MIGRAINE TREATMENT TOOLBOX

A PATIENT GUIDE TO MANAGING MIGRAINE

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
- ✓ Acute/Abortive
- ✓ Rescue
- ✓ Other options currently in the clinical pipeline



Non-Invasive Medical Devices

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



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 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.*

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UNDERSTANDING PRESCRIPTION MEDICATIONS: Preventives

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**®) – monoclonal antibody CGRP inhibitor (self-injection)
- Fremanezumab-vfrm (**Ajovy**®) – monoclonal antibody CGRP inhibitor (self-injection)
- Galcanezumab-gnlm (**Emgality**®) – monoclonal antibody CGRP inhibitor (self-injection)
- Eptinezumab-jjmr (**Vyepti**®) – monoclonal antibody CGRP inhibitor (IV infusion)
- Rimegepant (**Nurtec**® ODT) – oral tablet CGRP inhibitor
- Atogepant (**Qulipta**™) – oral tablet CGRP inhibitor
- Propanolol (**Inderal**®)
- Onabotulinum toxinA injection (**Botox**®)
- Timolol maleate (**Blocadren**®)
- Topiramate (**Topamax**®, **Trokendi** XR®, **Quedexy**® XR, Epronita™)
- Divalproex sodium (**Depakote**®)



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)
- Alzheimer's medications (e.g.: memantine)
- Triptans sometimes used as preventives for menstrual migraine (e.g.: frovatriptan, naratriptan)

Learn more about these medications: www.MigraineMeanderings.com/Medications

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UNDERSTANDING
PRESCRIPTION MEDICATIONS: Acute/Abortive

ACUTE/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)

- Ubrogepant (**Ubrelvy**®)—oral tablet
- Rimegepant (**Nurtec**® ODT)—oral dissolving tablet
- Zavegepant (**Zavzpret**™)—nasal spray

Ditans

- Lasmiditan (**Reyvow**®)—oral tablet, 5-HT_{1F} receptor agonist

Triptans

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

Ergotamines:

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

Butalbital compounds

- Butalbital, aspirin & caffeine (**Fiorinal**®)
- Butalbital, acetaminophen & caffeine (**Fioricet**®)

Anti-Emetics (anti-nausea)

- Prochlorperazine (**Compazine**®)
- Promethazine (**Phenergan**®)
- Ondansetron (**Zofran**®)
- Metoclopramide (**Reglan**®)

Muscle Relaxants

- Carisoprodol (**Soma**®)
- Tizanidine (**Zanaflex**®)
- Cyclobenzaprine (**Flexeril**®)

Prescription Strength NSAIDs

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



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®, Medrol®, Solu-Medrol®), Prednisone (Deltasone®, Prednisone Intensol®)

Ketamine

- IV infusion, nasal spray or oral tablet

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

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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



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



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



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



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



HeadaTerm

Worn on users' foreheads, HeadaTerm uses non-invasive neuronal electrical stimulation technology to prevent and treat primary headache, including migraine, tension headache, and cluster headache. The FDA-cleared device is HAS/FSA eligible and offers fast-acting relief without a prescription.

www.emeterm.com

Learn more about these devices:
www.MigraineMeanderings.com/devices

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UNDERSTANDING

TREATMENTS IN THE CLINICAL PIPELINE

There are several medications and medical devices currently at various stages of clinical trials, from early Phase 1 all the way to Phase 4.

- **Idebenone:** An oral tablet which improves energy metabolism similar to CoQ10 and is being investigated for migraine prevention. (Currently in Phase 4 studies in China)
- **AXS-07:** An oral, rapidly absorbed, tablet consisting of Meloxicam and Rizatriptan for the acute treatment of migraine. (Currently in Phase III Open Label clinical trials to study the safety and efficacy.)
- **TX360:** A device which delivers bupivacaine to the sphenopalatine ganglion for migraine prevention. (Currently in Phase III clinical trials)
- **Dysport:** An injectable formulation of Botulinum toxin type A. (Currently in Phase III clinical trials for the prevention of chronic and episodic migraine. Expected to be completed January 2026)
- **Tricaprilin:** An oral drug which has been designed to induce ketosis and improve mitochondrial metabolism, and is currently being investigated for preventive treatment of migraine. (A Phase 2 pilot study was completed July 2022 - no further updates)
- **Cannabis:** Inhaled cannabis being investigated for acute treatment of migraine. (Currently in Phase 2 clinical)
- **LY3451838:** A PACAP inhibitor which is being investigated for preventive migraine treatment. (Currently finished Phase 2 trials with positive results - we are waiting for more information on Phase 3 trials).
- **TNX-1900:** An intranasal oxytocin product being studies for migraine prevention for chronic migraine. (Currently finishing Phase 2)
- **Psilocybin:** Oral psilocybin being investigated for preventive treatment of migraine.
- **Protease Activated Receptor-2 (PAR-2) Inhibitors:** This is a novel class of small molecules which inhibit PAR-2, which generates cellular signals involved in inflammation and pain. Currently in preclinical trials for migraine.
- **XC101-D13H:** A 5-HT2B/2C receptor antagonist without serotonergic agonist-driven side effects, which is currently being investigated for preventive treatment of migraine. (Phase 1 clinical trial results were presented June 2020 - no further news currently)
- **Nocira:** an AVPI device for the acute treatment of migraine. It is currently in Phase I interventional clinical trials to evaluate safety and efficacy.
- **Pulsante:** Sphenopalatine Ganglion Stimulator. This device was FDA cleared April 2021 for the treatment of acute headache pain associated with chronic cluster headache. It is not yet FDA cleared for migraine in the USA, although it has received approval in Europe.
- **RELIEV-CM:** This study in Australia is an interventional study of Shiratronics' implantable craniofacial nerve stimulation system for migraine prevention. This initial trial is expected to be completed December 2024.



This information comes from 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.

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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.

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