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Key Inforbits

- What is a migraine?
- Top 10 Migraine Triggers
- Migraine and Headache Awareness Month
- Signs and Symptoms of a Migraine
- Current Migraine Management
- New Monoclonal Antibody Treatments

What is a Migraine?³



A migraine is an intense headache that is usually located in the frontotemporal area of the head. The cause and exacerbation of a migraine is not well understood. Generally, nerves and vascular dysfunction that arise within the trigeminovascular system are considered to be the root of migraine development. The activation of the trigeminal system leads to the release of vasoactive neuropeptides. These neuropeptides lead to vasodilation and plasma extravasation causing neurogenic inflammation. Pain sensory information is then relayed along the trigeminal fibers which, over time, become sensitized and hyperalgesic to other common stimuli such as light and sound.³

Premonitory symptoms can sometimes precede a migraine headache by hours or days. Auroras are also known to precede migraines in about a fourth of victims, however, auroras are not considered premonitory symptoms. Auroras usually develop over five minutes or greater and last for less than 60 minutes, the migraine may appear with the aura or appear within the hour.³

Migraines gradually appear and can reach their maximum intensity within minutes to hours. They can last anywhere from 4 to 72 hours, and they can cripple the victim's ability to function. Almost all of those who suffer from migraines have experienced reduced ability to carry out daily activities, from their ability to work to general care for themselves or their family. Disability due to migraines is caused by the intense pain as well as the accompanying sensory hyperactivity and neck pain.¹² It is important to be able to prevent and manage migraines in order to reduce the patient's lost work days as well as improve their overall quality of life.

Diagnosis and treatment of a migraine is carried out by the patient's physician or specialist. The treatment is customized to the patient, and in general, consists of pain management and symptom reduction medications. Prevention is one of the most important strategies in migraine management. Genetic factors are also an important consideration that can increase the risk for an individual to develop a migraine.



Top 10 Migraine Triggers¹

If you experience migraines, it is useful to know your triggers. Not everyone's triggers will be the same. The following list are some of the common triggers of migraines and how to handle them.

- 1. Stress** Find what causes stress and tension in your life and work towards reducing or eliminating those triggers. Exercise, meditation, and a regular sleep schedule can help with managing stress.
- 2. Irregular sleep schedule** To set a normal sleep schedule, try to go to bed at the same time every night. An adequate amount of sleep is at least 7-9 hours for most young adults and adults¹⁰. Also, avoid things like TV, cell phone usage, and listening to music right before bed.
- 3. Hormones** Women can be prone to migraines around their menstrual cycle. Birth control products prescribed by a physician can help stabilize hormones and prevent migraines around this time.
- 4. Caffeine and alcohol** Caffeine or alcohol are often culprits of migraines. Limiting consumption can help reduce the risk of a migraine.
- 5. Changes in weather** Stay indoors or limit time outdoors if cold or heat are triggers.
- 6. Diet** Common foods that can trigger migraines are chocolate, cheese/dairy, artificial sweeteners, cured meats, and foods with monosodium glutamate (MSG). Try to avoid these if they are a known trigger.
- 7. Dehydration** Be sure to drink plenty of water throughout the day. Carrying a water bottle with you can help remind you to drink more water.
- 8. Light** Certain types of light like sunlight or fluorescent lights can be a migraine trigger.¹¹ You can do things like wear sunglasses outdoors or eliminate the indoor light source.
- 9. Smells** Avoid strong smells such as perfumes, foods, chemicals, and gasoline.
- 10. Medication overuse** If you experience medication overuse headaches, talk to your physician about a new regimen to prevent this from happening.



Migraine and Headache Awareness Month

June is Migraine and Headache Awareness Month. This is a time for migraine physicians, other health care providers, patients' friends and families, and patients themselves to advocate for migraine recognition and treatment. Participation widens the recognition of headache and migraine pain as a legitimate condition as well as encourages people to seek diagnosis or treatment, and spread hope about new treatments and research. Become involved by following the American Migraine Foundation on social media for initiatives throughout June. More information is at: <https://americanmigrainefoundation.org/resource-library/migraine-headache-awareness-month-mham-2019/2>

Signs and Symptoms of Migraine³

Common Symptoms	Other Possible Symptoms
<ul style="list-style-type: none"> • Unilateral headache that is characteristically throbbing or pulsing • Nausea/vomiting • Sensory hyperacuity • Diaphoresis • Facial pallor • Blurred vision • Impaired Concentration • Irritability • Fatigue 	<ul style="list-style-type: none"> • Anorexia • Food cravings • Constipation • Diarrhea • Abdominal Cramps • Nasal Stuffiness • Localized facial swelling • Depression • Anxiety

For many patients, migraines can be made worse through physical activity or exposure to bright lights. It is not uncommon for the sufferer to seek relief from any stimulus that would exacerbate the migraine. Even once the migraine has resolved, other symptoms such as mood changes or drowsiness may continue.³

Current Migraine Management

Treatment strategies include ways to reduce the number of migraines a patient will have and reduce time migraines last when they develop. This can be done using a combination of possible medications for prophylactic prevention and treatment as well as non-pharm and lifestyle changes.



Pharmacological Treatments³

Prophylactic Therapy	Treatment
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)	NSAIDs
Beta blockers	Acetaminophen
Serotonin agonists (triptans)	Serotonin agonists (triptans)
Antidepressants	Ergotamine Tartrate
Histamine (Histatrol [®])	Dihydroergotamine
Calcitonin gene-related peptides (CGRP) antagonists	Metoclopramide
	Prochlorperazine

Non-pharmacologic treatment

Remove any aggravators	Find a dark, quiet room and apply ice. If possible, rest or sleep.
Avoiding triggers	As stated in the common trigger chart, it is important to identify and manage or avoid known triggers.
Behavioral intervention	Many have found relief or prevention through using stress management techniques such as relaxation therapy, biofeedback, cognitive therapy as well as counseling.
Use a headache diary	Using a headache diary to record the frequency, severity, and duration of migraine attacks can help in finding possible triggers and aid your primary care doctor in developing a management plan.

New Monoclonal Antibody Migraine Treatments

In 2018 there were three, FDA approved monoclonal antibodies for the treatment of migraines; Aimovig[®] (erenumab), Ajoovy[®] (fremanezumab), and Emgality[®] (galcanexumab). The method of action among these drugs are similar. Both Emgality[®] and Ajoovy[®] work by blocking the calcitonin gene-related peptides (CGRP) ligand from binding to its receptor.⁴ Aimovig[®] works by binding the CGRP receptor and antagonizes its function.⁴ The CGRP ligand is found throughout the nervous system, sometimes in high concentration in different areas of the body. One of those concentrated sites is the trigeminovascular system, the main system involved in the pathophysiology of migraines.⁴

These drugs are used for preventative treatment in patients with chronic migraine headaches (≥ 15 headaches per month with 8 of them being migraines).⁵ Aimovig[®] and Emgality[®] come in a prefilled auto-injectable syringe while Ajoovy[®] only comes in a prefilled syringe. All medications can be self-administered at home or at a doctor's office. Each of these drugs are given subcutaneously and can be dosed monthly. The exception is Ajoovy[®] whose frequency can be decreased so that patients can receive it every 3 months.

A study compiled all of the monoclonal antibodies' phase II trials summarizing the results of drug versus placebo in the reduction of headaches per month. Ajoovy[®] reduced migraines by 3.7 days at a dose of 225 mg in comparison to 2.2 days with placebo (HALO trial). Aimovig[®] decreased migraines by 3.2 and 3.7 days with doses of either 70 mg or 140 mg in comparison with 1.8 days with placebo (STRIVE trial). Emgality[®] dosed at 120 mg reduced migraine days to 4.8 less days in comparison with the 2.7 of the placebos (REGAIN trail). The study also dictated time to max concentration (T-max) with Ajoovy's[®] T-max of 3-20 days, Aimovig's[®] at 3-14 days, and Emgality's[®] at 7-14 days.⁸

Common adverse reactions include injection site reaction (occurs most with Ajoovy[®] at 43-45%), hypersensitivity to the drug, and antibody development, which is also called immunogenicity. In clinical trials, immunogenicity occurred at rates of 2 – 6% with Aimovig[®], 0.4 – 1.6% with Ajoovy[®], and 4.8 – 12.5% with Emgality[®].⁴ For each of these drugs, there is not enough data to demonstrate if neutralizing antibodies have an effect on their safety or efficacy.⁴

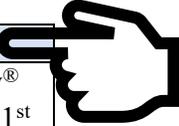
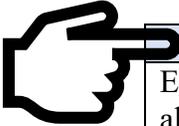


Aimovig[®] has additional adverse reactions including constipation (3%), muscle cramps ($\leq 2\%$), muscle spasms ($\leq 2\%$), erythema at injection site, and pain at injection site. There have been some reports of angioedema from Aimovig[®], but it is rare at $\leq 1\%$. The only contraindication for these drugs is hypersensitivity to the drug itself or their components.⁶ Importantly, there are no dosage adjustments for renal impairment, hepatic impairment or for the geriatric population (for complete dosing, see table below).⁷ Only Aimovig[®] and Emgality[®] have drug interactions and they cannot be given with Benlysta[®] (belimumab) (category X interaction) which can increase the adverse or toxic effects of belimumab.⁸

In regard to warnings and precautions, Aimovig[®] has a risk of hypersensitivity reactions and a statement that the syringe components could contain latex (the needle cap and the needle auto-injector shield). Ajovy[®] and Emgality[®] both have a warning for hypersensitivity, but additionally, they have warnings for cardiovascular disease (cardiovascular patients were excluded from trials so it is unknown how this population will tolerate these drugs), polysorbate 80 (delayed hypersensitivity reaction), and the possibility of patients developing drug neutralizing antibodies. There are no black box warnings for these drugs. The only monitoring parameter is to track monthly migraine days.⁶

Both Aimovig[®] and Emgality[®] require refrigeration and need to be kept out of the light although, they can be kept at room temperature for seven days before they must be discarded. Ajovy[®] requires refrigeration and light protection as well. However, Ajovy[®] only lasts for 24 hours at room temperature before it needs to be discarded. Once these drugs have warmed up to room temperature, they cannot be placed back into the refrigerator to prolong drug shelf life.⁶

In conclusion, the monoclonal antibodies are used for patients with chronic migraines to prevent and reduce migraine headaches. Ajovy[®] and Emgality[®] work by attaching to the CGRP ligand while Aimovig[®] blocks the receptor. Aimovig[®] has the most adverse drug reactions in comparison to Ajovy[®] and Emgality[®]. However, Aimovig[®] was tested in patients with cardiovascular disease, which makes it a safer choice for that population, and begins to work within 3-14 days.^{6,9} Their role in therapy is as a last line option since they are expensive drugs and still require more testing to be seen as more efficacious than current migraine prophylaxis drug therapies.⁶



Attention Community pharmacists: How to help patients save!

Each manufacturer has a coupon to help patients reduce the cost of their medications. Ajovy[®] allows patients to possibly pay nothing out of pocket for their prescription until December 31st of this year with the manufacturer's coupon.⁷ Emgality's[®] manufacturer coupon allows patients to pay nothing for their first 12 months.⁵ Finally, Aimovig[®] also has a coupon allowing for the first 12 doses for free then pay \$5.00 per month until the patient surpasses the \$2700 annual cut off.⁸ These coupons do not apply for uninsured patients and are only meant to be used to reduce their copays.^{5,7,8}

Dosing for New Monoclonal Antibodies ⁵

Drug Name	Dosing	Manufacturer	Dosage Forms	Storage
Aimovig[®] (erenumab)	70 mg subcutaneous monthly or 140 mg subcutaneous monthly	Amgen Inc	70mg/mL, 140mg/mL autoinjector	Refrigerate After removal may be stored at room temperature up to 7 days
Ajovy[®] (fremanezumab)	225 mg subcutaneous monthly or 675 mg subcutaneous every 3 months (when switching dosages, use the new dose at the next scheduled dose)	Teva Pharmaceuticals USA	225mg/1.5mL pre-filled syringe solution for injection	Refrigerate After removal may be stored at room temperature up to 24 hours
Emgality[®] (galcanexumab)	Single loading dose of 240 mg subcutaneous followed by 120 mg monthly	Eli Lilly and Co	120mg/mL pre- filled syringe solution for injection or autoinjector	Refrigerate After removal may be stored at room temperature up to 7 days
No renal, hepatic, or geriatric dosing adjustments for these drugs				

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The last “dose” ...

“Some pain you can distance yourself from, but a headache sits right where you live.”

– Mark Lawrence, American-British novelist, 1966-

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