Anti-CGRP Injectables for Migraine: Taking a Shot at the Cost and the Gain

Tina Ou, Pharm.D.
PGY-1 Pharmacy Resident
Central Texas Veterans Health Care System

Learning Objectives

<table>
<thead>
<tr>
<th>Describe</th>
<th>Describe the pathophysiology and epidemiology of migraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outline</td>
<td>Outline the current treatment options for migraine</td>
</tr>
<tr>
<td>Compare</td>
<td>Compare the injectable monoclonal antibodies as options for migraine treatment</td>
</tr>
<tr>
<td>Evaluate</td>
<td>Evaluate the cost-effectiveness of the injectable biologic agents</td>
</tr>
<tr>
<td>Discuss</td>
<td>Discuss the place in therapy of the injectable monoclonal antibodies and the pharmacists’ role</td>
</tr>
</tbody>
</table>

Abbreviations

- CGRP = calcitonin gene-related peptide
- MMD = monthly migraine day
- MHD = monthly headache day
- QALY = quality-adjusted life years
- ICER = incremental cost-effectiveness ratio

Migraine: What is it?

- Common chronic neurological disorder
- Recurring headaches that may be described as “throbbing”
- Often unilateral
- May be worsened physical activity
- Symptoms include:
  - Pain
  - Light sensitivity
  - Sound sensitivity
  - Vomiting
  - Nausea
  - Cutaneous allodynia
- About 1/3 are preceded by aura

Migraine: Why care?

- Second most disabling neurologic condition globally in years lost to disability according to Global Disease Burden
- Financial burden in the United States of $27 billion and possibly more
- Direct medical costs and indirect medical costs

Migraine: Who is affected?

- Experienced by 15% of the world’s population
- Possibly 3 billion people affected worldwide
- Underdiagnosed due to transience and variability
- Populations affected
  - Women
  - Ages 35-45 years old
  - Prevalence peaks between 25-35 years old
### Migraine: Characteristics

- **Episodic**
  - 0-14 headache days per month on average
  - ~90% of patients who suffer from migraine
  - At least 5 headache attacks must
  - Last 4-72 hours if untreated
  - Have concurrent nausea and/or vomiting or sensitivity to light and sound
  - Have at least two of these characteristics: unilateral location, pulsating quality, moderate to severe pain intensity, role of routine physical activity

- **Chronic**
  - Average of 15+ migraine-like or tension type-like headache days per month for 3+ months
  - At least 8 migraine days included
  - Patient belief that it is a migraine at onset
  - Relief from triptan or ergot derivative

### Migraine: How does it occur?

- CGRP serum levels are elevated during vascular headaches, which include migraines with or without aura
- CGRP levels are returned to baseline as headache pain is alleviated through triptan use
- Infusion of CGRP into susceptible subjects led to migraines and headaches

### Potential mechanism of inhibiting CGRP

A 32-40 otherwise healthy female states that she is experiencing 6 MMDs. She states that she misses about two social activities a month due to her pain, and she also takes at least one day off work every month.

She currently takes acetaminophen for her migraine pain and is wondering if there is anything else that she can try.
Treatment: Guidelines

- British Association for the Study of Headache
  - 2010 – first-line preventive treatment of beta-blockers, topiramate, valproate, and amitriptyline; onabotulinum toxin A for chronic migraine only
- American Academy of Neurology
  - 2016 – use of onabotulinum toxin A for chronic migraine
- National Institute for Health and Care Excellence
  - 2012 – antiepileptic drugs and beta-blockers for prevention of episodic migraine
- European Headache Federation
  - 2018 – topiramate and propranolol for prevention of migraine, choice determined by side effect profile and patient preference. Onabotulinum toxin A for chronic migraine with a target of at least 30% reduction in MHD after two treatment cycles or ≤15 MHDs

Treatment: Preventive options

- Oral preventive treatments were not designed specifically for migraine
- Adverse effect profiles
- Preventive treatment used by 3-13% of patients
- Adherence is low
- Consider for:
  - MHD >3
  - Significant interference with daily routines
  - Failure of or contraindication to acute treatments
  - Overuse of acute treatments

Treatment: Medication overuse headache

- Headache on 15+ days/month in a patient with a pre-existing headache disorder
- Overuse for >3 months of 1+ acute or symptomatic treatment options
- 10+ days/month for ergot derivatives, triptans, opioids, combination analgesics, or a combination of different classes though not individually overused
- 15+ days/month for nonopioid analgesics, acetaminophen, and NSAIDS

Treatment: When to offer

<table>
<thead>
<tr>
<th>Headache days per month</th>
<th>Degree of disability*</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFFER</td>
<td>None</td>
</tr>
<tr>
<td>6+</td>
<td>None</td>
</tr>
<tr>
<td>4+</td>
<td>Severe</td>
</tr>
<tr>
<td>3*</td>
<td>Severe</td>
</tr>
<tr>
<td>CONSIDER</td>
<td>None</td>
</tr>
<tr>
<td>4 or 5</td>
<td>Severe</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

* = Measured by Migraine Disability Assessment Scale

Treatment: Options
Treatment: Challenges

- Migraine severity, frequency, and characteristics:
  - differ in individuals
  - can change in an individual over time
- Lack of objective biomarkers and symptom profile
- Based on patient preference, “trial and error”, dependent on pregnancy/lactation, type of symptoms, contraindications, concomitant medication use
- Inadequate treatment of episodic migraine may lead to chronic migraine

Treatment: What is “success”?

- 50% decrease in frequency of MMDs/MHDs
- Significant decrease in attack duration or severity
- Improved response to acute treatment
- Reduction in migraine-related disability
- Improvements in health-related quality of life

Treatment: Counseling points

- Titration from a low dose to a target therapeutic dose
- Trial of at least 8 weeks on a therapeutic dose
- Combination of different classes
- Common adverse effects
- Continued use of up to 12 hours may result in cumulative benefits
- May need to re-evaluate therapeutic response over time due to changing characteristics of migraine

CGRP Antibodies

- Migraine-specific
- Monoclonal
- Injectable
- Act on the CGRP pathway
- Side effect profile appears favorable
- Recently approved by the FDA
- High cost

CGRP Antibodies: Approval

- May 2018 – FDA approves erenumab-aooe for migraine prevention
- September 2018 – FDA approves fremanezumab-vfrm for migraine prevention
- September 2018 – FDA approves galcanezumab-gnlm for migraine prevention
- June 2019 – FDA approves galcanezumab-gnlm for episodic cluster headache

CGRP Antibodies: Comparison

<table>
<thead>
<tr>
<th>Brandname</th>
<th>Erenumab-aooe</th>
<th>Fremanezumab-vfrm</th>
<th>Galcanezumab-gnlm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Amgen, Inc.</td>
<td>Teva Pharmaceuticals USA, Inc</td>
<td>Eli Lilly</td>
</tr>
<tr>
<td>Dosing</td>
<td>70 mg SQ once monthly OR 140 mg SQ once monthly</td>
<td>225 mg SQ once monthly OR 675 mg SQ once every 3 months</td>
<td>225 mg SQ loading dose THEN 120 mg SQ once monthly</td>
</tr>
<tr>
<td>FDA approvals</td>
<td>Episodic and chronic migraines</td>
<td>Episodic and chronic migraines</td>
<td>Episodic and chronic migraines Episodic cluster headache</td>
</tr>
<tr>
<td>Site of MOA</td>
<td>CGRP receptor</td>
<td>CGRP ligand</td>
<td>CGRP ligand</td>
</tr>
<tr>
<td>Current cost</td>
<td>$577.65 monthly for one 70 mg injector</td>
<td>$577.65 for one 225 mg syringe</td>
<td>$949.99 for one 120 mg pen</td>
</tr>
</tbody>
</table>
Trials: erenumab-aooe

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>Erenumab 140 mg</td>
<td>Mean change in MMD from baseline over 6 months</td>
<td>-3.2 MMD in 70 mg</td>
<td>P &lt; 0.001 for each treatment arm compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Erenumab 70 mg</td>
<td></td>
<td>-3.7 MMD in 140 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-1.8 MMD in placebo</td>
<td></td>
</tr>
</tbody>
</table>

ARISE

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
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<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>Erenumab 70 mg</td>
<td>Mean change in MMD from baseline over 3 months</td>
<td>-2.9 MMD in 70 mg</td>
<td>P &lt; 0.001 for each treatment arm compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-1.8 MMD in placebo</td>
<td></td>
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</tbody>
</table>

Tepper et al.

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic</td>
<td>Erenumab 140 mg</td>
<td>Mean change in MMD from baseline over 3 months</td>
<td>-6.6 MMD in 70 mg</td>
<td>P &lt; 0.001 for each treatment arm compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Erenumab 70 mg</td>
<td></td>
<td>-6.6 MMD in 140 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-4.2 MMD in placebo</td>
<td></td>
</tr>
</tbody>
</table>

Trials: fremanezumab-vfrm

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic</td>
<td>Fremanezumab 225 mg</td>
<td>Mean change in MMDs from baseline over 2 months</td>
<td>-4.0 MMDs in 225 mg</td>
<td>P &lt; 0.001 for each treatment arm compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Fremanezumab 675 mg</td>
<td></td>
<td>-3.9 MMDs in 675 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-2.6 MMDs in placebo</td>
<td></td>
</tr>
</tbody>
</table>

Silberstein et al.

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic</td>
<td>Fremanezumab 675 mg</td>
<td>Mean change in MMDs from baseline over 3 months</td>
<td>-4.3 MMDs in 675 mg</td>
<td>P &lt; 0.001 for each treatment arm compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Fremanezumab 225 mg after 675 mg loading dose</td>
<td></td>
<td>-4.6 MMDs in 225 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-2.5 MMDs in placebo</td>
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</table>


Trials: galcanezumab-gnlm

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVOLVE-1 Episodic</td>
<td>Galcanezumab 120 mg with a 240 mg loading dose on third monthly visit</td>
<td>Mean change from baseline in MHDs over 6 months</td>
<td>-4.7 MHDs for 120 mg</td>
<td>P &lt; 0.001 when compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Galcanezumab 240 mg</td>
<td></td>
<td>-4.6 MHD for 240 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-2.8 days for placebo</td>
<td></td>
</tr>
</tbody>
</table>

EVOLVE-2 Episodic

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Galcanezumab 240 mg</td>
<td>Mean change from baseline in MHDs over 6 months</td>
<td>-4.3 MHDs for 120 mg</td>
<td>P &lt; 0.001 when compared to placebo</td>
</tr>
<tr>
<td></td>
<td>Galcanezumab 120 mg after initial 240 mg loading dose</td>
<td></td>
<td>-4.3 MHDs for 240 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-2.3 days for placebo</td>
<td></td>
</tr>
</tbody>
</table>

REGAIN Chronic

<table>
<thead>
<tr>
<th>Migraine type</th>
<th>Treatment arms</th>
<th>Primary endpoint</th>
<th>Results</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Galcanezumab 120 mg after initial 240 mg loading dose</td>
<td>Mean change from baseline in MHDs over 3 months</td>
<td>-4.8 MHDs for 120 mg</td>
<td>P &lt; 0.001 when compared to placebo</td>
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<td></td>
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<tr>
<td></td>
<td>Placebo</td>
<td></td>
<td>-2.7 MHDs for placebo</td>
<td></td>
</tr>
</tbody>
</table>


Adverse events

- Nasopharyngitis
- Nausea
- Constipation
- Injection site reactions

Definitions and explanations

- Incremental cost-effectiveness ratio (ICER)
  - Used to compare costs and outcomes simultaneously between treatments
  - ICER = difference in costs / difference in outcomes

- Willingness-to-pay (WTP)
  - How much is a person willing to pay in order to reduce the likelihood of an adverse outcome?
  - Takes into account indirect aspects of a health condition

Case question

A 32-yo otherwise healthy female states that she is experiencing 6 MMDs. She states that she misses about two social activities a month due to her pain, and she also takes at least one day off work every month.

She currently takes acetaminophen for her migraine pain and is wondering if there is anything else that she can try.

What would you recommend?

a. Continue taking the acetaminophen. She probably is not using it enough.
b. Initiate a low dose of divalproex and titrate to a therapeutic dose for a trial of 12 weeks.
c. Recommend that she talk to a neurologist about trying erenumab.
d. Initiate a low dose of propranolol and titrate to a therapeutic dose for a trial of 12 weeks.

Definitions and explanations

- Incremental cost-effectiveness ratio (ICER)
  - Used to compare costs and outcomes simultaneously between treatments
  - ICER = difference in costs / difference in outcomes

- Willingness-to-pay (WTP)
  - How much is a person willing to pay in order to reduce the likelihood of an adverse outcome?
  - Takes into account indirect aspects of a health condition
Definitions and explanations

- Markov modeling
  - Health states that can result from interventions
  - Possible transitions between the health states
  - Cycle duration and number of cycles
  - Probabilities of transitioning between health states
  - Costs and outcomes for each option

- Monte Carlo simulation
  - Relies on repeated random sampling to simulate patient-level and parameter variability
  - Random patients are sent through the model one at a time and take different paths depending on their characteristics and the probabilities at chance nodes in the model

Cost-effectiveness analysis of erenumab for the preventive treatment of episodic and chronic migraine: results from the US societal and payer perspectives


Study design

- Treatment arms
  - Erenumab
  - No preventive treatment
  - OnabotulinumtoxinA (chronic migraine only)

- Inclusion criteria:
  - Adults > 18 years old
  - Episodic migraine (4-14 baseline MMDs) OR chronic migraine (15+ baseline MMDs)
  - Failed at least one previous preventive therapy

- Patients followed for 2 years
- Two cohorts: episodic migraine and chronic migraine
- Primary outcome: ICER as cost/QALY gained

Model design and methods

- Hybrid Monte Carlo patient simulation and Markov cohort model
- Patients enter model → baseline MMDs assigned from sampled distribution → simulation of receiving one of treatment arms
- Baseline MMDs and treatment effect were used to assign patients to post-treatment MMD category
- Treatment benefit was based on time to response in erenumab clinical trials
- Monthly treatment cycles per clinical trials
- Cost and utilities – literature-based, determined after MMD category assignment

Model flow

No preventive treatment

Simulate baseline MMDs → Calculate patients with EM or CM → Apply costs/utilities after each cycle → Assign probability of death → Continue to next cycle → Maintain baseline MMDs until death

Rascati, KL. Essentials of Pharmacoeconomics. 2nd ed.
1. Simulate baseline MMDs
2. Simulate change in MMDs
3. Calculate patients with EM or CM
4. Apply costs and utilities after each cycle
5. Assign probability of treatment discontinuation or death
6. Continue to next cycle, maintain MMDs from Cycle 1

Calculation of cost
- Direct costs
  - Monthly cost of $575 for erenumab per U.S. list price
  - One physician visit for administration education
  - Daily cost of acute medications
  - Estimation of one acute medical service use per one attack per MMD
- Indirect costs
  - Loss of work productivity (e.g., three hours of lost work per MMD)
  - Full-time and part-time division
  - Did not include adverse event-related costs due to low incidence
    - Nasopharyngitis
    - Sinusitis
    - Constipation
    - Arthralgia
    - Injection-site pain

Incremental Cost-Effective Ratios for the Base Case

Conclusions
- Cost-effectiveness threshold of ICER of $50,000-$150,000 per QALY is met in erenumab use for chronic migraine
- Erenumab use vs. no preventive treatment is predicted to be more clinically effective and less expensive

Limitations
- Lack of long-term clinical data
- MMDs were average estimates from the erenumab trials
Estimating the clinical effectiveness and value-based price range of erenumab for the prevention of migraine in patients with prior treatment failures: a US societal perspective

Study design
- Treatment arms
  - Erenumab
  - No preventive treatment
- Inclusion criteria:
  - Adults > 18 years old
  - Episodic migraine (4-14 baseline MMDs) OR chronic migraine (15+ baseline MMDs)
  - Failed at least one previous preventive therapy
- Patients followed for 10 years
- Episodic and chronic migraine cohorts modeled separately with outcomes combined (33% episodic and 67% chronic)
- Primary outcome: ICER as cost/QALY gained


Model design and methods
- Markov model
- Monthly treatment cycles per clinical trials
- Baseline persistence rates extrapolated from U.S. claims data of onabotulinum toxin A
- Medical resource use costs from literature

Modeling Results

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>Migraine days over 10 years</th>
<th>Mean duration of treatment, if any</th>
<th>Mean discounted costs related to migraine days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erenumab 140 mg monthly</td>
<td>1805</td>
<td>2 years</td>
<td>$121,407</td>
</tr>
<tr>
<td>No preventive treatment</td>
<td>1949</td>
<td>--</td>
<td>$129,889</td>
</tr>
</tbody>
</table>

Conclusions
- Some cost savings and gain in QALY due to erenumab intervention in patients who have failed at least one preventive therapy

Limitations
- Episodic and chronic migraine results combined
- Clinical data is limited
- Lack of long-term data

Calcitonin gene-related peptide (CGRP) inhibitors as preventive treatments for patients with episodic or chronic migraine: effectiveness and value

Study design
- Analysis of incremental cost-effectiveness of erenumab and fremanezumab when compared to no preventive treatment
- Galcanezumab not included due to lack of available data at time of publication
- Treatment arms:
  - CGRP inhibitor treatment
  - No preventive treatment
- Inclusion criteria:
  - Chronic and episodic migraine with failure of 1-3 preventive therapies
- Outcomes:
  - QAL Y
  - Reduction in migraine days
  - Total costs for interventions and comparators

Model design and methods
- Semi-Markov models for chronic and episodic migraine
- Patient baseline characteristics based on the average patient in the United States
- Treatment effect estimates from trial data in patients with 1-3 failed preventive therapies
- Base analyses from a payer perspective
  - Direct medical care costs
  - Monthly cycles over a 2-year duration
- Uncertainty in costs and health outcomes calculated through probabilistic sensitivity analyses

Calculation of cost
- Wholesale acquisition cost of erenumab: $6900/year
- Rounded to $5000 due to industry-wide discounts
- Pricing applied to fremanezumab as well
- Estimates of additional healthcare costs:
  - Daily acute migraine treatment
  - Adverse effects
  - Health care services for migraine treatment

Incremental Cost-Effective Ratios for the Base Case

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY gained</th>
<th>Cost per migraine-free day gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic migraine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab 140 mg</td>
<td>No preventive treatment</td>
<td>$110,000</td>
<td>$160</td>
</tr>
<tr>
<td>Fremanezumab 625/225 mg monthly</td>
<td>No preventive treatment</td>
<td>$120,000</td>
<td>$140</td>
</tr>
<tr>
<td>Episodic migraine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab 140 mg</td>
<td>No preventive treatment</td>
<td>$130,000</td>
<td>$160</td>
</tr>
<tr>
<td>Fremanezumab 225 mg monthly</td>
<td>No preventive treatment</td>
<td>$150,000</td>
<td>$150</td>
</tr>
</tbody>
</table>

Sensitivity Analyses

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ICER</th>
<th>Percentage of simulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab 140 mg</td>
<td>&lt;$100,000/QALY</td>
<td>67%</td>
</tr>
<tr>
<td>Fremanezumab 625/225 mg monthly</td>
<td>&lt;$150,000/QALY</td>
<td>79%</td>
</tr>
<tr>
<td>Episodic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab 140 mg</td>
<td>&lt;$100,000/QALY</td>
<td>&lt;3%</td>
</tr>
<tr>
<td>Fremanezumab 225 mg monthly</td>
<td>&lt;$150,000/QALY</td>
<td>44%</td>
</tr>
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</table>
Modified societal perspective

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QAL Y gained*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erenumab 140 mg monthly</td>
<td>No preventive treatment</td>
<td>$50,000</td>
</tr>
<tr>
<td>Fremanezumab 625/225 mg monthly</td>
<td>No preventive treatment</td>
<td>$80,000</td>
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<tr>
<td>Episodic migraine</td>
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<td></td>
</tr>
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<tr>
<td>Fremanezumab 225 mg monthly</td>
<td>No preventive treatment</td>
<td>$110,000</td>
</tr>
</tbody>
</table>

Conclusions

- Compared to not being on preventive treatment, CGRP inhibitors may be beneficial for patients with either chronic or episodic migraine pain who have previously failed 1-3 preventive therapies.
- Cost per QALY is more favorable in chronic migraine treatment.
- Erenumab and fremanezumab were below a $150,000 per QALY threshold for chronic migraine.
- When a modified societal perspective was used, incremental cost per QALY for erenumab was $50,000 and for fremanezumab was $80,000 in chronic migraine.

Limitations

- Models are based on data from clinical trials.
- Longer treatment duration has not been studied.
- Market price may fluctuate.

Future studies?

- More long-term studies in safety.
- More long-term studies in effectiveness over several years.
- Cost-effectiveness in chronic migraine with failed trials of preventive therapies.
- Second generation of CGRPs.
- New abortive class of acute medications.

Pharmacist role

- Manufacturers’ coupons.
- Patient education on evidence-based treatment and non-pharmacological treatment.
- Criteria for use – how strict should this be?
- Wide variability in patient characteristics and patient response.

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## Resources