Calcitonin Gene-Related Peptide (CGRP) Inhibitors as Preventive Treatments for Patients with Episodic or Chronic Migraine: Effectiveness and Value

Public Meeting – June 14, 2018

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Welcome and Introduction

- **Why are we here today?**
  - Innovation promising substantial benefits to patients and their families

- *You lose your sense of who you are, how to speak, how to think, how to move. You become a shell of your former self. The light hurts, that woman's perfume on the subway makes you sick, the sound of a baby's cry sends you into paralysis.*

  -- Patient comment on ICER draft report

- *I'm terrified of the day when I won't be able to work, as I have to spend so much money on medications and doctor appointments just to get out of bed, that there is no way a social security/disability income would support me let alone my family.*

  -- Patient comment on ICER draft report

Welcome and Introduction

- **Why are we here today?**
  - New mechanisms of action often raise questions about appropriate use, cost
    - *"An estimated 3.5 million patients have already tried a migraine preventative therapy and approximately 80% stop that therapy within a year, according to Amgen's calculations."*

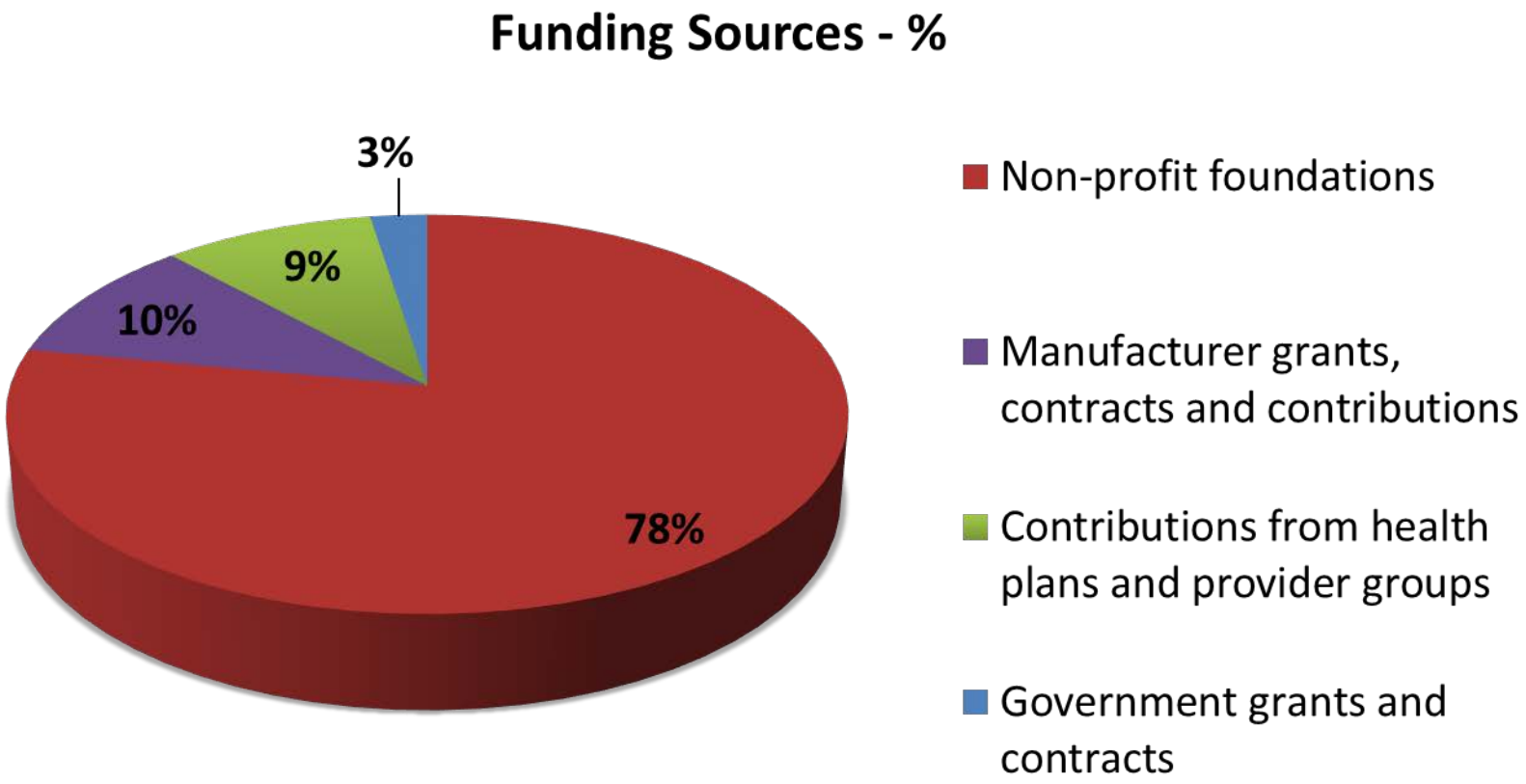
      -- Xconomy.com 6-1-18
  - Patients can have difficulty accessing new drugs
  - Need for objective evaluation and public discussion of the evidence on effectiveness and value

Welcome and Introduction

- California Technology Assessment Forum (CTAF)

- The Institute for Clinical and Economic Review (ICER)

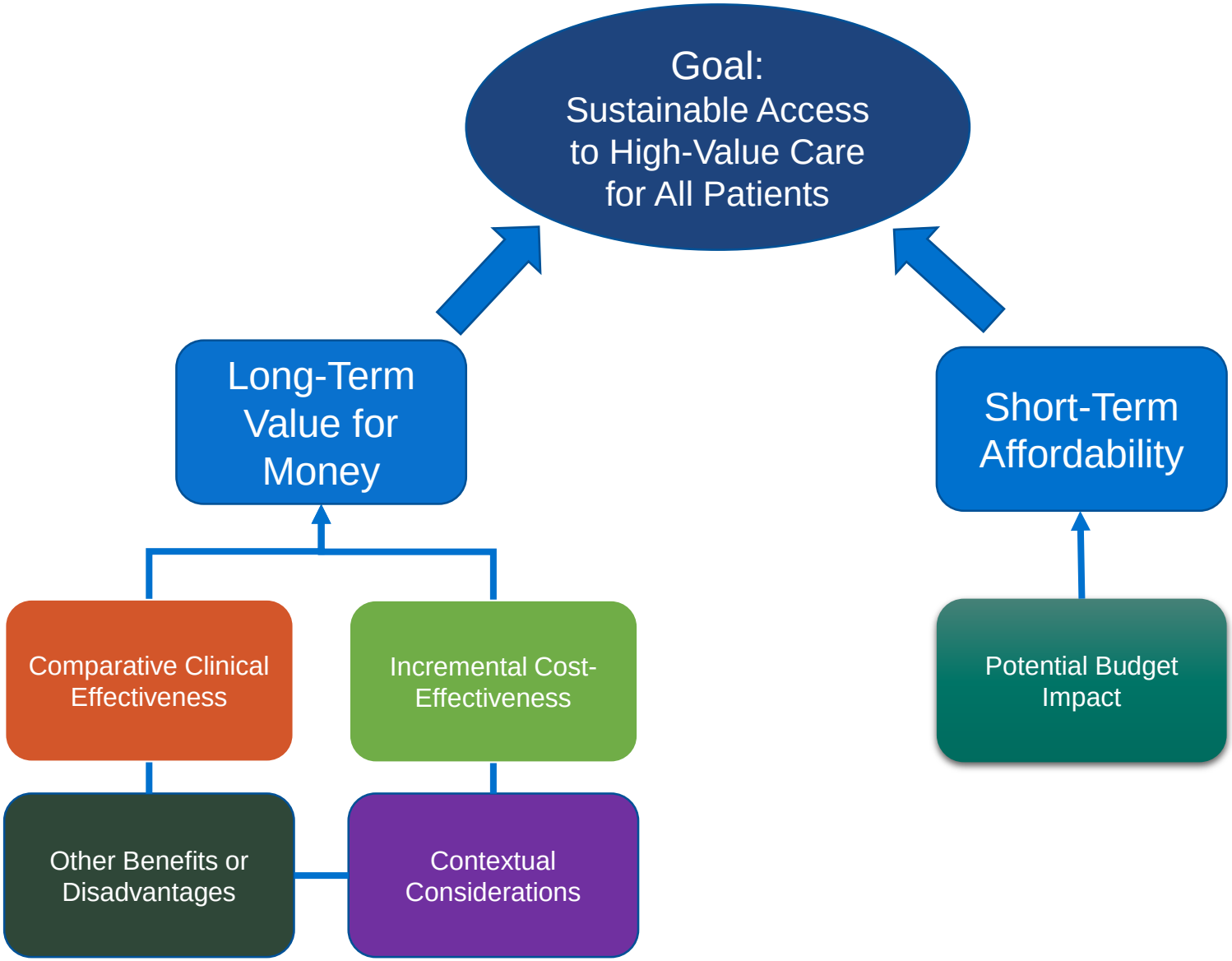
Sources of Funding, 2018



Welcome and Introduction

How was the ICER report on CGRP inhibitors for migraine developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- “Academic in confidence” data submitted by manufacturers
- Internal ICER staff evidence analysis
- University of Illinois, Chicago cost-effectiveness modeling
- Public comment and revision
- Expert report reviewers
  - Andrew Hershey, MD, PhD, FAHS (Cincinnati Children’s Hospital, AAN)
  - Annette Langer-Gould, MD, PhD (Kaiser Permanente)
  - Sonja Potrebic, MD, PhD (Kaiser Permanente)
  - Meghan Buzby, MBA (American Migraine Foundation)
- How is the evidence report structured to support CTAF voting and policy discussion?


Goal:
Sustainable Access to High-Value Care for All Patients
Long-Term Value for Money
Short-Term Affordability
Comparative Clinical Effectiveness
Incremental Cost-Effectiveness
Potential Budget Impact
Other Benefits or Disadvantages
Contextual Considerations

Agenda

10:00am: Welcome and Opening Remarks

10:15 am: Presentation of the Evidence

Evidence Review: Alexandra G. Ellis, PhD
Cost Effectiveness: Surrey Walton, PhD

11:15 am: Manufacturer Public Comment and Discussion

11:45 pm: Public Comments and Discussion

12:15 pm: Lunch

1:00 pm: CTAF Deliberation and Votes

2:15 pm: Break

2:25 pm: Policy Roundtable

3:40 pm: Reflections and Wrap Up

4:00 pm: Meeting Adjourned

Evidence Review

Alexandra G. Ellis, PhD

Senior Scientist, HTA and Economic Evaluation

ICER

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AND ECONOMIC REVIEW

Key Review Team Members

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Katherine Fazioli, BS

Disclosures:

We have no conflicts of interest relevant to this report.

Migraine

- Recurrent headache disorder affecting 20% of women and 6-10% of men in the US
- Associated with moderate-to-severe pain and other symptoms (e.g., nausea, vomiting, or sensitivity to light or to sound)
- Headaches among the top 5 reasons for emergency department (ED) visits

Diagnosis

- Chronic migraine
  - 15 or more headache days per month
  - 8 or more days with migraine features
  - Approximately 10% of patients with migraine
- “Episodic” migraine
  - Migraine not classified as chronic migraine
  - Not a clinical diagnosis
  - Approximately 90% of patients with migraine

Living With Migraine: Insights from Patients

- Feel frustrated, depressed, defeated, isolated, or a burden to society
  - Some patients experience suicidal thoughts
- Strained relationships with family, friends, and coworkers
  - Do not plan due to uncertainty when the next attack will occur
  - Feel stigmatized and that migraine pain is not taken seriously

Treatments for Migraine

- Non-pharmacologic
  - Diet, exercise, cognitive behavioral therapy, neuromodulator devices
- Pharmacologic
  - Acute (NSAIDs, triptans, Excedrin, opioids*)
  - Preventive

* Not recommended for first-line acute treatment

Preventive Treatments for Migraine

- Migraine (episodic or chronic)
  - Antidepressants (e.g., amitriptyline)
  - Anti-seizure medications (e.g., topiramate)
  - Beta-blockers (e.g., propranolol)
- Chronic migraine
  - Onabotulinum toxin A (Botox®, Allergan)

Preventive Therapy

- No strict guidelines on who is eligible
- Adequate therapeutic trial takes 2-6 months
- Patients frequently discontinue or switch therapies due to lack of efficacy or tolerability
  - Difficulty concentrating, remembering, or speaking clearly
  - Weight gain or loss

Treatments For Migraine: Insights from Patients

- “Guess and test” strategies can take many years before finding an effective treatment
- Some treatments work for a time, but stop working or are not tolerable
- Side-effects from some interventions can be as debilitating as migraine

CGRP Inhibitors

- Calcitonin gene-related peptide (CGRP)
- CGRP inhibitors for preventive therapy for patients with chronic or episodic migraine
  - Erenumab (Aimovig™, Amgen/Novartis)
    - FDA approved in May 2018
  - Fremanezumab (Teva)
  - Galcanezumab (Eli Lilly)

Scope of the Review

- **Population:** Adults with chronic or episodic migraine eligible for preventive treatment
  - Patients for whom preventive therapy has failed
- **Interventions:** Erenumab, fremanezumab, galcanezumab
- **Comparators:**
  - Oral preventives (amitriptyline, propranolol, topiramate)
  - Onabotulinum toxin A (chronic migraine only)
  - Placebo (i.e., no active preventive therapy)

Scope of the Review

- Efficacy
  - Monthly migraine days
  - ≥ 50% reduction in monthly migraine days
  - Days using acute medication per month
  - Quality of life
- Tolerability and harms
  - All-cause withdrawal
  - Withdrawal due to adverse events (AEs)
  - Serious AEs (SAEs)
  - Commonly reported AEs

Chronic Migraine: Evidence base

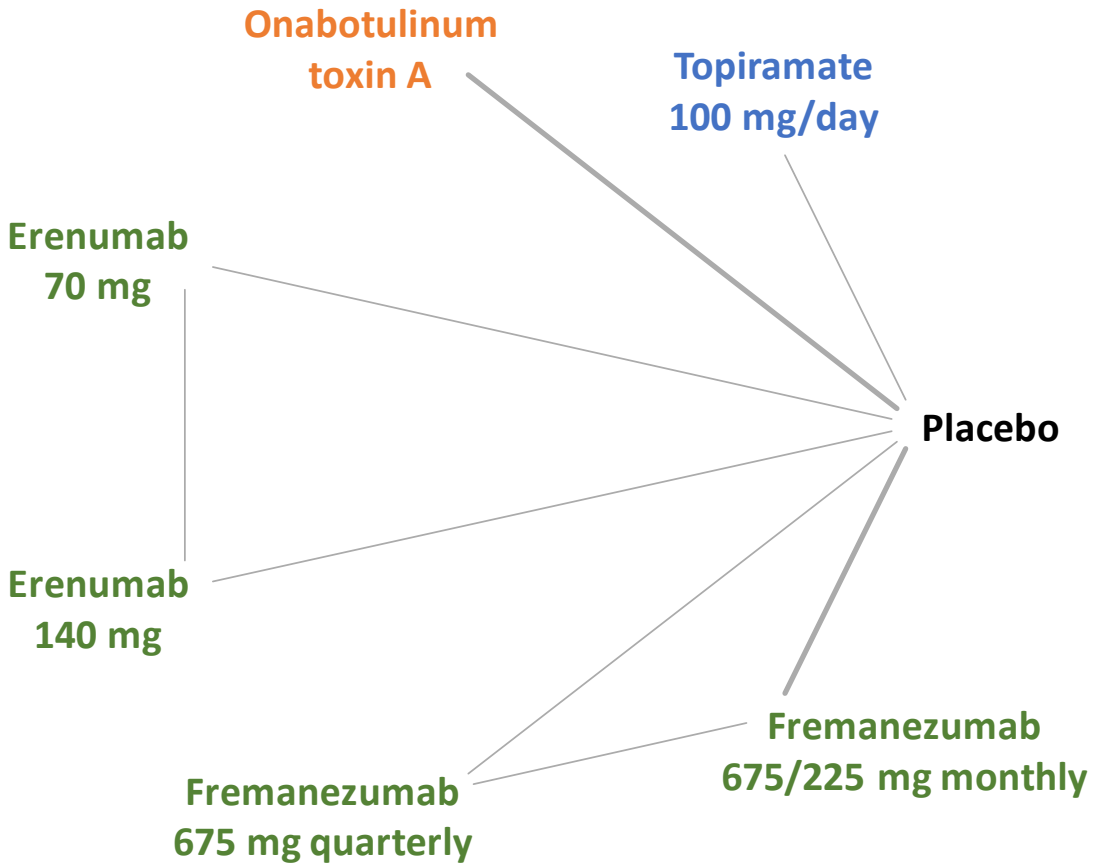
- 3 trials of CGRP inhibitors
- 13 trials of onabotulinum toxin A or topiramate
  - 11 trials included in efficacy analyses
- No trials of amitriptyline or propranolol

Chronic Migraine: CGRP Inhibitor Trials

Study / Phase	Arm	N	Mean Age (Years)	% Add-On Preventive Therapy	Mean Migraine Days per Month
Tepper 2017 Phase II	Erenumab 70 mg	191	41.4	0	17.9
	Erenumab 140 mg	190	42.9	0	17.8
	Placebo	286	42.1	0	18.2
Bigal 2015a Phase II	Fremanezumab 675/225 mg	88	40.0	40	17.2
	Placebo	89	40.7	43	16.8
Silberstein 2017 HALO-CM Phase III	Fremanezumab 675 mg quarterly	376	42.0	20	16.2
	Fremanezumab 675/225 mg	379	40.6	22	16.0
	Placebo	375	41.4	21	16.4

All trials included a 4-week baseline period, followed by a 12-week randomized phase

Chronic Migraine: Monthly Migraine Days



Chronic Migraine: Monthly Migraine Days

	Difference in Change From Baseline vs. Placebo (95% CrI)	Expected Change From Baseline (95% CrI)
Placebo	Reference	-4.0 (NA)
Erenumab 70 mg	**-2.4 (-4.8, 0.0)**	**-6.4 (-8.8, -4.0)**
Erenumab 140 mg	**-2.4 (-4.8, 0.0)**	**-6.4 (-8.8, -4.0)**
Fremanezumab 675 mg quarterly	-1.3 (-3.5, 0.9)	-5.3 (-7.5, -3.1)
Fremanezumab 675/225 mg	-1.7 (-3.5, 0.1)	-5.7 (-7.5, -3.9)
Onabotulinum toxin A 155U	**-2.0 (-3.6, -0.3)**	**-6.0 (-7.6, -4.3)**
Topiramate 100 mg/day	-1.7 (-4.2, 0.8)	-5.7 (-8.2, -3.2)

CrI: credible interval, NA: not applicable, bold text: statistically significant

Data on subgroup results among patients from whom preventive therapies have failed submitted in confidence

Chronic Migraine: Other Efficacy Outcomes

- Differences in definitions of 50% responders prohibited quantitative synthesis
- Approximately 2 fewer days using acute medications with CGRP inhibitors vs placebo
- Quality of life measures infrequently and inconsistently assessed
  - Where reported, larger improvements with active therapies than placebo

Episodic Migraine: Evidence Base

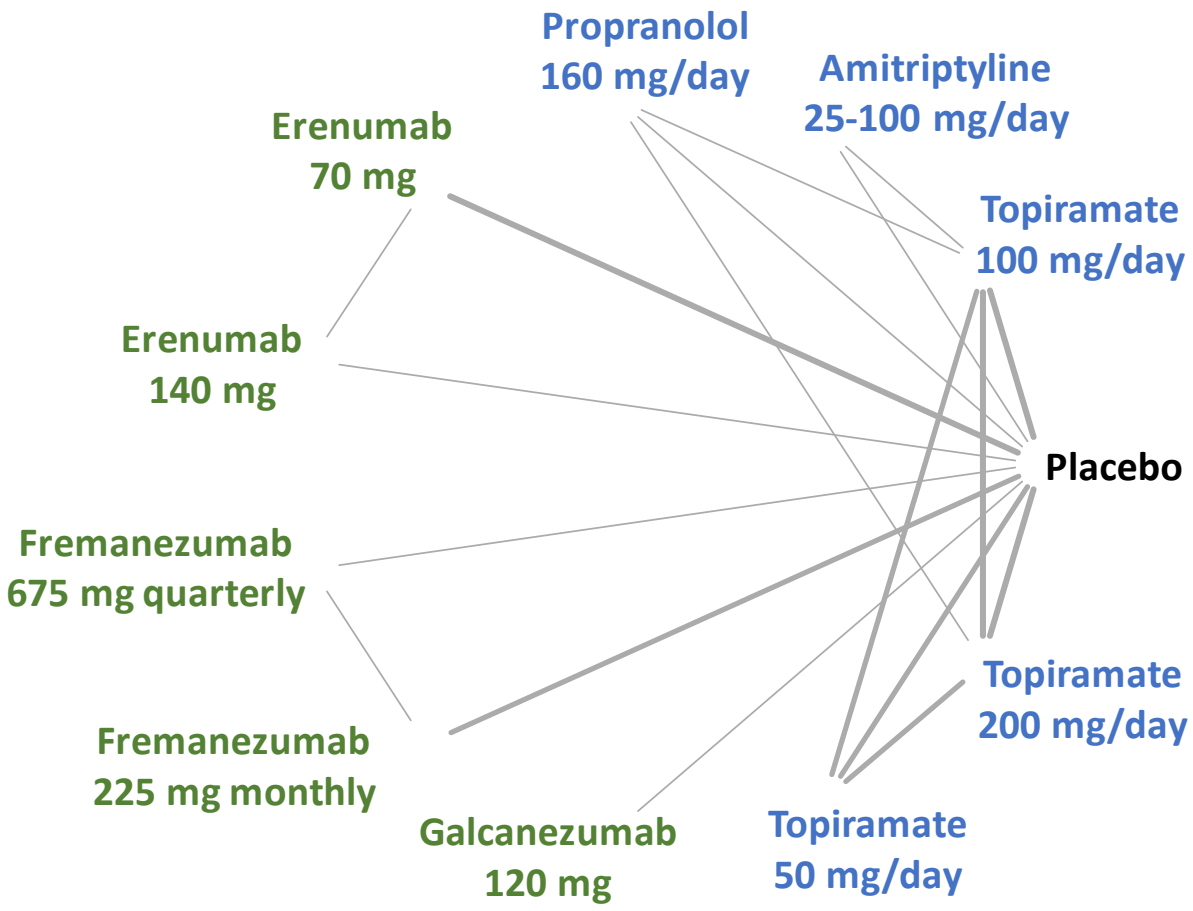
- 8 trials of CGRP inhibitors (1 open-label extension)
  - 6 trials of CGRP inhibitors included in efficacy analyses
  - 2 newly-published trials of galcanezumab
- 24 trials of oral preventive therapies
  - 16 trials included in efficacy analyses

Episodic Migraine: CGRP Inhibitor Trials

Study/ Phase	Arm	N	Mean Age (Years)	% Add-On Preventive Therapy	Mean Migraine Days per Month
Sun 2016 Phase II*	Erenumab 70 mg	107	42.6	0	8.6
	Placebo	160	41.4	0	8.8
Goadsby 2017 STRIVE Phase III	Erenumab 70 mg	317	41.1	2.8	8.3
	Erenumab 140 mg	319	40.4	2.5	8.3
	Placebo	319	41.3	3.1	8.2
Dodick 2018 ARISE Phase III	Erenumab 70 mg	286	42.0	6.6	8.1
	Placebo	291	42.0	5.5	8.4
Bigal 2015b Phase II	Fremanezumab 225 mg	96	40.8	34.0	11.5
	Placebo	104	42.0	27.0	11.5
Dodick 2018 HALO-EM Phase III	Fremanezumab 225 mg	290	42.9	21.4	8.9
	Fremanezumab 675 mg quarterly	291	41.1	19.9	9.3
	Placebo	294	41.3	21.1	9.1
Skljarevski 2018a Phase II	Galcanezumab (all doses)	273	40.6	0	8.4
	Placebo	137	39.5	0	8.0
Stauffer 2018 EVOLVE 1 Phase III*	Galcanezumab 120 mg	213	40.9	0	9.2
	Galcanezumab 240 mg	212	39.1	0	9.1
	Placebo	433	41.3	0	9.1
Skljarevski 2018b EVOLVE 2 Phase III*	Galcanezumab 120 mg	231	40.9	0	9.1
	Galcanezumab 240 mg	223	41.9	0	9.1
	Placebo	461	42.3	0	9.2

*24-week randomized phase; all other trials were 12 weeks

Episodic Migraine: Monthly Migraine Days



Episodic Migraine: Monthly Migraine Days

	Difference in Change From Baseline vs. Placebo (95% CrI)	Expected Change From Baseline (95% CrI)
Placebo	Reference	-2.7 (NA)
Erenumab 70 mg	**-1.3 (-1.9, -0.7)**	**-4.0 (-4.6, -3.4)**
Erenumab 140 mg	**-1.9 (-2.9, -1.0)**	**-4.6 (-5.6, -3.7)**
Fremanezumab 675 mg quarterly	**-1.2 (-2.3, -0.1)**	**-3.9 (-5.0, -2.8)**
Fremanezumab 225 mg	**-1.6 (-2.6, -0.7)**	**-4.3 (-5.3, -3.4)**
Galcanezumab 120 mg*	**-1.9 (-3.2, -0.6)**	**-4.6 (-5.9, -3.3)**
Topiramate 50 mg/day	-0.2 (-1.1, 0.7)	-2.9 (-3.8, -2.0)
Topiramate 100 mg/day	**-1.2 (-1.7, -0.6)**	**-3.9 (-4.4, -3.3)**
Topiramate 200 mg/day	**-1.0 (-1.6, -0.4)**	**-3.7 (-4.3, -3.1)**
Amitriptyline 25-100 mg/day	-1.1 (-2.4, 0.2)	-3.8 (-5.1, -2.5)
Propranolol 160 mg/day	**-1.2 (-2.2, -0.3)**	**-3.9 (-4.9, -3.0)**

CrI: credible interval, NA: not applicable, bold text: statistically significant
*Results from EVOLVE 1 & 2 are similar in magnitude

Data on subgroup results among patients from whom preventive therapies have failed submitted in confidence

Episodic Migraine: Other Efficacy Outcomes

- Odds for 50% reduction in migraine days per month approximately 2 times higher with CGRP inhibitors than placebo
- Approximately 1 fewer day using acute medications with CGRP inhibitors vs placebo
- Quality of life measures infrequently and inconsistently assessed
  - Where reported, greater improvements with active therapies than placebo

Tolerability and Harms

- CGRP inhibitors well-tolerated with non-serious and uncommon harms
- No differences in the meta-analyzed odds of discontinuations or SAEs with the CGRP inhibitors versus other preventive therapies
- Most commonly reported AEs with CGRP inhibitors involved injection-site reactions
- Fatigue, memory-loss, difficulty concentrating, and paresthesia commonly reported in oral preventive therapies but not CGRP inhibitors

Controversies and Uncertainties

- **Short-term trials:** Uncertainty in any durability of effects from prolonged use
- **First in CGRP inhibitor class:** Concerns about the long-term effects of continuous blocking of CGRP or its receptor
- **Results may not generalize:** Patients likely to be treated with CGRP inhibitors include those who tried more than three prior treatments and those with comorbidities

Summary

- Preventive treatment with CGRP inhibitors provide some clinical benefit
- Few harms observed
- The short-term trials limit certainty about the safety of these agents with a novel mechanism of action
- Longer-term studies ongoing

ICER Evidence Ratings

- Chronic migraine and eligible to receive preventive therapy with oral agents or onabotulinum toxin A
  - **Insufficient (“I”)** for erenumab and fremanezumab
- Chronic migraine for whom prior preventive therapy has failed
  - **Comparable or better (“C+”)** for erenumab and fremanezumab
- Episodic migraine and eligible to receive preventive therapy with oral agents
  - **Insufficient (“I”)** for erenumab and fremanezumab
- Episodic migraine for whom oral preventive therapies have failed
  - **Promising but inconclusive (“P/I”)** for erenumab and fremanezumab
- **Insufficient (“I”)** for galcanezumab for all populations and comparisons
- **Insufficient (“I”)** for erenumab versus fremanezumab for all populations

Other Benefits and Contextual Considerations

- Monthly (or quarterly) administration may reduce burden of migraine, but subcutaneous injection may add complexity
- If tolerable and effective:
  - Less likely to discontinue treatment
  - Increase ability to work and improve overall productivity
- Novel mechanism of action

Public Comments

- The review should evaluate CGRP inhibitors only in their likely treatment paradigm (i.e., among patients for whom preventive therapies have failed)
  - The wider migraine population and this subgroup were of interest to many stakeholders including clinicians and patients
- Phase II and Phase III studies should not be assessed together
  - Included if similar studies/populations
  - Due to smaller sample sizes or larger variances, Phase II trials have less weight in the analyses
- Galcanezumab should not be included in review
  - Stakeholders beginning to make decisions about erenumab and other CGRP inhibitors
  - Due to limited data, included in clinical review not economic assessment

Cost Effectiveness

Surrey Walton, PhD

Todd Lee, PharmD, PhD

University of Illinois at Chicago College of Pharmacy

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Key Review Team Members

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Varun Kumar, MBBS, MPH, MSc (ICER)

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Disclosures:

We have no conflicts of interest relevant to this report.

Objective

- To estimate the cost-effectiveness of erenumab and fremanezumab compared to no preventive treatment for patients with chronic and episodic migraines for whom other preventive migraine medications had failed.

Methods in Brief

Methods Overview

- **Model Type**: Semi-Markov models with time-dependent efficacy and mortality rates.
- **Setting:** United States (US)
- **Perspective:** Health sector perspective
- **Time Horizon**: 2 years
- **Discount Rate:** 3% per year (costs and outcomes)
- **Cycle Length**: 1 month
- **Outcomes by Intervention:** Costs, quality-adjusted life years (QALYs), migraine days reduced
- **Primary Outcome:** Cost per QALY Gained

Patient Population

- US patients seeking care for migraine

Patient Baseline Characteristics	Chronic Migraine	Episodic Migraine
Mean Age	39 Years	40 Years
Proportion Female	80.5%	76.4%
Mean Migraine Days per Month	17.7	8.0

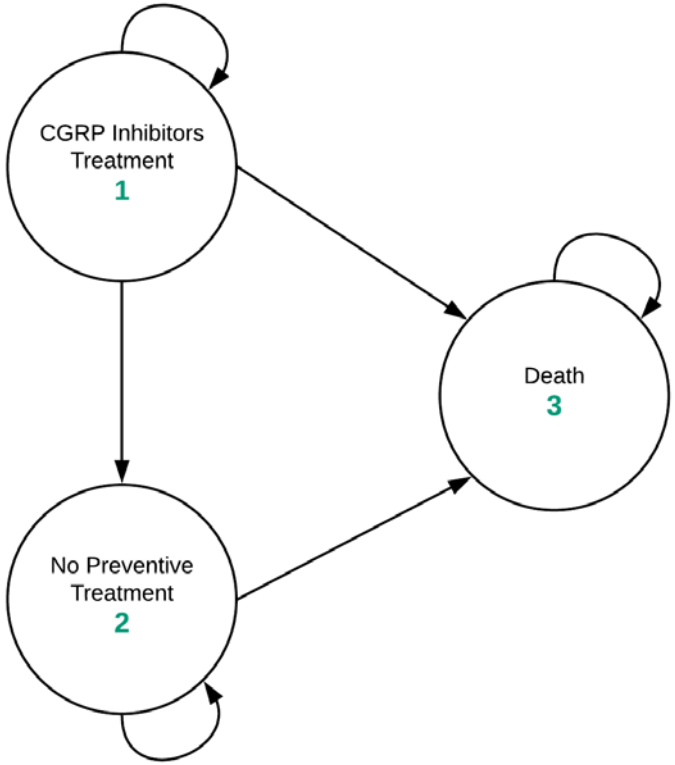
Parameters: Drug Regimens

	Dosage	Schedule	Route
Erenumab (Chronic and Episodic)	140 mg	1 injection per month	Subcutaneous
Fremanezumab (Chronic and Episodic)	225 mg*	1 injection per month	Subcutaneous

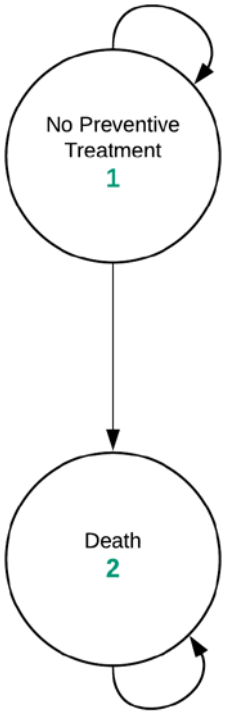
* 675 mg dose for first month in fremanezumab chronic migraine patients

Model Overview

Treatment Model

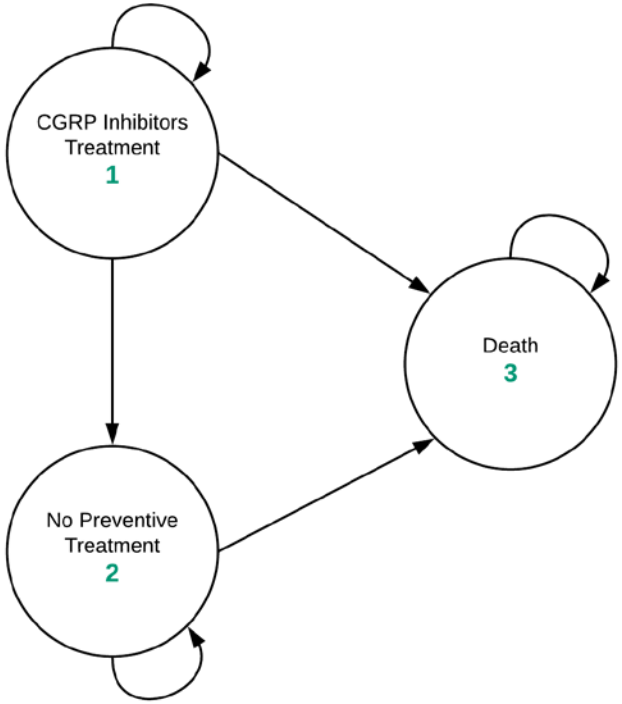


Placebo Model



Model Transitions

- Discontinuation from “CGRP Inhibitor Treatment” to “No Preventive Treatment” was based the ICER NMA.
- Mortality was based on age- and gender-adjusted mortality estimates for the general population (CDC/NCHS National Vital Statistics System).



Key Assumptions

- CGRP inhibitors have no direct effect on mortality, outcomes, or cost of treating underlying conditions other than migraines.
- Effect of migraine days on utilities based on disutility weights for mild, moderate, and severe migraine days from the literature.
- Changes in the distribution of mild, moderate, and severe migraine days were modeled based on available evidence for fremanezumab that was also applied to erenumab.
- Reduction in migraine days resulted in proportional reductions in other forms of heath care utilization for migraine such as number of hospitalizations, ED visits, PCP visits.
- AEs were assumed to result in a cost associated with a primary care physician office visit and an assumed disutility of 0.05.
- Costs of CGRPs were based on erenumab's initial launch price discounted by 27% and rounded.

Key Model Inputs: Clinical Inputs

Treatment	Chronic Migraine: Monthly Discontinuation Rate (95% CI)	Episodic Migraine: Monthly Discontinuation Rate (95% CI)
Erenumab 140 mg monthly	0.031 (0.010, 0.084)	0.041 (0.017, 0.090)
Fremanezumab 675/225 mg monthly	0.062 (0.034, 0.114)	0.084 (0.044, 0.160)

Monthly migraine day reduction data from the trials have been redacted here, but included in the model since they were submitted to us as academic-in-confidence data

Key Model Inputs: Drug Costs

Drug	Annual WAC	Annual Net Drug Costs
Erenumab 140 mg	$6,900	$5,000
Fremanezumab 675*/225 mg	NA	$5,000

NA: not available
*675 mg fremanezumab dose is given for first month in chronic patients only. Same estimated costs.
Also an administration fee of $74 per monthly injection is added to the estimated drug costs in the first month.

Key Model Inputs: Acute Drug Use Days and Costs

Migraine Type	Baseline Acute Drug Use Days per Month	Acute Drug Cost per Day
Chronic	7.62	$24
Episodic	2.97	$21

Drug	Acute Medication Use Days Reduction per Month (Chronic Migraines)	Acute Medication Use Days Reduction per Month (Episodic Migraines)
Erenumab 140 mg	2.67	1.76
Fremanezumab 675/225mg	2.33	1.31

Key Model Inputs: Healthcare Utilization Costs per Month at Baseline

Direct Costs Type	Chronic Migraines	Episodic Migraines
ED Visits*	$16	$6
Hospitalizations**	$1	$1
PCP/Nurse Practitioner/ Specialist Visits	$93	$30
Other Direct Costs	$31	$10

* The cost of one ED visit was $949 and the rates were 1.7% per month for chronic and 0.7% for episodic. (costs: Insinga 2011, rates: Mesalli 2016)
** The cost of one hospitalization was $8,996 and the rate was 0.00009% per month. (costs: Insinga 2011, rates: Lucado 2006). Rest are Mesalli 2016.

Key Model Inputs: Adverse Events Monthly Rates and Costs

Drug	Monthly Rate (Chronic)	Monthly Cost (Chronic)
Erenumab 140 mg	0.027	$2
Fremanezumab 675/225mg	0.117	$9

Drug	Monthly Rate (Episodic)	Monthly Cost (Episodic)
Erenumab 140 mg	0.056	$4
Fremanezumab 675/225mg	0.066	$5

NMA for rates. Assigned physician office visit cost ($73.93).

Key Model Inputs: Utilities

Model Inputs	Base-Case Value	Distribution Within Migraine Days**	References
Severe Migraine Day	0.440	51.9%	Xu 2011 Lipton 2007
Moderate Migraine Day	0.773	41.0%	Xu 2011 Lipton 2007
Mild Migraine Day	0.835	7.1%	Xu 2011 Lipton 2007
No Migraine Day*	0.959	For all non-migraine days	Xu 2011

*Utility associated on days that patient did not experience a migraine
**Based on patients with 4-14 Migraines days per month
In addition, adverse events resulted in a assigned disutility of 0.05

Results

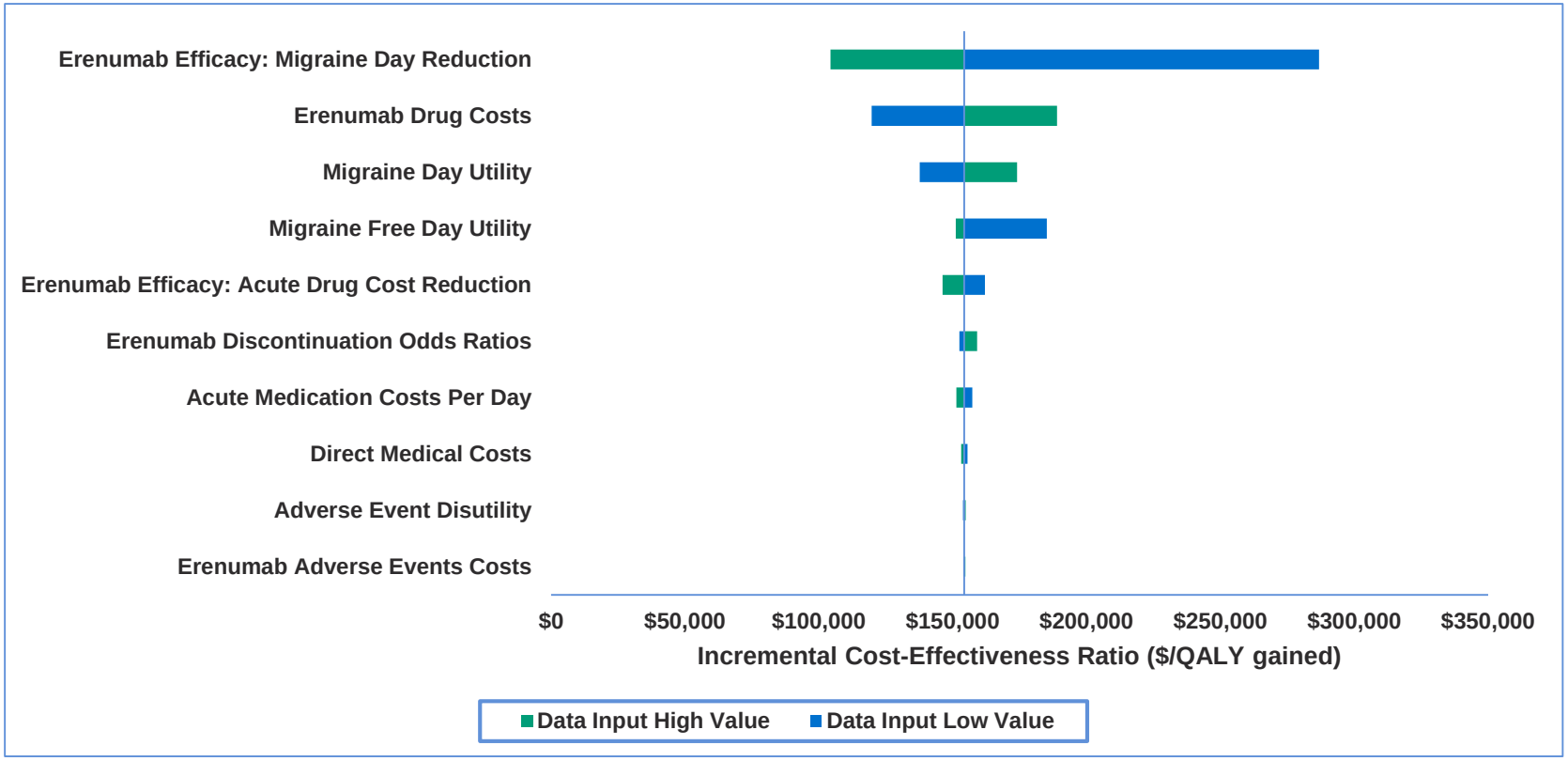
Model Results: Incremental Cost per QALY

Regimen	Incremental Cost-Effectiveness Ratios (Chronic)	Incremental Cost-Effectiveness Ratios (Episodic)
Erenumab	**$90,000**	**$150,000**
Fremanezumab	**$120,000**	**$150,000**

Costs and QALYs are discounted at 3% per annum
Results are rounded to the nearest $10,000, as confidential data were used in their generation

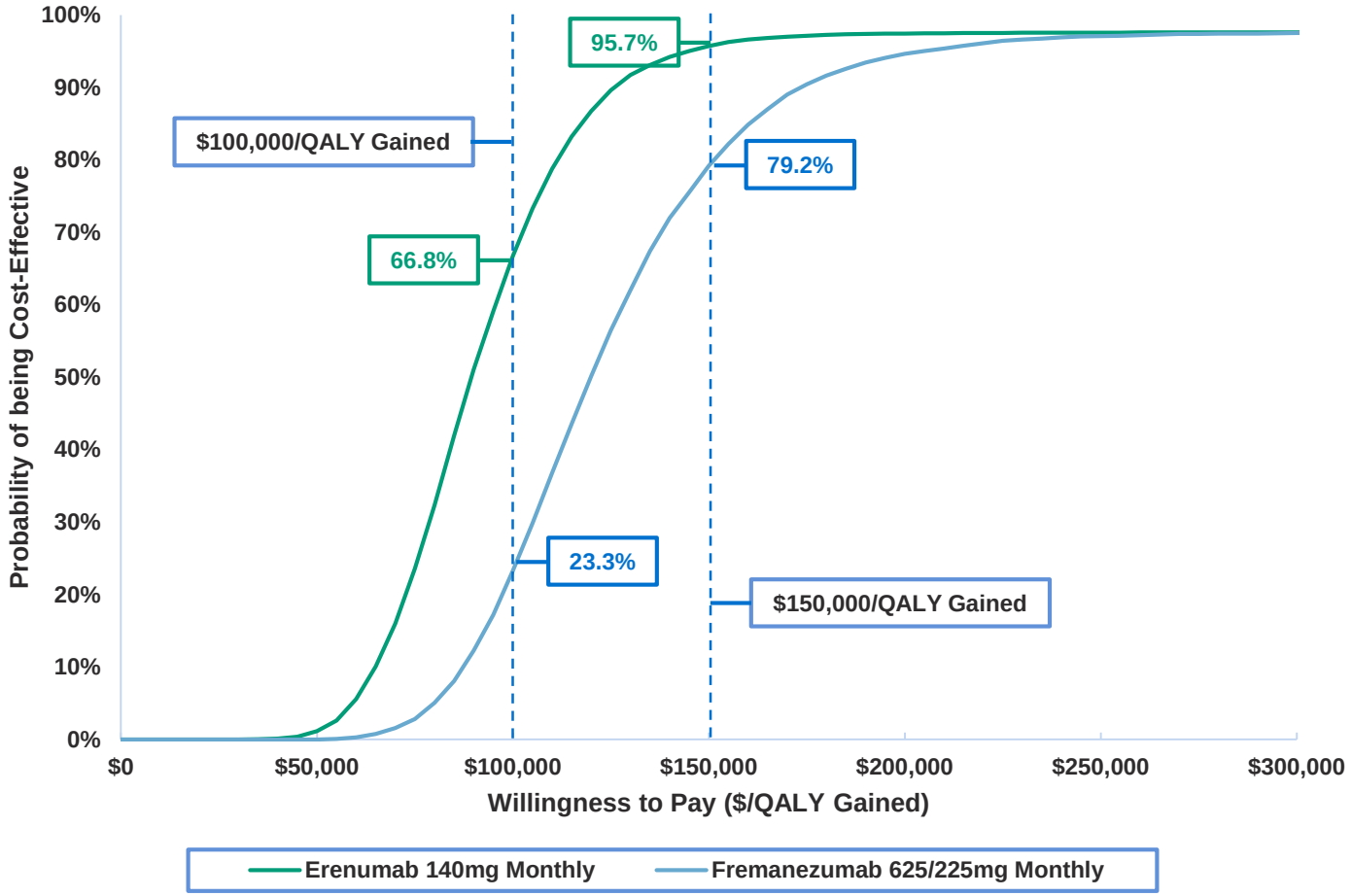
One-Way Sensitivity Analyses

Erenumab vs. No Preventive Treatment (Episodic)

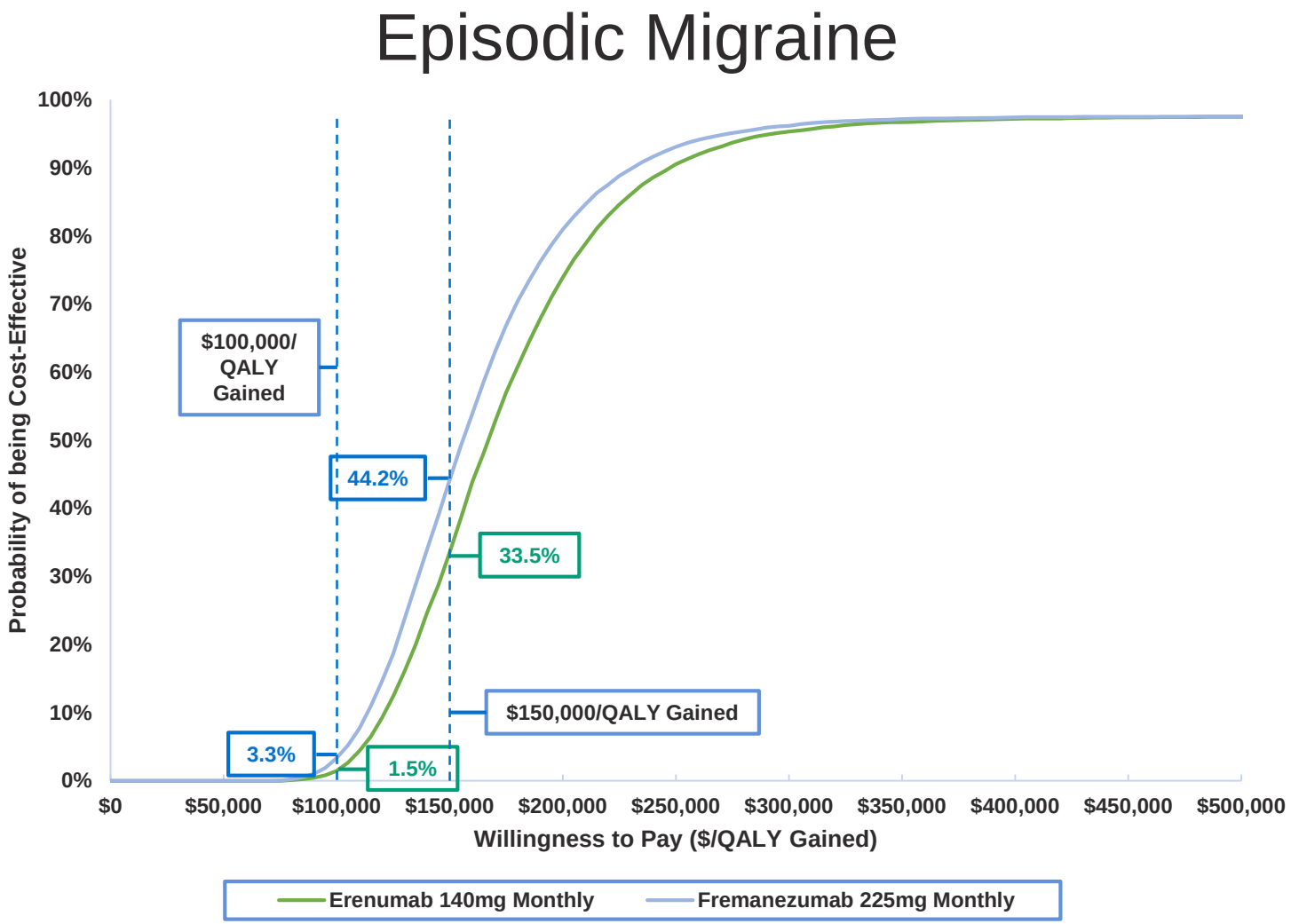


Probabilistic Sensitivity Analyses

Chronic Migraine



Probabilistic Sensitivity Analyses



Scenario Analyses

Chronic

Scenario Analysis	Erenumab 140 mg	Fremanezumab 625/225 mg
Vs. Current Preventive Treatments	$345,000/QALY	$12,780,000/QALY
Modified Societal Perspective	$50,000/QALY	$80,000/QALY

Episodic

Scenario Analysis	Erenumab 140 mg	Fremanezumab 225 mg
Vs. Current Preventive Treatments	$410,000/QALY	$1,040,000/QALY
Modified Societal Perspective	$110,000/QALY	$110,000/QALY

Limitations

- The models are inherently based on clinical trial data over relatively short time periods that may not reflect longer time horizons or real world use.

- The model applies to an average patient with chronic or episodic migraine for whom other preventive treatment has failed, but may not reflect particular sub-populations.

Comments Received

- A societal perspective should be employed, as CGRPs will have productivity effects
- CGRPs will help with depression as well as migraine
- CGRPs will reduce issues with opioid addiction
- Non-responders will discontinue leaving only responders such that long-run cost effectiveness of CGRPs will improve over time
- CGRPs may impact schooling achievement and impact future employment status (including job promotions)

Summary

- Erenumab and fremanezumab are projected to reduce migraine days and improve patient health.
- At currently expected discounted prices erenumab and fremanezumab are projected to have incremental cost effectiveness ratios between $90,000 and $150,000 for patients with chronic migraine for whom other preventive therapy has failed.
- CGRPs are projected to have cost effectiveness ratios around but likely above $150,000 when used in patients for whom prior preventive therapy has failed.
- Including productivity effects for CGRPs results in more favorable incremental cost effectiveness ratios.
- CGRPs compared to currently available therapies are projected to have incremental cost effectiveness ratios greatly exceeding commonly-cited thresholds.

Manufacturer Public Comment and Discussion

Speakers

Name	Title	Company
Sandhya Sapra, PhD	Director, Global Health Economics, Global Product Lead, Erenumab	Amgen
Joshua Cohen, MD, MPH, FAHS	Therapeutic Area Lead, Migraine and Headache, Global Medical Affairs	Teva
Eric Pearlman, MD, PhD	Medical Fellow, Medical Lead - Migraine	Eli Lilly
Jonathan W. Kowalski, PharmD, MS	Vice President, US Health Outcomes and Value	Allergan

Public Comment and Discussion

Katie Golden

Professional Patient, Advocate, and Writer

Conflicts of interest:

- Other relationship that could be reasonably be considered a financial conflict of interest.

Katie has participated in events run by Amgen and Teva, but received less than $5,000 in honoraria payments in aggregate.

Katie also serves as:

- *Steering committee member, Coalition for Headache and Migraine Patients (CHAMP)*
- *Migraine Advocacy Liaison, US Pain Foundation*
- *Staff writer, migraine.com*
- *Senior contributing writer, Invisible Project Magazine*
- *Member of adult headache prevention treatment guideline committee, AAN/AHS*

Mary Franklin
National Headache Foundation
Executive Director

Conflicts of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies

The National Headache Foundation receives over 25% of its funding from life sciences companies, including:

- *Allergan*
- *Allergan Foundation*
- *Amgen*
- *DepoMed*
- *Diamond Headache Clinic, Chicago*
- *Eli Lilly*
- *Novartis*
- *Presence Saint Joseph Hospital, Chicago*
- *Promius*
- *Supernus*
- *Ter Sera Therapeutics*
- *Teva*

Lynn Kaufman
Attorney

Conflicts of interest:

- None declared

Shirley Kessel
Miles for Migraine
Executive Director

Conflicts of interest:

- Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000

Miles for Migraine receives sponsorship for programs from the organizations below. Less than 30% of Shirley's compensation comes from these funds.

- *Companies that sponsor MFM salaries*
  - *Allergan Foundation*
  - *Depomed*
  - *eNeura*
- *Companies that support MFM programs*
  - *Alder Biopharmaceuticals*
  - *Amgen*
  - *Eli Lilly*
  - *Novartis*
  - *Teva*
  - *Supernus Pharmaceuticals*

Brian Gifford, PhD
Integrated Benefits Institute
Director, Research and Analytics

Conflicts of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies

- *Several health plans or life sciences companies serve on the IBI board:*
  - *United HealthCare*
  - *Health Care Service Corporation*
  - *Teladoc*

- *IBI receives membership dues from the pharmaceutical manufacturers, including:*
  - *Abbot*
  - *AbbVie (board member)*
  - *Amgen (board member)*
  - *GlaxoSmithKline*
  - *Johnson & Johnson (board member)*
  - *Merck*
  - *National Pharmaceutical Council*
  - *Novo Nordisk (board member)*
  - *Pfizer (board member)*
  - *PhRMA*
  - *Sanofi (board member)*
  - *Walgreens*

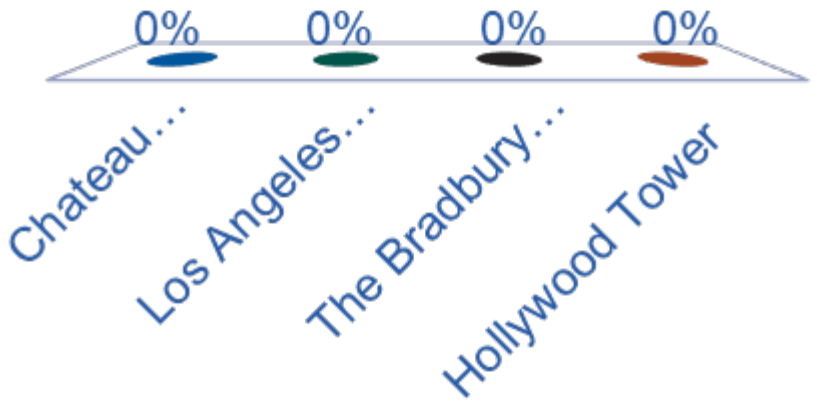
Lunch

Meeting will resume at 1:00 pm

Voting Questions

0. What Los Angeles building served as inspiration for the Disney theme park ride “The Tower of Terror”?

A. Chateau Marmont Hotel
B. Los Angeles City Hall
C. The Bradbury Building
D. Hollywood Tower



Patient population for questions 1-4: Adult patients with 15 or more headache days per month (i.e., chronic migraine).

1. Is the evidence adequate to distinguish the net health benefits among the CGRP inhibitors erenumab, fremanezumab, and galcanezumab?

A. Yes

B. No

Patient population for questions 1-4: Adult patients with 15 or more headache days per month (i.e., chronic migraine).

2. Is the evidence adequate to distinguish the net health benefit between treatment with CGRP inhibitors and oral preventive therapies (e.g., amitriptyline, topiramate, or propranolol)?

A. Yes

B. No

Patient population for questions 1-4: Adult patients with 15 or more headache days per month (i.e., chronic migraine).

3. Is the evidence adequate to distinguish the net health benefit between treatment with CGRP inhibitors and onabotulinum toxin A (Botox®, Allergan)?

A. Yes

B. No

Patient population for questions 1-4: Adult patients with 15 or more headache days per month (i.e., chronic migraine).

4. For patients who have no other options for preventive therapy, is the evidence adequate to demonstrate a net health benefit for treatment with CGRP inhibitors compared with no treatment?

A. Yes

B. No

Patient population for questions 5-7: Adult patients with 14 or fewer migraine days per month.

5. Is the evidence adequate to distinguish the net health benefits among the CGRP inhibitors erenumab, fremanezumab, and galcanezumab?

A. Yes

B. No

Patient population for questions 5-7: Adult patients with 14 or fewer migraine days per month.

6. Is the evidence adequate to distinguish the net health benefit between treatment with CGRP inhibitors and oral preventive therapies (e.g., amitriptyline, topiramate, or propranolol)?

A. Yes

B. No

Patient population for questions 5-7: Adult patients with 14 or fewer migraine days per month.

7. For patients who have no other options for preventive therapy, is the evidence adequate to demonstrate a net health benefit for treatment with CGRP inhibitors compared with no treatment?

A. Yes

B. No

Patient population for questions 8-9: Adult patients with migraine for whom other preventive treatments have failed.

8. Does treating patients with CGRP inhibitors offer one or more of the following "other benefits?" (select all that apply)

A. Reduced complexity

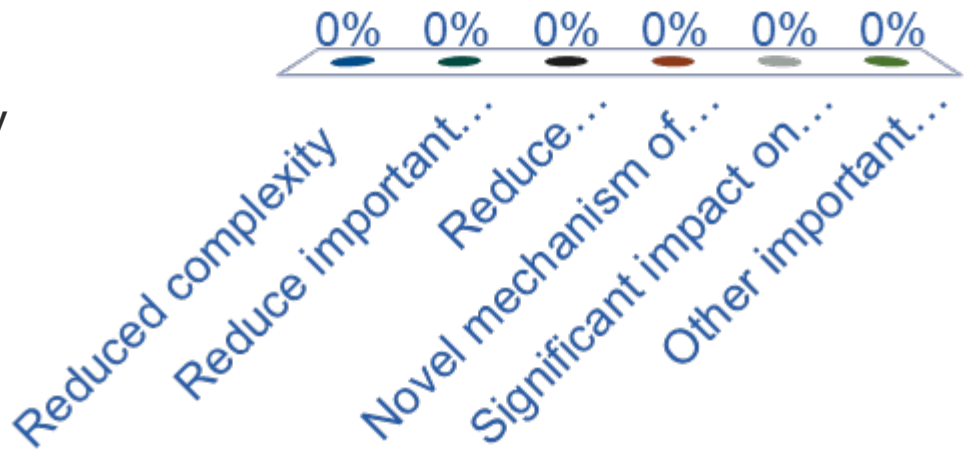
B. Reduce important health disparities

C. Reduce caregiver/family burden

D. Novel mechanism of action or approach

E. Significant impact on improving return to work/overall productivity

F. Other important benefits or disadvantages. _____



Patient population for questions 8-9: Adult patients with migraine for whom other preventive treatments have failed.

9. Are any of the following contextual considerations important in assessing CGRP inhibitors' long-term value for money? (select all that apply)

A. Care of individuals with condition of high severity

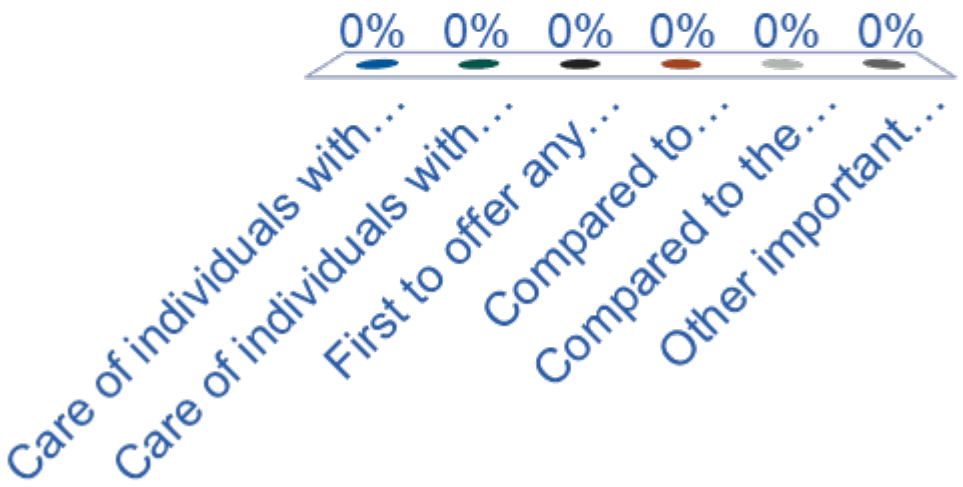
B. Care of individuals with condition with high lifetime burden of illness

C. First to offer any improvement

D. Compared to comparator, there is significant uncertainty about long-term risk of serious side effects

E. Compared to the comparator, significant uncertainty about magnitude or durability of the long term benefits of this intervention

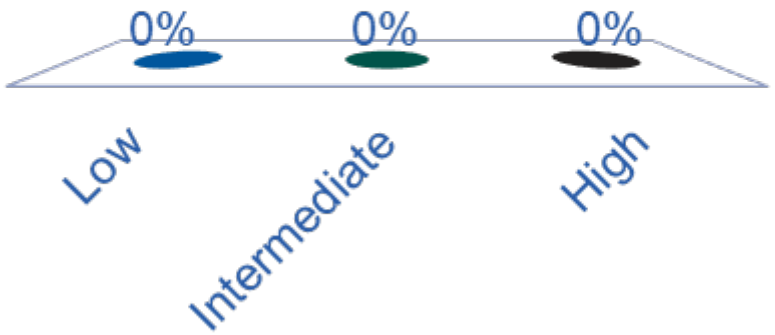
F. Other important contextual considerations. _____



Patient population for question 10: Adult patients with 15 or more headache days per month (i.e., chronic migraine) for whom other preventive therapies have failed.

10. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with erenumab versus no treatment?

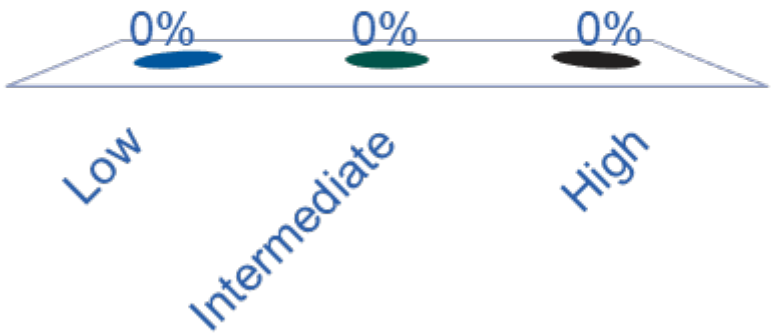
A. Low
B. Intermediate
C. High



Patient population for question 11: Adult patients with 14 or fewer migraine days per month for whom other preventive therapies have failed.

11. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with erenumab versus no treatment?

A. Low
B. Intermediate
C. High



Break
Meeting will resume at 2:25 pm

Policy Roundtable

Policy Roundtable Participants

Name	Title	COI Declaration
Amy Benavente, BA	Executive Director, Reimbursement, Access, and Value, Neuroscience, Amgen	Full-time employee of Amgen
Jill Dehlin, RN, MA, MPH, CHES	Migraine Patient, Former President of American Headache and Migraine Association	None
Aaron Deves, BS	Global Disease Lead, Migraine and Headache, Teva Pharmaceuticals	Full-time employee of Teva
Kevin Lenaburg, MA	Executive Director, Coalition for Headache and Migraine Patients (CHAMP), Caregiver for Person With Migraine	CHAMP receives funding from Alder, Amgen, Eli Lilly, MigraineAgain, migraine.com, Novartis, Teva, The Migraine World Summit, Supernus
Everett Neville, RPh	Executive Vice President, Strategy, Supply Chain, and Specialty, Express Scripts	Full-time employee of Express Scripts
Sonja Potrebic, MD, PhD	Residency Program Director, Headache Specialist, and Co-Assistant Chief of Neurology, Southern California Permanente Medical Group, Kaiser Permanente	None
Richard KP Sun, MD, MPH	Medical Consultant and Chief, Clinical Programs and Appeals Section, Health Plan Administration Division, California Public Employees' Retirement System (CalPERS)	None
Yvette Yeung, MD	Neurologist, Clinical Pod Lead, HealthCare Partners Medical Group	None

CTAF Panel Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published in early July. Includes description of CTAF votes, deliberation; policy roundtable discussion
- Materials available at

  https://icer-review.org/topic/migraines/

Adjourn