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

Model Overview†

<table>
<thead>
<tr>
<th>Overview</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>Structure</strong></td>
<td>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.</td>
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<tr>
<td><strong>Perspectives</strong></td>
<td>• Societal (direct + indirect costs) – base case • Payer (direct costs only) – scenario analysis</td>
</tr>
<tr>
<td><strong>Population Modeled</strong></td>
<td>Episodic Migraine:*  • ≥ 4–14 migraine days per month  • &lt; 15 headache days per month²⁻³  • ≥ 1 prior preventive treatment failure</td>
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<tr>
<td><strong>Intervention</strong></td>
<td>Aimovig® 70 mg injected subcutaneously every 4 weeks  Aimovig® 140 mg injected subcutaneously every 4 weeks</td>
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<tr>
<td><strong>Comparators</strong></td>
<td>EM: No preventive treatment (NPT)</td>
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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).¹²⁴ 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 In ARISE, patients were randomly assigned to subcutaneous placebo (n = 291) or Aimovig® 70 mg (n = 286), given every 4 weeks for 12 weeks.¹²³
†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).¹⁵ 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.¹³

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.¹ 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†:**

<table>
<thead>
<tr>
<th></th>
<th>Alimovig® 70 mg</th>
<th>Alimovig® 140 mg</th>
<th>OnabotulinumtoxinA</th>
</tr>
</thead>
<tbody>
<tr>
<td>EM</td>
<td>−3.29 MMD</td>
<td>−3.79 MMD</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>CM</td>
<td>−6.45 MMD</td>
<td>−6.35 MMD</td>
<td>−6.05 MMD</td>
</tr>
</tbody>
</table>

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.² 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.³
†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 (6.86 MMD) and CM (18.44 MMD) clinical trials.¹

Healthcare economic value analysis was performed using a Markov health state transition structure with patients compartmentalized into one of three health states: (1) OnabotulinumtoxinA: Fitted exponential curve, (2) Alimovig® 70 mg: Estimated using NMA RR, and (3) Alimovig® 140 mg: Estimated using NMA RR. The analysis evaluated adult migraine patients who initiated preventive treatment and experiencing reductions in monthly migraine days (MMDs). The time horizon was one year, with 28-day cycles. 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.
Contraindication:

Aimovig® is contraindicated in patients with serious hypersensitivity to erenumab (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.

Constitution with Serious Complications: Constitution 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 constitution 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. Constitution was one of the most common (up to 3%) adverse reactions reported in clinical studies. Monitor patients treated with Aimovig® for severe constitution and manage as clinically appropriate. Concurrent use of medications associated with decreased gastrointestinal motility may increase the risk for more severe constitution and the potential for constitution-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.

This resource contains healthcare economic information and is intended only for formulary committees or other similar entities with drug selection responsibilities, pursuant to Section 114 of the FDA Modernization Act.