEVICES

## MIGRAINE DEVICES

Non-invasive, FDA-cleared, medical devices for migraine can help block the pain of a migraine or cluster attack, or even prevent attacks from starting. These devices can dramatically increase the quality of life for those with migraine disease without the side effects that sometimes accompany medications.



### CEFALY®

An external trigeminal nerve stimulation device (eTNS), CEFALY sends tiny electrical impulses through a self-adhesive electrode placed on the forehead. This stimulates and desensitizes the trigeminal nerve, reducing the frequency and intensity of migraine attacks. The CEFALY DUAL is FDA-cleared as a migraine abortive and preventive for adults only. Available over the counter without a prescription, there is a 60-day money back guarantee as well as an optional payment plan.

[www.cefaly.us](http://www.cefaly.us)



### gammaCore™

By activating the vagus nerve with a gentle, 2-minute electrical stimulation, gammaCore, a noninvasive vagus nerve stimulator (nVNS), helps block the pain signals that cause migraine and cluster attacks. Convenient and handheld, this device offers up to 24 stimulations each day. It is FDA-cleared both as a migraine abortive and preventive for adults and adolescents (12 & older), and for preventive treatment of cluster headache, as well as the acute treatment of episodic cluster headache. A copay assistance program is available for those who have commercial insurance.

[www.gammacore.com](http://www.gammacore.com)



### Nerivio®

A wireless, smartphone-controlled, wearable device, Nerivio is FDA-cleared as a migraine abortive and preventive for both adults and adolescents (12 & older) who have episodic or chronic migraine. This remote electrical neuromodulation device (REN) is placed on the upper arm to stimulate peripheral nerves, which signal the brain to alleviate migraine pain.

[www.nerivio.com](http://www.nerivio.com)



### Relivion® MG

A brain neuromodulation system, Relivion MG stimulates both the trigeminal and occipital nerve branches to maximize relief from a migraine attack. There are 3 components to the system which is designed to optimize treatment for each attack: the headset, the patient app to track attacks and treatment, and the Physician Management Interface. Relivion MG is FDA-cleared as a migraine abortive in adults and is in clinical trials for preventive treatment.

[www.neurolief.com](http://www.neurolief.com)



### SAVI Dual™

Using single pulse transcranial magnetic stimulation, the SAVI Dual is a handheld device. It works by generating a magnetic pulse that affects electrical signaling in the brain. The device is FDA-cleared as a migraine abortive and preventive for adults and adolescents (12 & older).

[www.eneura.com](http://www.eneura.com)

Talk with your doctor to see if they would be good options to add to your treatment toolbox.

There are several medications and medical devices currently at various stages of clinical trials, from early Phase 1 all the way to Phase 4. In addition to those listed below, there are several trials investigating CGRP inhibitor medications in children and adolescents.

- **AG09222**  
A PACAP inhibitor which is being investigated for preventive migraine treatment. (Currently in Phase 2 clinical trials)
- **Tricaprilin**  
An oral drug which has been designed to induce ketosis and improve mitochondrial metabolism. It is being investigated for preventive treatment of migraine. (Currently in Phase 2 clinical trials)
- **Idebenone**  
An oral tablet which improves energy metabolism similar to CoQ10 and is being investigated for migraine prevention. (Currently in Phase 3 and 4 clinical trials)
- **Psilocybin**  
This is being investigated for preventive treatment of migraine. (Currently in Phase 1 clinical trials)
- **Cannabis**  
This is being investigated for both the acute and preventive treatment of migraine. (Currently there are multiple clinical trials ranging from Phase 1 to Phase 4)
- **XC101-D13H**  
A 5-HT<sub>2B/2C</sub> receptor antagonist without serotonergic agonist-driven side effects, which is currently being investigated for preventive treatment of migraine. (Currently in Phase 1 clinical trials)
- **TRV250**  
Targeting the delta receptor, with potential to be a first-in-class, non-narcotic mechanism, this is being investigated for the acute treatment of migraine. (Currently terminated due to enrollment issues from COVID)
- **Pulsante**  
Sphenopalatine Ganglion Stimulator. This device was FDA cleared April 2021 for the treatment of acute headache pain associated with chronic cluster headache. It has not yet received FDA clearance for migraine management in the USA, although it has received approval in Europe.
- **BIIB074/vixotrigine**  
A voltage- and use-dependent sodium channel blocker. It is a centrally and peripherally acting small molecule. It is currently being studied in trigeminal neuralgia & small fiber neuropathy. (Phase 3 clinical trials are estimated to start March 2023)
- **UB-313**  
This first in-human (FIH) study of UB-313, an anti-calcitonin gene-related peptide based immunotherapeutic candidate, is designed to assess the safety, tolerability, and immunogenicity of 4 selected UB-313 dose regimens in healthy adults. (Currently in Phase 1 clinical trials)
- **XC101-D13H**  
This is a serotonergic oral therapy for the prevention of migraine with a novel mechanism of action. (Currently in Phase 1 clinical trials)



This information comes from [ClinicalTrials.gov](https://clinicaltrials.gov) as well as pharmaceutical and medical device company websites.

*Disclaimer:  
We are not responsible for any errors in this information, or any updates which are not accurately updated online or made available to the public.*

*(Last Updated  
2/9/23)*

# UNDERSTANDING NON-PHARMACEUTICAL OPTIONS

A wholistic approach to migraine treatment often helps yield the best results. In addition to medications and devices, consider adding some non-traditional options to your treatment toolbox.



## Lifestyle Modifications

- Regular sleep
- Trigger management
- Regular exercise
- Healthy diet
- Hydration
- Stress management
- Creative activities
- Self-advocacy
- Connection with others



## Alternative Treatments

- Acupuncture
- Biofeedback
- Cognitive behavioral therapy
- Mindfulness and meditation
- Massage therapy
- Restorative yoga
- Acupressure
- Physical therapy
- Tai Chi



## Supplements

There are few quality studies for the efficacy of supplements for preventive migraine treatment, however the following six options all suggest there may be some evidence of efficacy:

- B2 (riboflavin)
- Butterbur (Petadolex)
- CoQ10
- Feverfew
- Magnesium
- Melatonin



## Over-the-Counter Tools

- Ice and heat packs
- Eye masks
- Light filtering glasses
- Light filtering screens
- Green light therapy
- Orthopedic pillows
- Massage & acupressure gadgets
- Soft clothing
- Weighted blankets
- Essential oils (if these are not migraine triggers for you)

## INSURANCE TERMINOLOGY

**Prior Authorization (PA):** Some of the treatment options require a “Prior Approval” to be completed by your doctor so that your insurance will approve coverage. These are often treatments that are already on your insurance company’s formulary, but for which additional information is needed to show the company how necessary the prescription is.

**Step Therapy:** Some treatments will require that you go through “Step Therapy” before they are approved by your insurance company. This is where you will have to try, and experience treatment failure with, specific other treatments first. Sometimes this is required in combination with a PA.

**Formulary Exception:** There are some medications that require a “Formulary Exception” request to be completed by your doctor. This is normally needed when the medication is not listed on your insurance company’s formulary list either because it is not “preferred” or because it has only recently been FDA-approved. Additional information is needed to explain why currently listed medications are not appropriate.

**Not Covered:** Some of the medications and many of the devices are not covered by insurance. At times it is possible to appeal this with a letter of medical necessity from your doctor together with a history of failed alternative treatments.