Health Economic Value of Aimovig® (erenumab-aooe) in the Preventive Treatment of Migraine

Model Overview[1]

Overview	Description	
Structure	A semi-Markov health state transition structure with patients compartmentalized into one of three health states, based on preventive treatment status and death. The model assumes a 10-year time horizon with 28-day cycles, with a 3% annual discount.	
Perspectives	• Societal (direct + indirect costs) – base case • Payer (direct costs only) – scenario analysis	
Population Modeled	**Episodic Migraine:*** • 4–14 migraine days per month • < 15 headache days per month[2,3] • ≥ 1 prior preventive treatment failure	**Chronic Migraine:†** • ≥ 8 migraine days per month • ≥ 15 headache days per month • ≥ 1 prior preventive treatment failure
Intervention	• Aimovig® 70 mg injected subcutaneously every 4 weeks • Aimovig® 140 mg injected subcutaneously every 4 weeks	
Comparators	EM: No preventive treatment (NPT)	CM: OnabotulinumtoxinA
Inputs	**Clinical Inputs** • Mean baseline MMD frequency • Change from baseline in MMDs • Discontinuation rates, by treatment • Health utilities, by MMD frequency	**Economic Inputs** • Preventive medication costs • Other direct costs (acute medication use and health resource utilization) • Indirect costs (lost productivity)
Outcomes	• Incremental cost-effectiveness ratios (ICERs)	

CM: chronic migraine; EM: episodic migraine; MMD: monthly migraine day
*Based on two pivotal, phase 3, randomized, double-blind, placebo-controlled, multicenter studies of Aimovig® for adults aged 18–65 years with EM in North America and Europe: STRIVE (121 centers) and ARISE (69 centers)[1,2,4]. In STRIVE, patients were randomly assigned to subcutaneous placebo (n = 319), Aimovig® 70 mg (n = 317), or Aimovig® 140 mg (n = 319), given every 4 weeks for 24 weeks.[1,4] In ARISE, patients were randomly assigned to subcutaneous placebo (n = 291) or Aimovig® 70 mg (n = 286), given every 4 weeks for 12 weeks.[1,2]
†Based on a pivotal, phase 2, randomized, multicenter, double-blind, placebo-controlled study of Aimovig® for adults aged 18–65 years with CM in North America and Europe (69 centers).[1,5] Patients were randomly assigned to subcutaneous placebo (n = 286), Aimovig® 70 mg (n = 191), or Aimovig® 140 mg (n = 190), given every 4 weeks for 12 weeks[1,5]

Health States Contained in the Cost-Effectiveness Model

On Preventive Treatment: All patients modeled to start on a preventive treatment and experiencing reductions in monthly migraine days (MMDs). The time- and treatment-dependent discontinuation rates determine the time on preventive therapy.[1]

Off Preventive Treatment: All patients modeled to receive no preventive treatment (NPT) for episodic migraine (EM) or patients who discontinue their active preventive therapy for both EM and chronic migraine (CM). The model assumes that treatment effect of any active therapy is instantaneously lost once patients discontinue their treatment, and MMD returns to the baseline frequency.[1]

Death: Patients from both the "On Preventive Treatment" and "Off Preventive Treatment" health states can transition to the "Death" health state at any time, and are assumed to experience general population mortality, based on US life tables.[6] Migraine- or treatment-related mortality was not considered significant enough to warrant incorporation into the model.[1]

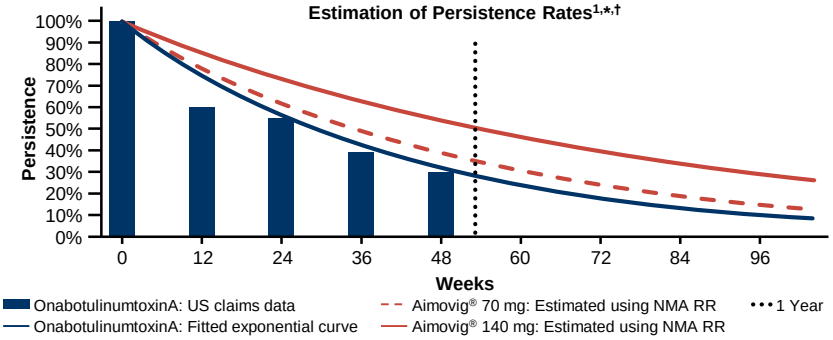
Clinical Inputs:

Absolute Reduction* in MMD From Baseline[1,†]

	Aimovig® 70 mg	Aimovig® 140 mg	OnabotulinumtoxinA
EM	–3.29 MMD	–3.79 MMD	Not Applicable
CM	–6.45 MMD	–6.35 MMD	–6.05 MMD

CM: chronic migraine; EM: episodic migraine; MMD: monthly migraine day
*Change from baseline in the placebo groups of the Aimovig® clinical trials was estimated using a longitudinal regression model and subsequently added to the relative reductions in MMDs for migraine preventive therapies drawn from a network meta-analysis (NMA) to calculate absolute reductions from baseline in MMDs. This absolute reduction from baseline was modeled over the timeframe of the analysis. The NMA is based on a systematic review of identified randomized clinical trials searched in June 2015 and updated in October 2018 that compared the efficacy and safety of preventive migraine therapies in migraine sufferers.[7] The data provided by the systematic literature review evidence were summarized by means of Bayesian NMA. Outcomes of interest were analyzed using a fixed and a random effects model.[1]

† Baseline monthly migraine frequency was calculated using a negative-binomial distribution of the mean baseline migraine day frequency of the patient population with ≥ 1 prior preventive treatment failure from the Aimovig® EM (8.66 MMD) and CM (18.44 MMD) clinical trials.[1]



NMA: Network meta-analysis; RR: rate ratio

*OnabotulinumtoxinA persistence rates were derived using claims data from the Truven Health MarketScan® databases. The analysis evaluated adult migraine patients who initiated preventive medication and were continuously enrolled in the health plan for ≥ 12 months before and after the start of treatment between 2010 and 2014. Patients followed for 12 months after treatment initiation were categorized by whether they ended the year on the same treatment or stopped treatment without starting a new treatment, defined as a gap in therapy of > 60 days. The annual probabilities were converted to monthly risks of discontinuation, assuming constant rates across the 12 months. The predicted real-world discontinuation and switch rates for Aimovig® were assumed to equal the trial-based discontinuation rates and were estimated using the NMA of all-cause clinical trial discontinuation to calculate a rate-ratio derived from the CM clinical study data, where the switch rate-ratio was assumed to be the same as the discontinuation rate-ratio (Aimovig® 70 mg: 0.83 (95% CI 0.10–6.51); Aimovig® 140 mg: 0.54 (95% CI 0.06–4.6).[1,8] Discontinuation rate-ratios were applied to the persistence curves with the equation:

$$\text{Aimovig® persistence rate (week x)} = e^{[-(\text{week x}) * (\text{onabotulinumtoxinA regression constant rate of persistence decline}) * (\text{Aimovig® vs onabotulinumtoxinA discontinuation rate-ratio})]}$$

†The model assumed that treatment effects of preventive therapies are lost instantaneously, and monthly migraine day (MMD) returns to the baseline value once patients discontinue treatment. The same persistence rates were assumed for episodic migraine (EM) and chronic migraine (CM).[1]

Indication: Aimovig® (erenumab-aooe) is indicated for the preventive treatment of migraine in adults.

Important Safety Information

Contraindication: Aimovig® is contraindicated in patients with serious hypersensitivity to erenumab-aooe or to any of the excipients. Reactions have included anaphylaxis and angioedema.

Please see additional Important Safety Information on reverse.

aimovig (erenumab-aooe) injection 70 mg/mL • 140 mg/mL

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USA-334-83898

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Clinical Inputs:[1] Health Utilities*

Mean utility value range	0–7 MMD	8–14 MMD	15–21 MMD	22–28 MMD
Aimovig® 70 mg	0.8170–0.7204	0.7043–0.5978	0.5788–0.4616	0.4422–0.3310
Aimovig® 140 mg	0.8204–0.7250	0.7090–0.6033	0.5843–0.4673	0.4478–0.3361
Placebo	0.8146–0.7171	0.7009–0.5940	0.5749–0.4577	0.4383–0.3275

MMD: monthly migraine day

*Patient-reported outcomes from the Aimovig® clinical trials were captured using a migraine-specific questionnaire. These values were mapped to EuroQoL five-dimensional (EQ-5D) utility values, using previously published and validated algorithms.[3] A nonlinear, multilevel beta regression model was used to predict patient utilities based on the patient's MMDs, while controlling for other patient and treatment factors. Utility values for placebo were applied either to patients who were modeled to receive no preventive treatment (NPT) or to patients who discontinued an active treatment in the model. The utility values for Aimovig® (70 mg or 140 mg) were assumed to be equal to the utility values for active treatment with onabotulinumtoxinA. Quality-adjusted life years (QALYs) were estimated using these utility values, applied to the MMD experienced in each 28-day cycle, over the model time horizon.

Economic Inputs[1]

Drug	WAC per Administration*
Aimovig® 70 mg	$528.95
Aimovig® 140 mg	$528.95
OnabotulinumtoxinA	$1,202.00

WAC: wholesale acquisition cost

*WAC prices for Aimovig® were based on an assumed annual price of $6,900, with administration every 4 weeks. The WAC price for Aimovig is $575 per month, however, the model uses a 28-day frequency which corresponds to a WAC price of $528.95.[1,9] WAC prices for onabotulinumtoxinA (200 U) were based on AnalySource (October 2019)[9] and costs were applied for administration every 12 weeks. The 200 U vial was used to account for potential drug wastage. Administration costs for onabotulinumtoxinA were to equal $177.32 per administration, assuming a 50% facility (CPT 99212) and 50% nonfacility (CPT 64615) site of care for administration, based on the Centers for Medicare and Medicaid Services Physician Fee Schedule.[1]

Medical Resource Costs per Migraine Day*				Acute Medication Costs per Migraine Day†		Lost Productivity Costs per Migraine Day‡	
Physician Visits	ER Visits	Hospitalization	Specialist Visit	Migraine Specific	Nonmigraine Specific	Absenteeism	Presenteeism
$4.55	$8.54	$46.00	$1.59	$7.95 (EM)/$9.05 (CM)	$1.38 (EM)/$2.13 (CM)	$219.84	$109.92

CM: chronic migraine; EM: episodic migraine; ER: emergency room; WAC: wholesale acquisition cost

*Based on a 5-year, US national, longitudinal American Migraine Prevalence and Prevention (AMPP) survey evaluating the impact of migraine on health care resource utilization. 7,796 adults with EM were asked to report the number of visits to each defined medical resource, in the preceding 12 months of the survey.[10] Average use for each resource was calculated as a weighted average of EM and CM, assuming 24.34 headache days per year as reported by the survey respondents. Costs were based on a 2010–2014 study period of the retrospective claims analysis of the Truven Health Analytics MarketScan® Commercial Claims and Medicare Supplemental databases, where migraine-specific costs were estimated over a 12-month period.[11] Costs are presented in 2019 dollars.

†Based on WAC obtained from AnalySource (October 2019),[9] weighted by the relative probability of use for each medication in the class, as defined by previously published studies. Acute medication utilization was based on a prediction model fitted to the pooled data (EM and CM) of acute medication use, collected in the Aimovig® pivotal trials.[2,4,5] The identified relationship was applied to the change from baseline in MMDs to calculate the costs associated with incremental use. Migraine-specific acute medications comprised triptans and ergotamine derivatives. Nonmigraine-specific acute medications comprised acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), barbiturates, opioids, isometheptene compounds, and other over-the-counter medications. However, it must be noted that there was very limited use of opioids in Aimovig® clinical trials (< 3% in clinical trials vs 11%–21% in real world).[12]

‡Absenteeism defined as a full day lost and presenteeism defined as a half-day lost, based on an 8-hour work day and a median hourly pay of $27.48/hour, as reported by the 2018 US Bureau of Labor Statistics.[13] The numbers of absenteeism and presenteeism days associated with therapies were estimated from patient responses to the Migraine Disability Assessment (MIDAS) questionnaire collected in the Aimovig® pivotal trials. The identified relationship was based on regression models used to estimate the number of absenteeism and presenteeism days as a function of MMD in the pivotal trials.

Aimovig® is Cost-Effective Across All Populations and Doses in the Base Case[1]

Treatment	Episodic Migraine			Chronic Migraine		
	NPT	Aimovig® 70 mg	Aimovig® 140 mg	OnabotulinumtoxinA	Aimovig® 70 mg	Aimovig® 140 mg
Total Costs (USD)*	$119,241	$121,774	$122,157	$230,940	$230,477	$229,891
Total QALYs*	5.847	5.899	5.943	4.637	4.657	4.709
ICER	Not Applicable	**$48,586**	**$30,325**	Not Applicable	**Less Costly, More Effective**	**Less Costly, More Effective**

ICER: incremental cost-effectiveness ratio; NPT: no preventive treatment; QALY: quality-adjusted life year

*Base-case results (societal perspective) include indirect costs of lost productivity in patients that have failed at least one prior therapy. Total costs and QALYs are based on a 10-year time horizon and are discounted at a 3% annual rate.

- ICERs from a scenario analysis of a payer perspective (direct costs only) for EM were $76,895 and $56,701 for Aimovig® 70 mg and 140 mg, respectively.[1]
- ICERs from a scenario analysis of a payer perspective (direct costs only) for CM were $19,189 and $25,158 for Aimovig® 70 mg and 140 mg, respectively.[1]

Select Assumptions:

- The statistical approaches adopted in the model assume identical distribution of patient cohorts with the same mean MMD. [1]
- The population modeled requires long-term prevention for the duration of the model, which represents the patient population in which Aimovig® will be used. [1]

Limitations:

- The model only assesses patients who failed ≥ 1 prior preventive therapy and were not treatment naïve. [1]
- Discontinuation rate-ratios used to derive the Aimovig® persistence rates are based on all-cause clinical trial discontinuation rates and may not be reflective of the real-world persistence rates.[1]
- The model does not differentiate between lost productivity in the workplace and at home due to lack of available evidence.[1]

References:

1. Data on file, Amgen; [Aimovig® Cost-Effectiveness Analysis; 2019]. 2. Dodick DW, et al. *Cephalalgia*. 2018;38:1026-1037.* 3. Gillard PJ, et al. *Value Health.* 2012;3:485-494. 4. Goadsby PJ, et al. *N Engl J Med*. 2017;377:2123-2132.* 5. Tepper S, et al. *Lancet*. 2017;16:425-434.* 6. Kochanek KD, et al. *Deaths: Final Data for 2014.* Hyattsville, MD: National Center for Health Statistics; 2016. National Vital Statistics Reports, Vol 65, No. 4. 7. Data on file, Amgen; [NMA of Migraine Preventatives; 2019]. 8. Data on file, Amgen; [Patient Flow Characteristics; 2019]. 9. AnalySource. https://www.analysource.com/products/active/. Accessed October 21, 2019. 10. Munakata J, et al. *Headache*. 2009;49:498-508. 11. Data on file, Amgen; [Unit Medical Resource Utilization Costs; 2019]. 12. Bigal ME, et al. *Cephalalgia*. 2009;29:891-897. 13. Bureau of Labor Statistics. https://www.bls.gov/news.release/archives/realer_01182017.pdf. Accessed October 22, 2019.

*The following research/publications utilized in the economic model were funded by Amgen, Inc. At the time of publication, the following authors had received financial compensation/funding from Amgen, Inc for these studies: Dodick, DW; Ashina, M; Brandes, JL; Kudrow, D; Lanteri-Minet, M; Palmer, K; Lenz, RA; Broessner, G; Goadsby, PJ; Hallström, Y; Reuter, U; Lenz, R; Mikol, D; Picard, H; Sapra, S; Zhang, F; Tepper, S; Doležil, D; Silberstein, S; Winner, P; Leonardi, D

Important Safety Information

Contraindication: Aimovig® is contraindicated in patients with serious hypersensitivity to erenumab-aooe or to any of the excipients. Reactions have included anaphylaxis and angioedema.

Hypersensitivity Reactions: Hypersensitivity reactions, including rash, angioedema, and anaphylaxis, have been reported with Aimovig® in post marketing experience. Most reactions were not serious and occurred within hours of administration, although some occurred more than one week after administration. If a serious or severe reaction occurs, discontinue Aimovig® and initiate appropriate therapy.

Constipation with Serious Complications: Constipation with serious complications has been reported following the use of Aimovig® in the postmarketing setting. There were cases that required hospitalization, including cases where surgery was necessary. The onset of constipation was reported after the first dose in a majority of these cases, but patients also reported later on in treatment. Aimovig® was discontinued in most reported cases. Constipation was one of the most common (up to 3%) adverse reactions reported in clinical studies.
Monitor patients treated with Aimovig® for severe constipation and manage as clinically appropriate. Concurrent use of medications associated with decreased gastrointestinal motility may increase the risk for more severe constipation and the potential for constipation-related complications.

Hypertension: Development of hypertension and worsening of pre-existing hypertension have been reported following the use of Aimovig® in the postmarketing setting. Many of the patients had pre-existing hypertension or risk factors for hypertension. There were cases requiring pharmacological treatment and, in some cases, hospitalization. Hypertension may occur at any time during treatment but was most frequently reported within seven days of dose administration. In the majority of the cases, the onset or worsening of hypertension was reported after the first dose. Aimovig® was discontinued in many of the reported cases.
Monitor patients treated with Aimovig® for new-onset hypertension, or worsening of pre-existing hypertension, and consider whether discontinuation of Aimovig® is warranted if evaluation fails to establish an alternative etiology.

Adverse Reactions: The most common adverse reactions in clinical studies (≥ 3% of Aimovig®-treated patients and more often than placebo) were injection site reactions and constipation.

Please see accompanying Aimovig® full Prescribing Information.

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