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Aimovig®: A Novel Therapy for Preventive Treatment of Migraine

Michelle Vanderhoof, PharmD Candidate

In the Global Burden of Disease Study 2015, migraine was ranked the third-highest cause of disability worldwide in both males and females under the age of 50.[1] In 2015, 20% of adult women and 9.7% of adult men in the US reported having a severe headache or migraine in the past 3 months.[2] Migraine is a disabling headache disorder typically characterized by recurrent unilateral headaches with pulsating quality and moderate to severe intensity. Most migraine attacks last around 4-72 hours, can be aggravated by routine activity, and are associated with nausea, photophobia, and/or phonophobia.[1] People who experience frequent migraines are classified as having episodic migraine (≤14 migraine days per month) or chronic migraine (>15 migraine days per month).[3] Employees with frequent migraines can cost employers thousands of dollars per year with the majority of costs result from absenteeism/disability or being less productive while at work.[4] It is estimated that frequent migraines cost employers between $2,400 and $7,000 yearly for women and $4,000 and $13,000 yearly for men.[4-6]

Migraine pharmacological therapy includes acute and preventative treatments. Acute migraine-specific abortive medications, such as serotonin receptor agonists (triptans), are used to abort migraines. Preventative treatments aim to reduce the frequency and severity of migraine.[7] Commonly used migraine-preventative therapies include topiramate, propranolol, and amitriptyline among others. However, it is estimated that more than 80% of patients treated with these preventative medications discontinue them within 12 months of initiation due to significant side effects.[8] This demonstrates a need for newer migraine-specific agents for the preventative treatment of migraines.

Aimovig® (erenumab-aooe) is the first monoclonal antibody CGRP-receptor antagonist FDA approved for the preventative treatment of migraines. The purpose of this article is to evaluate erenumab's safety and efficacy data from clinical trials in the prevention of migraine.

Pharmacology

Erenumab is a human immunoglobulin G2 monoclonal antibody that binds to the calcitonin gene-related peptide (CGRP) receptor and antagonizes CGRP receptor function. It is thought that a migraine attack begins by activation of the trigeminovascular system, which causes the release of CGRP, a potent vasodilator.[9] Studies have shown that CGRP is increased during a migraine attack and can induce migraine-like headaches.[9] It was thus identified that blocking CGRP or its receptor might treat an acute migraine attack or prevent migraines from occurring. Erenumab is a potent, selective, and full competitive antagonist of the CGRP receptor that prevents native CGRP ligand binding.[10]

Pharmacodynamics

Inhibition of dermal blood flow (DBF) was assessed in phase I trials using the capsaicin-induced DBF model. Capsaicin induces the local release of CGRP and increases the DBF. Erenumab was found to inhibit dermal blood flow after capsaicin challenge at doses of 7 mg or greater in healthy patients or those with migraines, demonstrating peripheral vasoconstriction.[13] Despite this effect, erenumab at recommended doses does not affect resting systolic or diastolic blood pressure in healthy patients.[11,12] Erenumab, at recommended doses, does not affect mean 24-hour or nocturnal blood pressure in healthy patients or in patients with migraine.[10]

Pharmacokinetics

Erenumab exhibits nonlinear elimination kinetics that are similar to other monoclonal antibodies that target membrane-bound receptors.[10,11] After subcutaneous injection, Erenumab is estimated to have a bioavailability of 82%.[11] Following a single IV dose of erenumab 140 mg, the mean volume of distribution during the terminal phase (V_2) was estimated to be 3.86 L.[11] Monoclonal antibodies such as erenumab are not eliminated through hepatic, renal, or biliary processes. Erenumab is predominately metabolized via proteolytic mechanisms and is degraded into peptides and single amino acids.[14] Erenumab undergoes two parallel elimination pathways: a slow non-specific elimination pathway through the hepatic reticuloendothelial system and a rapid saturable elimination pathway mediated by degradation or internalization of the erenumab-receptor complex.[13] The effective half-life of erenumab is approximately 28 days and reaches steady state after 3 months of dosing.[11] Erenumab is unlikely to be affected by renal or hepatic impairment due to its proteolytic metabolism/elimination. The pharmacokinetic parameters for erenumab are

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Table 1 | Select Erenumab Pharmacokinetics[10,11]

Parameters	Erenumab 70 mg
Absorption	
C_{max}	6.1 mcg/mL
AUC_{last}	159 mcg*day/mL
Distribution	
V_d	3.9
Metabolism	
Proteolytic*	
Elimination	
Half-life	~28 days

-Values reported represent mean levels

*Degradation/internalization = the erenumab-receptor complex is broken down by proteases into peptides and single amino acids which are incorporated into body proteins

AUC_{last} = area under the curve after last dose in trial; **C_{min}** = trough concentration prior to next dose; **C_{max}** = peak concentration; **mcg** = microgram; **mg** = milligram; **mL** = milliliter; m**L** = milliliter; **Vd** = volume of distribution

summarized in **Table 1.**

Clinical Trials

Two phase II studies and two phase III studies established erenumab safety and efficacy for preventative treatment of migraines. Three of the four trials studied the use of erenumab in episodic migraine, while one trial studied its use in chronic migraine. In each trial, episodic migraine was defined as a minimum of 4 and maximum of 14 migraine days per month and less than 15 headache days per month. Chronic migraine was defined as headaches occurring for 15 days or more per month for 3 months or more. Each trial had the same primary endpoint of change from baseline in monthly migraine days (MMD). For each trial, an MMD was defined as any calendar day on which the patient had an onset, continuation, or recurrence of a qualified migraine. Any calendar day on which an acute migraine-specific medication (i.e. triptan) was used was counted as a migraine day. For each trial, patients recorded the incidence of headaches, presence of aura, time of onset and resolution of headaches, severity, pain features, and other migraine symptoms using an electronic headache diary.[15,16,17,18] In the following section the clinical trials are discussed, and a summary of results can be seen in **Table 2** and **Table 3**. Safety and adverse reactions in clinical trials are discussed separately below.

Phase II Trials

Sun H et al. conducted a double-blind, placebo-controlled, dose-finding phase 2 trial to assess the safety and efficacy of erenumab for the prevention of migraine.[15] The trial consisted of four phases: screening (up to 3 weeks of initial screening and 4 weeks of baseline), double-blind treatment (12 weeks), open-label extension (up to 256 weeks), and a safety follow-up phase (12 weeks after last dose of investigational product). The open-label extension phase is ongoing at the time of this manuscript writing. Patients were randomly allocated 3:2:2:2 to a monthly subcutaneous injection of placebo (n=153), erenumab 7 mg (n=107), erenumab 21 mg (n=102), or erenumab 70 mg (n=104), respectively. Study eligibility included adult patients with episodic migraine for ≥12 months before screening. Patients were excluded if they had a history of cluster headaches or hemiplegic migraine, no therapeutic response to more than 2 preventative treatments after 6 weeks of treatment, or overuse of acute headache treatments.[15] The included patients had a mean monthly MMD of 8.7 days.[15] The primary endpoint was the change in MMD from baseline to week 12 of the double-blind treatment phase.

For the primary endpoint, erenumab 70-mg (-3.4 MMD change from baseline) demonstrated a significant reduction in MMD from baseline compared with placebo (-2.3 MMD) at week 12 (difference = -1.1 MMD; 95% CI, -2.1 to -0.2 MMD). Additionally seen was a significant reduction in weekly migraine days at week 2 as determined in a post-hoc analysis (difference = -0.5 MMD; 95% CI, -0.8 to -0.1 MMD).[15] There was no significant difference in the reduction in MMD at lower doses of erenumab compared to placebo.[15]

Secondary endpoints included the proportion of patients with at least a 50% reduction from baseline in MMD and change in monthly migraine attacks from baseline at week 12.[15] There was a significantly greater proportion of patients with at least a 50% reduction in MMD in the 70-mg erenumab group compared to the placebo group at week 12 (46% vs 30%; odds ratio [OR] = 2.0; 95% CI, 1.2 to 3.4). There was no significant difference in the proportion of patients with 50% reduction in MMD with the lower dose groups of erenumab compared to placebo.[15] Patients in the 70-mg erenumab group reported significantly greater reductions in the number of headache days compared to the placebo group at week 12 (-3.5 days vs -2.4 days; difference = -1.2 days; 95% CI, -2.1 to -0.20 days). Patients in the 70-mg erenumab group also saw a reduction in the number of days using acute medications (-2.5 days vs -1.4 days; difference = -1.2 days; 95% CI, -2.0 to -0.30 days) and days using migraine-specific medications (-1.6 days vs -0.70 days; difference = -1.0 days; 95% CI, -1.6 to -0.30 days). No statistical difference was reported between groups for cumulative hours of migraine pain, fewer cumulative hours of headache, and fewer migraine days per week. Overall, significant differences were not recorded between the erenumab 7 mg or 21 mg doses compared to placebo for the exploratory endpoints.[15]

Tepper S et al. studied the safety and efficacy of erenumab for the preventative treatment of chronic migraine in a randomized, placebo-controlled phase 2 trial.[16] The study was comprised of an initial screening phase (up to 3 weeks), a baseline phase (4 weeks), a double-blind treatment phase (12 weeks), and a safety follow-up phase (12 weeks). Patients were randomly allocated 3:2:2 to receive placebo (n=281), erenumab 70 mg (n=188), or erenumab 140 mg (n=187) subcutaneously once every 4 weeks for the 12-week double-blind treatment phase. The primary endpoint of this study was the mean change in MMD from baseline to the last 4 weeks of the 12-week treatment phase. Secondary endpoints included ≥ 50% reduction from baseline in MMD, change from baseline in cumulative headache hours, and change form baseline in monthly acute migraine-specific medications days (MSMD) assessed during the last 4 weeks of the 12-week treatment phase.[16]

Adults aged 18-65 years with a history of chronic migraine were eligible to participate in this study. Exclusion criteria were patients who were older than 50 years at migraine onset, history of cluster headache, hemiplegic migraine, or chronic migraine with continuous pain. Patients were also excluded if they had no therapeutic response after at least a 6-week trial with more than three FDA approved preventative treatment therapies.[16]

For the primary endpoint of reduction in MMD from baseline, both the 70 mg and 140 mg erenumab groups had a mean reduction of 6.6 migraine days compared to a reduction of 4.2

days in the placebo group (difference = -2.5 MMD; 95% CI, -3.5 to -1.4 MMD). The secondary outcome of ≥50% reduction in MMD was achieved by 40% of patients in the 70 mg erenumab and by 41% in the 140 mg erenumab group compared to 23% in the placebo group (70 mg vs placebo OR = 2.2; 95% CI, 1.5 to 3.3; 140 mg vs placebo OR = 2.3; 95% CI, 1.6 to 3.5). Significant reductions from baseline in MSMD were also observed for both the 70 mg (-3.5 MSMD) and 140 mg (-4.1 MSMD) groups compared to placebo (-1.6 MSMD) (70 mg vs placebo: difference = -1.9 MSMD; 95% CI, -2.6 to -1.1 MSMD; 140 mg vs placebo: difference = -2.6; 95% CI, -3.3 to -1.8 MSMD).[16]

Phase III Trials

The ARISE trial was a phase 3 randomized placebo-controlled trial that evaluated erenumab's safety and efficacy in prevention of migraine.[17] The study consisted of 3 phases: a screening phase, a 4-week baseline phase, and a 12-week double-blind treatment phase. Patients were randomly allocated 1:1 to a monthly subcutaneous injection of erenumab 70 mg (n=286) or placebo (n=291). The primary objective was change from baseline in MMD during the last month (month 3) of treatment. Secondary endpoints included achievement of ≥50% reduction from baseline in MMD, change from baseline MSMD, and achievement of at least a 5-point reduction in monthly average Physical Impairment (PI) domain scores and Impact on Everyday Activities (EA) domain scores as measured by the Migraine Physical Function Impact Diary (MPFID). The MPFID score is reported as a scale of 0 to 100, with higher values representing greater physical impairment or greater interference of migraine with everyday activity. Patients used an electronic headache diary daily throughout the baseline and treatment phase to complete this patient reported outcome (PRO).[17]

For the primary endpoint of change in MDD, the erenumab group had a mean -2.9 MMD change from baseline compared to -1.8 MMD for placebo (difference = -1.0 MMD; 95% CI, -1.6 to -0.5 MMD).[17] The secondary outcome of ≥50% reduction in MMD was achieved by 39.7% of patients in the erenumab group compared to 29.5% in the placebo group (OR = 1.59; 95% CI, 1.12 to 2.27). For change in MSMD, those receiving erenumab experienced a mean -1.2 MSMD change from baseline compared to a -0.6 MSMD change for placebo (difference in MSMD= -0.6; 95% CI, -1.0 to -0.2). For the secondary endpoint of the proportion of patients that achieved ≥5-point reduction (improvement) in the MPFID-EA and MPFID-PI scores, there were no significant differences between 70 mg erenumab and placebo.[17]

The STRIVE trial was a phase 3 randomized, double-blind, placebo controlled trial that studied the efficacy of erenumab 70 mg and 140 mg compared to placebo for the preventative treatment of episodic migraines.[18] The trial consisted of 4 phases: the screening phase (≥3 weeks of initial screening and a 4-week baseline phase), the double-blind treatment phase (24 weeks), the active treatment phase (patients underwent repeat randomization and received 70 mg or 140 mg of erenumab for 28 weeks), and a safety follow-up phase (12 weeks). The results from the active treatment phase and the safety follow-up have not yet been analyzed at the time of this manuscript writing. Patients were randomly allocated in a 1:1:1 ratio to receive monthly subcutaneous injections of 70 mg erenumab (n=312), 140 mg erenumab (n=318), or placebo (n=316). The primary objective was the change in mean number of MMD from baseline to the final 3

Table 2 | Summary of Erenumab Clinical Trials—Primary Endpoints

Trial	Intervention	Primary Endpoint	Results
Phase 2 Sun et al.[15]	Erenumab 70 mg subQ monthly (n=104) -vs- placebo (n=153)	Change from baseline in MMD in month 3 of a 12-week trial	-3.4 vs -2.3 MMD Difference: -1.1 MMD 95% CI: -2.1 to -0.2 MMD
Phase 2 Tepper et al.[16]	Erenumab 70 mg subQ monthly (n=188) -vs- placebo (n=281) Erenumab 140 mg subQ monthly (n=187) -vs- placebo (n=281)	Change from baseline in MMD in month 3 of a 12-week trial	70 mg vs placebo: -6.6 vs -4.2 MMD Difference: -2.5 MMD (95% CI: -3.5 to -1.4 MMD) 140 mg vs placebo: -6.6 vs -4.2 MMD Difference: -2.5 MMD (95% CI: -3.5 to -1.4 MMD)
ARISE[17]	Erenumab 70 mg subQ monthly (n=286) -vs- placebo (n=291)	Change from baseline in MMD in month 3 of a 12-week trial	-2.9 vs -1.8 MMD Difference: -1.1 MMD (95% CI: -1.6 to -0.5 MMD)
STRIVE[18]	Erenumab 70 mg subQ monthly (n=312) -vs- placebo (n=316) Erenumab 140 mg subQ monthly (n=318) -vs- placebo (n=316)	Change from baseline in MMD in last 3 months of a 6-month trial	70 mg vs placebo: -3.2 vs -1.8 MMD Difference: -1.4 MMD (95% CI: -1.9 to -0.9 MMD) 140 mg vs placebo: -3.7 vs -1.8 MMD Difference: -1.9 MMD (95% CI: -2.3 to -1.4 MMD)

All data is reported as least squares mean; **95% CI** = 95% confidence interval; **mg** = milligram; **MMD** = Monthly migraine days; **subQ** = subcutaneous

Table 3 | Summary of Erenumab Clinical Trials—Secondary Endpoints

Trial	Intervention	Secondary Endpoint	Results
Phase 2 Sun et al.[15]	Erenumab 70 mg subQ monthly (n=104) -vs- placebo (n=153)	Proportion achieving ≥50% reduction from baseline in MMD at week 12 of a 12-week trial	46% vs 30% OR: 2.0 (95% CI: 1.2 to 3.4)
Phase 2 Tepper et al.[16]	Erenumab 70 mg subQ monthly (n=188) -vs- placebo (n=281) Erenumab 140 mg subQ monthly (n=187) -vs- placebo (n=281)	Proportion achieving ≥50% reduction from baseline in MMD at week 12 of a 12-week trial	70 mg vs placebo: 40% vs 23% OR: 2.2 (95% CI: 1.5 to 3.3) 140 mg vs placebo: 41% vs 23% Odds ratio: 2.3 (95% CI: 1.6 to 3.5)
ARISE[17]	Erenumab 70 mg subQ monthly (n=286) -vs- placebo (n=291)	Proportion achieving ≥50% reduction from baseline in MMD in month 3 of a 12-week trial	39.7% vs 29.5% OR: 1.59 (95% CI: 1.12 to 2.27)
		Proportion achieving ≥5-point reduction in MPFID-EA score	40.4% vs 35.8% OR: 1.22 (95% CI: 0.87 to 1.71)
		Proportion achieving ≥5-point reduction in MPFID-PI score	33.0% vs 27.1% points OR: 1.33 points (95% CI: 0.92 to 1.90 points)
STRIVE[18]	Erenumab 70 mg subQ monthly (n=312) -vs- placebo (n=316) Erenumab 140 mg subQ monthly (n=318) -vs- placebo (n=316)	Proportion achieving ≥50% reduction from baseline in MMD in the last 3 months of a 6-month trial	70 mg vs placebo: 43.3% vs 26.6% OR: 2.13 (95% CI: 1.52 to 2.98) 140 mg vs placebo: 50% vs 26.6% OR: 2.81 (95% CI: 2.01 to 3.94)
		Change from baseline in monthly MPFID-EA score	70 mg vs placebo: -5.5 vs -3.3 points Difference: -2.2 points (95% CI: -3.3 to -1.2 points) 140 mg vs placebo: -5.9 vs -3.3 points Difference: -2.6 points (95% CI: -3.6 to -1.5 points_)
		Change from baseline in monthly MPFID-PI score	70 mg vs placebo: -4.2 vs -2.4 points Difference: -1.9 points (95% CI: -3.0 to -0.8 points) 140 mg vs placebo: -4.8 vs -2.4 points Difference: -2.4 points (95% CI: -3.5 to -1.4 points)

All data is reported as least squares mean, except for ≥ 50% reduction endpoints, which were reported as percentages; **95% CI** = 95% confidence interval; **mg** = milligram; **MMD** = Monthly migraine days; **MPFID-EA** = Migraine Physical Function Impact Diary – Everyday Activities (scored on scale of 0 to 100); **MPFID-PI** = Migraine Physical Function Impact Diary – Physical Impairment (scored on scale of 0 to 100); **OR** = odds ratio; **subQ** = subcutaneous

months (months 4 through 6) of the double-blind treatment phase. Secondary endpoints included ≥50% reduction from baseline in the MMD and change from baseline in mean number of days MSMD use. Other secondary endpoints included the change from baseline in the MPFID-PI score and MPFID-EA score.[18]

Eligible patients were adults 18-65 years of age who had a history of migraine with or without aura for at least 12 months before screening. Patients were excluded if they had no therapeutic response to more than 2 migraine-preventative treatment categories.[18] During baseline, all three groups had a mean MMD of 8.3 per month.

For the primary endpoint, placebo change in MMD was -1.8 days compared to -3.2 days for the 70 mg erenumab group (difference vs placebo = -1.4 MMD; 95% CI, -1.9 to -0.9 MMD) and -3.7 days for the 140 mg erenumab group (difference vs placebo = -1.9 MMD; 95% CI, -2.3 to -1.4 MMD).[18] For secondary endpoints, 43.3% of patients in the 70 mg erenumab group and 50% of patients in the 140 mg erenumab group achieved a ≥ 50% reduction in MMD per month from baseline compared with 26.6% of patients in the placebo group (70 mg vs placebo: OR = 2.1; 95% CI, 1.52 to 2.98; 140 mg vs placebo: OR = 2.8; 95% CI, 2.01 to 3.94). The MSMD per month was reduced from baseline by 1.1 days in the 70-mg erenumab group and by 1.6 days in the 140-mg erenumab group compared with 0.2 days for the placebo group (P<0.001 for each dose vs. placebo).[18] Significant reductions in the MPFID-EA and MPFID-PI scores were seen with both 70 mg and 140 mg of erenumab compared to placebo. The 70 mg erenumab dose reduced the monthly MPFID-EA score by 5.5 points compared to 3.3 points with placebo (difference = -2.2 points, 95% CI, -3.3 to -1.2 points) and reduced the monthly MPFID-PI score by 4.2 points compared to 2.4 points with placebo (difference = -1.9 points, 95% CI, -3.0 to -0.8 points). The 140 mg erenumab dose reduced the monthly MPFID-EA score by 5.9 points compared to 3.3 points with placebo (difference = -2.6 points, 95% CI, -3.6 to -1.5 points) and reduced the monthly MPFID-PI score by 4.8 points compared to 2.4 points with placebo (difference = -2.4 points, 95% CI, -3.5 to -1.4 points).

SAFETY

Adverse reactions for erenumab were assessed in every clinical trial. The most common adverse events reported for erenumab were injection site pain, nasopharyngitis, upper respiratory tract infections, nausea, fatigue, and muscle spasms.[15,-18] The occurrence of any adverse event was similar between placebo and erenumab groups in each trial. In the STRIVE trial, patients in the erenumab 70 mg group had numerically more instances of injection site pain compared to those in the placebo and 140 mg groups.[18] In the phase 2 trial conducted by Sun H et al., two patients had serious adverse events that were considered to be unrelated to treatment: one in the 7 mg group had a ruptured ovarian cyst and one in the 70 mg group had vertigo and migraine.[15] In the ARISE trial, 1 patient (0.3%) in the placebo group and 5 patients (1.8%) in the erenumab group experienced adverse events that led to treatment discontinuation.[17]

Anti-erenumab antibodies were also assessed in these clinical trials. However, during the clinical trials no apparent association was recorded between patients with positive erenumab antibodies and adverse events.

In the STRIVE trial, no clinically meaningful differences between the erenumab groups and the placebo group were observed in hepatic function testing, total neutrophil counts, creatinine levels, vital signs, or electrocardiographic findings.[18] Since monoclonal antibodies are not metabolized hepatically, erenumab treatment did not result in any observable effect on liver enzymes[18] Overall, erenumab appears to be safe and relatively tolerable.

Table 4 | Select Adverse Events from Clinical Trials

Trial	Intervention	Any AE	Serious AE	Injection Pain
Phase 2: Sun et al.[15]	**Placebo (n=153)**	54%	0%	-
	Erenumab 70 mg (n=106)	54%	1%	-
Phase 2: Tepper et al.[16]	**Placebo (n=282)**	39%	2%	1%
	Erenumab 70 mg (n=190)	44%	3%	4%
	Erenumab 140 mg (n=188)	47%	1%	4%
Phase 3: ARISE[17]	**Placebo (n=289)**	54.7%	1.7%	4.2%
	Erenumab 70 mg (2n=83)	48.1%	1.1%	6%
Phase 3: STRIVE[18]	**Placebo (n=319)**	63%	2.2%	0.3%
	Erenumab 70 mg (n=314)	57.3%	2.5%	3.2%
	Erenumab 140 mg (n=319)	55.5%	1.9%	0.3%

IC50 = half-maximum inhibitor concentration; **nM** = nanomolar; **SGLT** = sodium-glucose transporter;

Clinical Implications

The clinical trials for erenumab report significant reductions in the mean frequency of MMD. However, this reduction was only by about 1 to 2.5 days per month for the 70 mg erenumab dose and by about 2 to 2.5 days per month for the 140 mg erenumab dose compared to placebo. When looking at secondary endpoints, there were 10-17% more patients that achieved at least a 50% reduction from baseline in MMD with 70 mg erenumab compared to placebo, and approximately 18-23% more patients with 140 mg erenumab compared to placebo. On average, erenumab 70 mg reduced MSMD by about 0.5 to 2 days per month while the 140 mg erenumab reduced MSMD by about 1.5 to 3 days per month compared to placebo.[15,-18] A significant reduction in weekly migraine days was seen starting at week 2, which suggests that some benefit may be seen after 2 weeks of therapy although the full effect may take 12 weeks.[15]

It is also interesting to note that the clinical trials excluded patients with previous failures with two to three FDA approved preventative treatment therapies for migraines. This means there is a lack of data on whether erenumab would be efficacious in this population of patients.

Although side effects were reported in about 50% of patients taking placebo or erenumab, the side effects appear to be mild. There were no significant differences observed between the rate of side effects with erenumab compared to placebo. Also, the rate of side effects did not appear to increase with increasing doses of erenumab.

Although these results were shown to be statistically significant in these trials, the question remains as to whether these reductions in MMD or MSMD represent a clinical benefit for patients. For patients with chronic or episodic migraine, as assessment will need to be made as to whether a reduction in migraine frequency by about 2.5 days per month is worth the cost of Aimovig®. Based on clinical trials, it appears erenumab 140 mg is more effective at reducing MMD and MSMD compared to erenumab 70 mg. Since erenumab has a low rate of side effects and does not have drug interactions or cause hepatic or renal harm, it may be appropriate for all patients to start on erenumab 140 mg.

Dosing and Administration

Aimovig® comes as a 70 mg/mL solution in a pre-filled syringe or SureClick® autoinjector for subcutaneous injection.[11] Patients can either receive 70 mg or 140 mg of Aimovig® subcutaneously once monthly in the abdomen, thigh, or upper arm. If the patient needs 140 mg, it should be administered as two consecutive subcutaneous injections of 70 mg in separate locations since the maximum recommended subcutaneous injection volume per site is about 1 mL (although the manufacturer does not specify). If a patient misses their monthly dose, it should be administered as soon as possible, and the next dose should be scheduled monthly from the date of administration. Aimovig® should be kept in the refrigerator but it can be stored at room temperature for up to 7 days. Prior to administering, Aimovig® should be left at room temperature for at least 30 minutes. Aimovig® currently does not have any contraindications for use. Aimovig® is not excreted renally, therefore it does not require dose adjustment for renal impairment nor does it require hepatic impairment adjustments. Aimovig® is not metabolized by CYP450 enzymes and has no significant drug interactions at this time.[12] Part of the prefilled syringe and autoinjector is made from latex, so it is recommended to use caution in patients with a latex allergy.[11]

Cost and Availability

Aimovig® is currently priced in the US at $575 per month for a 70 mg single-use prefilled SureClick® autoinjector, which comes to $6,900 annually.[11] this cost would be doubled for those requiring 140 mg monthly dose. Lipton RB, et al. conducted a cost-effectiveness study in 2017 on erenumab from the US societal perspective.[4] The investigators used a Markov health state transition model to estimate the incremental costs and quality-adjusted life years (QALYs) of erenumab 140 mg for migraine prevention. The study used the mean reduction in MMD observed in the clinical trials previously mentioned. In the analysis, 6,108 patients receiving only supportive care for migraines were estimated to experience an average of 1,949 migraine days over 10 years. Those who were treated with erenumab were estimated to experience a reduction of 144 MMD with a mean treatment duration of ~2 years.[4] As a result of migraine day reductions, erenumab was associated with increased total QALYs per person of 0.1849 over 10 years. The cost associated with only supportive care of migraines was estimated to be $129,889 over 10 years. With the reduction in MMD, erenumab was expected to reduce the total migraine day-related cost by $8,482 over 10 years.[4] In comparison, the cost of 70 mg monthly over 10 years would be $69,000 which shows poor cost-effectiveness with this therapy. The Aimovig® manufacturer, Amgen Inc., offers a Copay Program that can reduce a patient's out-of-pocket costs to as little as $5 per month for eligible patients with commercial insurance.[11]

Conclusion

Erenumab is an FDA approved medication for the prevention of episodic and chronic migraines. Erenumab is the first monoclonal antibody that targets and antagonizes the CGRP receptor. Clinical trials have demonstrated that erenumab is statistically effective at reducing the frequency of migraine days per month at doses of 70 mg and 140 mg. Erenumab well-tolerated by patients and is currently only associated with some mild to moderate adverse events but cost may be a limiting factor for use in some patients. Overall, erenumab appears to be a safe and effective preventative treatment option to decrease the frequency of migraine days in patients with episodic and chronic migraine.

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