



# A Comprehensive Guide to Preventative Migraine Drugs

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## Types of Preventative Migraine Medicine

Prevention is key when someone with migraines experiences frequent and disabling attacks. If your migraine attacks are persistent, last for long durations, are severe and do not respond well to treatment, preventative migraine medicine may be recommended by your doctor. For instance, someone with chronic migraines who has 15 or more migraines a month would benefit from taking a preventative medication.

There are several common preventative migraine medicine treatments that are prescribed to help lower the frequency, duration and severity of migraine attacks, and also help them to better respond to acute medications. Blood pressure lowering medications, antidepressants, anti-seizure drugs, Botox injections and calcitonin gene-related peptide (CGRP) monoclonal antibodies are what we will be addressing today in terms of prevention.

### **Blood Pressure Lowering Medications**

Some options when being prescribed a blood pressure lowering medication are beta blockers, ACE inhibitors, angiotensin II receptor blockers and calcium channel blockers.

#### **Beta-Blockers**

Beta blockers decrease the heart rate, which helps to lower blood pressure. Propranolol (Inderal) and metoprolol tartrate (Lopressor) are often prescribed in helping to prevent migraines.

#### **ACE Inhibitors**

Angiotensin is a chemical that causes the narrowing of the arteries, especially in the kidneys, but also throughout the body. ACE stands for enzyme converting angiotensin. ACE inhibitors help the body produce less angiotensin which helps relax and expand the blood vessels. This then lowers blood pressure.

#### **Angiotensin II Receptor Antagonists (ARBs)**

This medication blocks the effects of angiotensin, a chemical that causes narrowing of the arteries. To constrict the blood vessel, angiotensin needs a receptor— like a chemical "slot" to fit in or bind with. ARBs block the receptors and prevent angiotensin from constricting the blood vessels. This ensures that the blood vessels remain open and that blood pressure decreases.

Research has shown that both ACE inhibitors (enalapril, lisinopril) and angiotensin II receptor antagonists (candesartan, telmisartan) have been effective in reducing both the frequency and severity of migraine attacks with minimal side effects.

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## Calcium Channel Blockers

Calcium channel blockers, such as verapamil (Isoptin, Calan), relax and expand compressed blood vessels, lower heart rate and lower blood pressure. This medication blocks calcium from reaching cardiac and arterial smooth muscle cells. This induces a stronger and faster contraction as calcium reaches these organs. So, by reducing the calcium, the contracting of the hearts is not as intense.

Potential side effects of blood pressure lowering medications include fatigue, depression, nausea, insomnia, dizziness, low blood pressure, weight gain and constipation.

## Antidepressants

Tricyclic antidepressants, specifically amitriptyline, can prevent migraines. Amitriptyline reduces norepinephrine and serotonin absorption. Its ability to block sodium channels may clarify other possible mechanisms in migraines, improve GABA-mediated inhibition, potentiate endogenous opioids and enhance lessening inhibition on nociceptive pathways.

Other antidepressants may be prescribed if the side effects of weight gain and sleepiness of amitriptyline are intolerable, such as paroxetine (Paxil), fluoxetine (Prozac), or sertraline (Zoloft). Some other potential side effects of taking an antidepressant for prevention of migraines can include dry mouth and low libido.

## Anti-Seizure Medications

Migraines and their associated symptoms may result from neuronal hyperexcitability and migraine attacks can be avoided if this can be suppressed. Drugs, such as topiramate (Topamax) and gabapentin (Neurontin) may be first-line prevention measures. This is especially true when beta-adrenergic antagonists or tricyclic antidepressants become contraindicated, or when there are comorbid medical and/or psychiatric conditions such as seizures or mood disorders.

Antiseizure medications and their side effects depend on the type of drug you are taking:

- Diarrhea
- Dizziness
- Drowsiness
- Weight changes
- Visual changes
- Fatigue
- Confusion
- Difficulty concentrating
- Loss of appetite
- Constipation

Since the use of topiramate can cause decreased sweating and increased body temperature, it is important to wear light clothes and drink plenty of water, especially during warmer months. If your body temperature rises, contact your physician immediately.

## Botox Injections

Botox injections are currently FDA-approved for the prevention of migraines in people who experience 15 or more headache days per month, or who have been diagnosed with chronic migraines.

Botox may have anti-migraine effects by inhibiting the release of calcitonin-related gene peptide from activated sensory trigeminal neurons. A series of 31 injections are administered every 12 weeks. These injections are usually given by a physician or headache specialist who is experienced in using Botox.

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Common side effects of Botox injections for migraines:

- Dry mouth
- Discomfort or pain at the injection site
- Tiredness
- Headaches
- Neck pain
- Eye problems
- Drooping eyebrows

## **CGRP Inhibitors**

CGRP is a neuropeptide that is thought to play a key role in the pathophysiology of a migraine. The CGRP works as a neurotransmitter in the central and peripheral nervous systems and also acts as a vasodilator. Studies have suggested that the levels of CGRP increase during a migraine attack.

CGRP inhibitors are used to block the CGRP receptor that inhibits the inflammatory response in the central and peripheral nervous systems. These classes of drugs are the first to be developed specifically for the prevention of migraines. This makes them one of the most significant preventative migraine medicine options.

### **Erenumab-Aooe (Aimovig)**

Erenumab was the first CGRP drug approved by the FDA for the prevention of episodic and chronic migraines. It is a fully human monoclonal antibody that binds to the CGRP receptor. Erenumab is given by a self-administered injection on a monthly basis. Dosage is one to two injections. Those with chronic migraines commonly receive two injections per month.

The most reported side effects are pain, redness, or swelling at the injection site and constipation. Out of the 631 patients enrolled in the three-month, double-blind study, 39.9% of responders on the one-injection dose and 41.2% on the two-injection dose had over 50% in the reduction of migraine days.

### **Fremanezumab-Vfrm (Ajovy)**

Ajovy is a humanized monoclonal antibody (derived from rats) that targets the CGRP ligand. Dosage comes in either quarterly or monthly self-administered injections. The quarterly dose is 675 milligrams given as three 225 milligram subcutaneous injections every three months. Monthly doses are one 225 milligram subcutaneous injection each month.

Allergic reactions such as itching, rash and hives were reported by some patients within an hour and up to one month after receiving Ajovy. However, 2% of patients reported adverse reactions, with some reporting mild to moderate injection-site reactions. Ajovy decreased migraine days by an average of five days per month in chronic migraine patients and reduced migraine days by an average of three and a half days per month in patients with episodic migraines when administered weekly or quarterly over a 12-week period.

### **Galcanzumab-Glnm**

Galcanzumab is preventative medication for the treatment of migraines in adults who have four or more migraine days per month, as well as for the treatment of episodic cluster headaches. Like fremanezumab, it is a humanized monoclonal antibody that binds to and inhibits activity of the calcitonin gene-related peptide.

Galcanzumab is a self-administered injection. The first, or loading dose, will be two injections. After the initial dose, one injection will be administered once per month via a subcutaneous injection. Each dose comes in a pre-filled pen. The most reported side effects of galcanzumab are injection site reactions. Clinical trial data shows that for patients with 15 or more headache days per month, 62% had over 50% reduction in migraine days, 39% had over 75% reduction and 16% had 100% reduction.