Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value

New England Comparative Effectiveness Public Advisory Council (CEPAC)

Public Meeting — September 24, 2021

Meeting materials available at: https://icer.org/assessment/myasthenia-gravis/#timeline

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Patient and Clinical Experts

- **Adrejia Boutté, JD, LLM**, Patient Expert
  - *No financial conflicts to disclose*
- **Marcia Lorimer, MSN, CPNP,** Board Chair Emerita, Myasthenia Gravis Foundation of America
  - *The MGFA receives >25% of its funding from health care companies, including Alexion and argenx.*
- **Dr. Pushpa Narayanaswami,** MD, Vice-Chair, Clinical Operations, Beth Israel Deaconess Medical Center and Associate Professor of Neurology, Harvard Medical School
  - *Dr. Narayanaswami has received funding in excess of $5,000 from Alexion, argenx, and UCB, and has received research support from Momenta/Janssen, Alexion, and UCB.*
- **Dr. A. Gordon Smith,** MD, Professor and Chair of Neurology, Virginia Commonwealth University
  - *Dr. Smith has received funding in excess of $5,000 from Alexion, argenx, Eidos, and Lexicon.*

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Why are we here today?

A diagnosis with myasthenia gravis is like a full-time job. The length of time it takes to find a treatment that is going to possibly improve your condition while keeping the distraction in your life to a minimum all while knowing there is currently no cure is a heavy load to bear. Not to mention the impact of living with a chronic rare disease such as myasthenia gravis and the impact it has on your relationships, your family, your career and just about everything else you can think of. These are factors and burdens that cannot be dismissed and must valued when looking at the overall picture.

Justin, Person with Myasthenia Gravis

Why Are We Here Today?

- What happens the day these treatments are approved by the FDA?
- Patients can have difficulty accessing drugs
  - Coverage eligibility
  - Costs (out-of-pocket and insurance premiums)
- What happens to others in the health care “system”?

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The Impact of Rising Health Care Costs

Leonard Edloe
Richmond, Virginia

The Whitman family
Bird City, Alaska

The Maccoux family
Brooklyn Park, Minnesota

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Organizational Overview

- New England Comparative Effectiveness Public Advisory Council (CEPAC)
- The Institute for Clinical and Economic Review (ICER)

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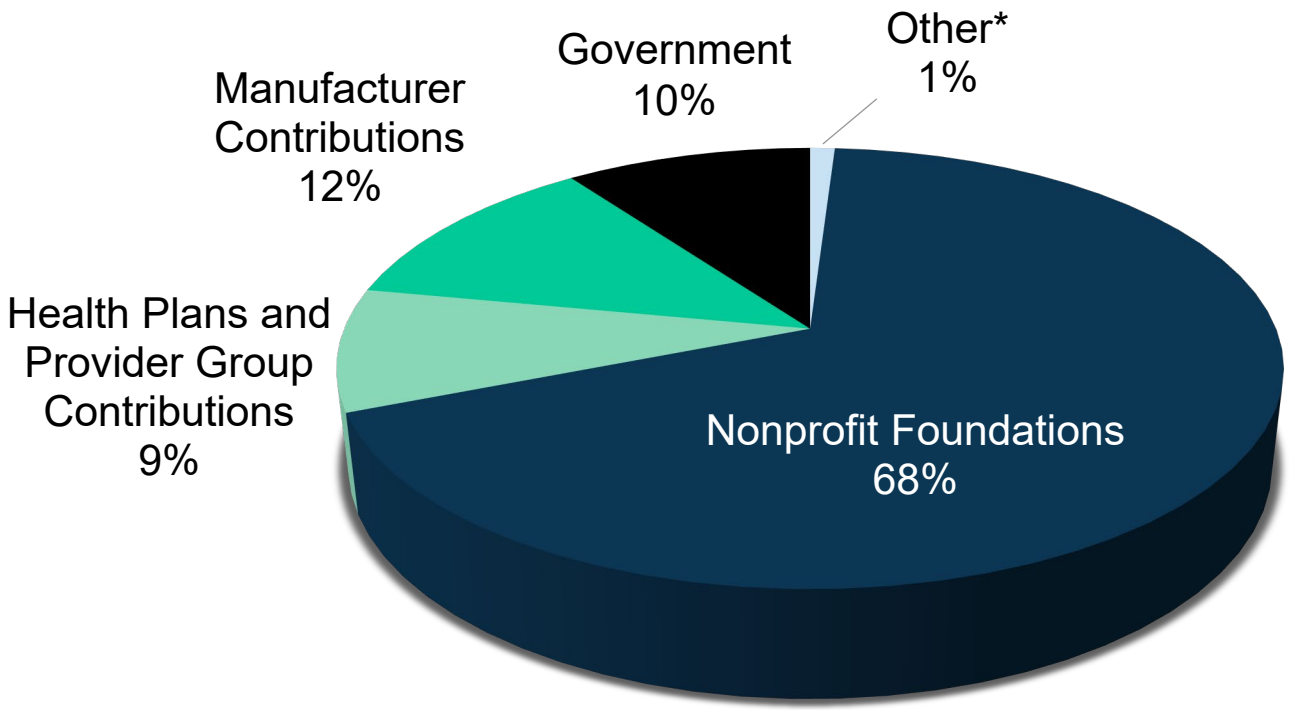
Sources of Funding, 2021

https://icer.org/who-we-are/independent-funding/



*Individual / matching contributions and speech stipends

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How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Illinois at Chicago cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Aaron Lewis, MD**, San Francisco Kaiser Neurology, Neuromuscular Medical Director, NCAL
  - **Samantha Masterson,** President and CEO, Myasthenia Gravis Foundation of America
  - **Pushpa Narayanaswami, MD, FAAN,** Vice-Chair, Clinical Operations, Beth Israel Deaconess Medical Center and Associate Professor of Neurology, Harvard Medical School
  - **A. Gordon Smith, MD, FAAN,** Professor and Chair of Neurology, Virginia Commonwealth University
- How is the evidence report structured to support CEPAC voting and policy discussion?

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Value Assessment Framework: Long-Term Value for Money

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Agenda

Time (ET)	Activity
10:00am – 10:20am	Meeting Convened and Opening Remarks
10:20am - 11:00am	Presentation of the Clinical Evidence
11:00am – 11:40am	Presentation of the Economic Model
11:40am - 12:05pm	Public Comments and Discussion
12:05pm – 12:50pm	Lunch Break
12:50pm – 2:00pm	New England CEPAC Vote on Clinical Effectiveness and Value
2:00pm – 2:10pm	Break
2:10pm – 3:30pm	Policy Roundtable
3:30pm – 4:00pm	Reflections from New England CEPAC
4:00pm	Meeting Adjourned

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Presentation of the Clinical Evidence

Jeffrey A. Tice, MD

Professor of Medicine

University of California, San Francisco

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Key Collaborators

- **Dmitriy Nikitin, MSPH,** Research Lead, Evidence Synthesis, ICER
- **Avery McKenna,** Senior Research Assistant, Evidence Synthesis, ICER

Disclosures:

We have no conflicts of interest relevant to this report.

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Background: Myasthenia Gravis (MG)

- Autoimmune disease affecting the neuromuscular junction (NMJ)
- Key feature: “fatigable weakness”
  - Eyelids, swallowing, breathing…
- Often starts with ocular disease, but may progress over about 2 years to involve muscles throughout the body (generalized MG or gMG)
- Chronic disease, but not progressive
- Autoantibodies
  - Acetylcholine receptor (AChR) – most common, classic form: 85%
  - Muscle specific kinase (MuSK): 6%; low density lipoprotein receptor-related protein 4 (LRP4): 2%
  - None / not identified
- Prevalence: 14-20 per 100,000 people

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Impact on Patients

- Long and frustrating path to diagnosis
- Unexpected flares, chronic fatigue
  - Impacts school, work, personal relationships
- Side effects of treatments can be worse than disease
  - Corticosteroids
- Challenges with therapies requiring infusions
  - Travel time, impacts on jobs, barriers to home infusion

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Additional Insights from Discussions with Patients

- Impact of COVID-19 pandemic
  - Fear of going to medical centers for visits, infusions, provider visits
  - Higher risk for severe COVID-19 disease: respiratory compromise and immunosuppressed
  - Poor response to vaccinations
- Race / ethnicity / gender disparities
  - Earlier disease in women compared with men
  - Earlier disease in Black / African American women than others
- Impact of delayed or lost childbearing due to risks from medications
- Financial burden / out-of-pocket costs

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Standard of Care and Management

- Pyridostigmine
- Corticosteroids
- Corticosteroid-sparing immunosuppressive drugs
  - Azathioprine, mycophenolate mofetil, rituximab, maintenance IVIG, others
- IVIG or plasma exchange for crises
- Mortality has improved over time, but not remission

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Scope of Review

- Population
  - Adults with generalized myasthenia gravis who have failed or are intolerant of standard therapy
- Interventions
  - Eculizumab and Efgartigimod: focus of the review
- Comparators
  - Standard of care / other interventions
  - Rituximab and maintenance IVIG: limited data
- Outcomes
  - Physician assessed: quantitative myasthenia gravis scale (QMG)
  - Patient reported: myasthenia gravis activities of daily living scale (MG-ADL)

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Main Interventions

- Eculizumab (Soliris®): monoclonal antibody inhibiting C5 cleavage reducing compliment deposition at NMJ
  - IV infusion every 2 weeks
  - FDA approval for AChR-Ab+ gMG in October 2017
- Efgartigimod: Immunoglobulin G1 Fc fragment antibody that decreases IgG levels
  - IV infusion weekly x 4 weeks, then as needed in cycles of 4 weekly infusions
    - Unclear if real world dosing will reflect clinical trial protocol
  - FDA decision expected December 17, 2021

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Outcomes

- QMG: Physician assessments including measures of strength and breathing.
  - Minimum clinically important difference (MCID) is 2 points for mild to moderate disease (QMG<16) and 3 points for severe disease (QMG≥16)
- MG-ADL: Patient-reported symptoms
  - MCID 2 points

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Clinical Evidence

Key Clinical Trials Population Differences

- Eculizumab: REGAIN
  - Patients who are AChR Ab positive and refractory to treatment (2+ immunosuppressive therapies or 1 plus IVIG or plasma exchange given at least 4 times per year for at least one year) with MG-ADL score ≥ 6
- Efgartigimod: ADAPT
  - Patients who are AChR Ab positive OR negative with MG-ADL score ≥ 5 on stable dose of at least one treatment for gMG
  - Primary outcome is in AChR Ab **positive** patients

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Results: AChR Ab+ Patients in Pivotal Trials

Trial	Arms	Change in MG-ADL		Change in QMG	
		4 weeks	8 weeks	4 weeks	8 weeks
REGAIN	Eculizumab	-3.5	-3.7	-3.3	-4.0
	Placebo	-1.5	-1.8	-1.5	-1.4
ADAPT	Efgartigimod	-4.6	-2.2	-6.2	-2.9
	Placebo	-1.8	-1.7	-1.0	-1.2

Primary outcome:
REGAIN: LSMR 56.6 versus 68.3, p=0.0698, change in MG-ADL at 26 weeks using worst-rank ANCOVA score
ADAPT: 68% versus 30%, $p < 0.001$, responders in MG-ADL in first cycle for at least 4 consecutive weeks

LSMR: least-squares mean rank

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Rituximab and IVIG

- Rituximab: unpublished BeatMG trial: no difference from placebo in ≥75% reduction in prednisone (60% vs. 56%, p NR)
- IVIG: No difference in reduction in prednisone dose (primary outcome), but greater reduction in QMG (-4.6 vs. -2.7, p NR)
- Trial results remain unpublished

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AChR Ab Negative Patients in ADAPT Trial

- Efgartigimod only, exploratory analyses
- N=38, 19/19
- No p-values or confidence intervals reported
- MG-ADL response in cycle 1: 68% versus 63%
- QMG response in cycle 1: 53% versus 37%

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Harms

- Fewer SAEs versus placebo for both new therapies
- More discontinuations due to SAEs for eculizumab (6% vs. 0%), but not for efgartigimod (3% vs. 3%)
- Black box warning for eculizumab: Meningococcal infections

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Controversies and Uncertainties

- Unclear when or if to stop either eculizumab or efgartigimod once started
- Insufficient data on important subgroups
  - AChR Ab negative patients
  - MUSK Ab positive patients
  - LRP4 Ab positive patients
  - Non-white populations
- Appropriate dosing regimen for efgartigimod
  - Unlikely that clinicians will wait until benefits gone to re-treat patients
- Very limited comparative effectiveness data for maintenance IVIG or rituximab

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Potential Other Benefits and Contextual Considerations

- MG is a serious, lifelong illness with 60% to 80% of patients not achieving treatment goals with current therapies
- MG affects women in the early working lives leading to reduced work hours, slow career progression, and early retirement. This is particularly true for Black / African American women
- Caregivers may be needed to help with travel, feeding, and communication
- Patients with MG are particularly vulnerable during the COVID-19 pandemic

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Public Comments Received

- Prioritize the patient voice: We agree! See Section 2: Patient and Caregiver Perspective
- Death due to MG crisis while on eculizumab occurred after stopping eculizumab, so should not be considered an AE
- Use real world data: No published comparative analyses
- Rituximab should be limited to MuSK+ patients: Not according to MGFA guidelines, nor inclusion criteria for BeatMG trial

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Summary: AChR Ab Positive Patients

- Eculizumab
  - Did not meet its primary endpoint, but had consistent, clinically important improvements in MG-ADL and QMG scores at 26 weeks that were maintained through 130 weeks in continuation studies for
  - Black box warning for meningococcal infections (vaccinate prior to starting)
- Efgartigimod
  - Significant improvements in MG-ADL and QMG after first cycle that decline by 8 weeks
  - No harms identified
  - Dosing uncertain: Potential for more harms if more frequent dosing than in ADAPT
- Insufficient data on rituximab and IVIG; eculizumab versus efgartigimod

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ICER Evidence Ratings for AChR Ab+ Patients

- Eculizumab versus placebo: B+
  - Moderate certainty of small to substantial net health benefit
- Efgartigimod versus placebo: C++
  - Moderate certainty of comparable, small, or substantial net health benefit
- Eculizumab versus efgartigimod: I, Insufficient evidence
- Ecu/Efgar versus rituximab: I, Insufficient evidence
- Ecu/Efgar versus IVIG: I, Insufficient evidence

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Summary: AChR Ab Negative Patients

- Efgartigimod
  - Small subgroup in ADAPT trial
  - Exploratory analyses suggest potential benefits

ICER Evidence Ratings for AChR Ab- Patients

- Efgartigimod versus placebo: I Insufficient evidence

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Questions?

Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value

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Objective

To evaluate the cost effectiveness of **eculizumab** and, separately, **efgartigimod**, each added to conventional therapy versus conventional therapy alone, among patients with **refractory, AChR Ab+ gMG** and **gMG**, respectively (i.e., the corresponding populations evaluated in the pivotal trials)

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Treatments, Comparators and Patient Populations per Analyses

Analysis	Treatment	Comparator	Patient Population
Base-case	**Eculizumab + CT**	**CT**	**refractory, AChR Ab+ gMG (REGAIN trial)**
Base-case	**Efgartigimod + CT**	**CT**	**gMG (ADAPT trial)**
Scenario	Efgartigimod + CT	CT	refractory, AChR Ab+ gMG ([resembling] REGAIN trial)
Scenario	Eculizumab + CT	Efgartigimod + CT	refractory, AChR Ab+ gMG ([resembling] REGAIN trial)
Scenario	Efgartigimod + CT	CT	AChR Ab+ gMG (ADAPT trial)
Scenario	IVIG + CT	CT	AChR Ab+ gMG (IVIG's trial)
Scenario	Rituximab + CT	CT	AChR Ab+ gMG (rituximab's trial)

CT: conventional therapy, AChR-Ab+: Anti-acetylcholine receptor antibody positive, gMG: generalized myasthenia gravis
*Efgartigimod intermittent: four weeks on, four weeks off, using efficacy at four and eight weeks from the ADAPT trial
**Sequential: eculizumab or efgartigimod, followed by IVIG or rituximab (4 combinations)
***using trial-derived utilities provided by argenx

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Methods in Brief

Methods Overview

- **Model**: Markov model with time varying proportions of achieving ≥ 3-point reduction in QMG, health state-based probability of MG-related hospitalizations or emergency room visits, and mortality
- **Setting**: United States
- **Perspective**: Health Care Sector Perspective
- **Time Horizon**: 2 years (MG is not considered progressive; onset of action/maximal effect would be achieved within few cycles and maintained stable throughout two-year time period)
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 4 weeks
- **Primary Outcome**: Cost per quality-adjusted life year (QALY) gained; cost per life year (LY) gained; cost per equal value life year gained (evLYG); mean QMG; and time in "improved" state (i.e., 3-point or greater improvement in QMG)

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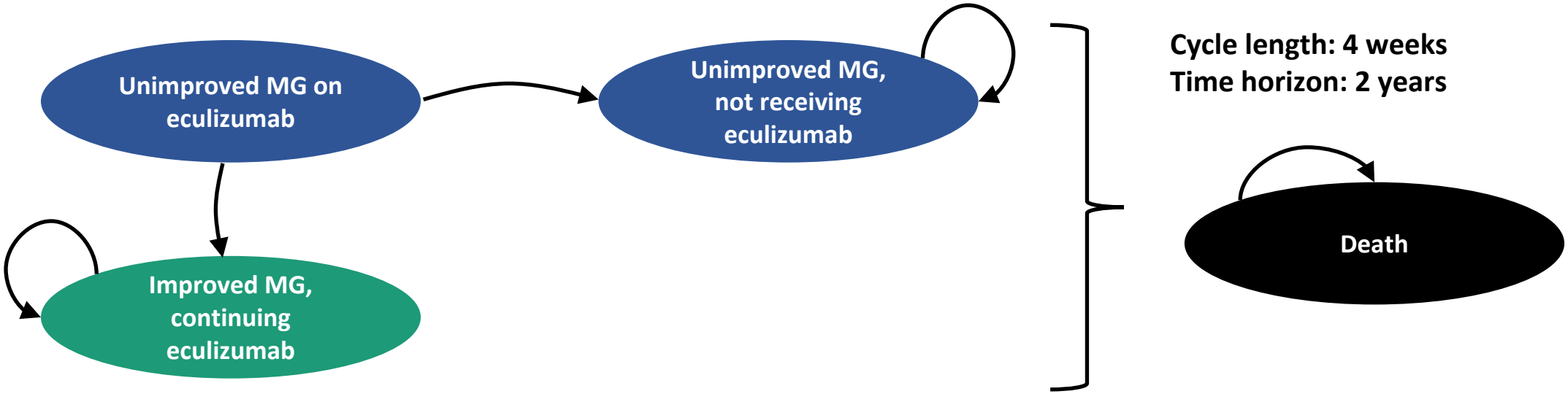
Model Schematic



Transition States includes:
- MG-related hospitalizations
- MG-related emergency room visits

*Patients who do not respond to initial treatment will have eculizumab discontinued and remain in the unimproved MG state, except for those transitioning to the death state.

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Model Characteristics

- **Target Population**
  - Base case
    - Refractory, AChR Ab+ gMG (eculizumab)
    - gMG (efgartigimod)
  - Other target populations evaluated in scenario analyses
  - Starting mean age
    - Male: 54 years
    - Female: 44 years
  - Gender: 71% female

AChR-Ab+: Acetylcholine receptor antibody positive
gMG: generalized myasthenia gravis

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Key Model Assumptions

- Base-case efgartigimod efficacy was assigned based on weekly dosing without discontinuation between treatment cycles
- Patients who respond to treatment will remain in an improved MG state; patients who do not respond to treatment will have that treatment discontinued and remain in an unimproved MG state
- Change in utility is linearly associated with change in QMG, regardless of baseline QMG score
- There are no differences in mortality among living model states

QMG: quantitative myasthenia gravis score

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Key Model Inputs: Transition Probability from Unimproved to Improved State (Proportion Achieving ≥ 3-point Reduction in QMG)

Time Point	Treatments	Input	Source
Population: Refractory, AChR Ab+ gMG			
Week 4	Eculizumab	0.53	Bootstrapped value derived from Howard 2017
Week 8	Eculizumab	0.58	
Week 4, 8	CT (eculizumab comparator)	0.37	
Population: gMG			
Week 4, 8	Efgartigimod	0.73	Bootstrapped value derived from Howard 2021
Week 4, 8	CT (efgartigimod comparator)	0.38	

CT: conventional therapy

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Key Model Inputs: Probability of Hospitalizations and Emergency Visits

Markov State	Event	Probability of Occurrence per Cycle	Source
Unimproved MG	Hospitalizations	0.04	Harris 2020
Improved MG	Hospitalizations	0.02	
Unimproved MG	Emergency Visits	0.04	
Improved MG	Emergency Visits	0.03	

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Key Model Inputs: Drug Costs

Treatment	Annual Net Price	Source
Eculizumab	$653,100	Federal Supply Schedule 2021
Efgartigimod	$418,400*	Keith Woods, argenx COO, The Motley Fool 2020. (https://www.fool.com/earnings/call-transcripts/2020/10/22/argenx-se-argx-q3-2020-earnings-call-transcript/) assumption

*Placeholder price: midpoint between annual cost of eculizumab and maintenance IVIG

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Key Model Inputs: Drug Administration Costs per Injection

Treatment	Cost per Infusion	Source
Eculizumab	$230	https://hcpcs.codes/j-codes/J1300/
Efgartigimod	$230	Assumed

*Placeholder price: midpoint between annual cost of eculizumab and IVIG

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Key Model Inputs: Health Care Utilization Costs

Item	Input	Source
Cost per Hospitalization	$109,609	Omorodion 2017
Cost per Emergency visit	$563	Healthcare Cost and Utilization Project 2021

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Key Model Inputs: Utilities

Item	Input	Source
Utility at baseline	0.47	Barnett 2021
Increase in utility for each 1-point reduction in QMG score	0.03	
Disutility of hospitalizations (applied for 1 week)	-0.22	Used mean values from two studies: Lin. Int J Environ Res Public Health. 2020 Ambrosy. Eur J Heart Fail 2016
Disutility of emergency room visits (applied for 1 day)	-0.22	

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Results

Base-Case Results

Treatment	Drug Cost	Total Cost	QALYs/evLYGs	Life Years	Time in Improved State (years)
Population: Refractory, AChR Ab+ gMG (eculizumab's trial)					
Eculizumab + CT	$760,700	$855,400	1.13	1.93	1.13
CT	$0	$95,500	0.98	1.93	0.71
Population: gMG (efgartigimod's trial)					
Efgartigimod + CT	$595,100*	$692,700	1.27	1.93	1.41
CT	$0	$94,800	0.98	1.93	0.74

CT: conventional therapy, evLYG: equal value of life years gained, QALY: quality-adjusted life year

*Efgartigimod evaluated using a placeholder price

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Base-Case Incremental Results

Treatment	Comparator	Cost per QALY Gained (Same as Cost per evLYG)	Cost per Year in Improved State
Population: Refractory, AChR Ab+ gMG (eculizumab's trial)			
Eculizumab + CT	CT	$5,210,200	$1,831,300
Population: gMG (efgartigimod's trial)			
Efgartigimod + CT	CT	$2,076,100*	$891,500*

CT: conventional therapy, evLYG: equal value of life years gained, QALY: quality-adjusted life year

There were no differences in survival. Cost per life-year gained could not be calculated whereas cost per evLYG is equal to the cost per QALY gained

*Efgartigimod evaluated using a placeholder price

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Scenario Incremental Results

Treatment	Comparator	Cost per QALY Gained (same as Cost per evLYG)	Cost per Year in Improved State
Population: Refractory, AChR Ab+ gMG (resembling eculizumab's trial population)			
Efgartigimod + CT	CT	$1,976,600‡	$824,200‡
Population: AChR Ab+ gMG (efgartigimod's trial)			
Efgartigimod + CT	CT	$1,892,600‡	$673,000‡
Population: AChR Ab+ gMG (IVIG's trial)			
IVIG + CT	CT	$1,504,300	$624,400
Population: AChR Ab+ gMG (rituximab's trial)			
Rituximab + CT	CT	$358,500	$118,900

CT: conventional therapy, evLYG: equal value of life years gained, QALY: quality-adjusted life year
*Efgartigimod intermittent: four weeks on, four weeks off, using efficacy at four and eight weeks from the ADAPT trial
**Using trial-derived utilities provided by argenx
‡Efgartigimod evaluated using a placeholder price

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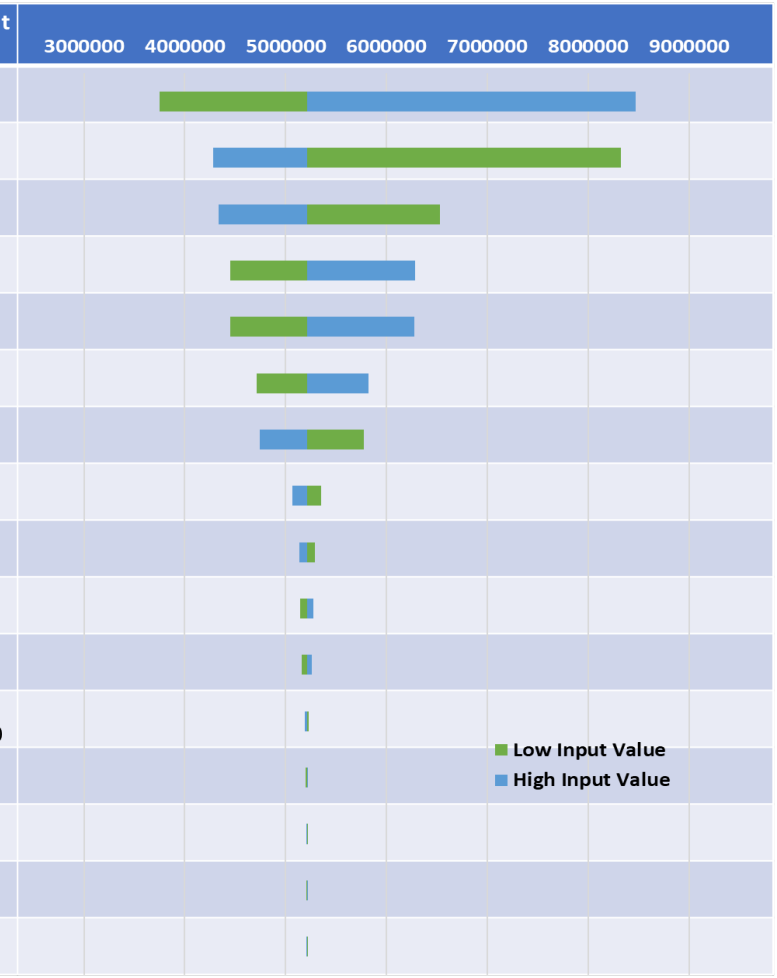
One Way Sensitivity Analyses: Eculizumab plus Conventional Therapy versus Conventional Therapy in Patients with Refractory, AChR Ab+ gMG

Parameter	Low input Value	High Input Value
Proportion of patients achieving 3 point or more QMG reduction week 4, eculizumab	0.25	0.48
Proportion of patients achieving 3 point or more QMG reduction week 8, eculizumab	0.40	0.76
Mean QMG change, unimproved MG, week 4	0.61	2.20
Mean QMG change, improved MG, week 8	-8.03	-6.47
Slope of the linear regression between QMG and EQ-5D	-0.036	-0.026
Mean QMG change, unimproved MG, week 8	-0.16	1.17
Mean QMG change, improved MG, week 4	-7.20	-5.86
Hospitalization probability per cycle, unimproved MG	0.01	0.07
Proportion of patients achieving 3 point or more QMG reduction, at week 4,	0.40	0.65
Hospitalization probability per cycle, improved MG	0.01	0.04
Mean change in QMG of improved MG at week 4	-7.70	-6.20
Cost per hospitalization	$74,500	$151,400
Mean Change in QMG of unimproved MG at week 4	0.07	1.46
Emergency Care visit rate in unimproved MG per month	0.01	0.08
Emergency Care visit rate in improved MG per month	0.01	0.04
Cost per ED visit	$280	$2,250



CT: conventional therapy, MG: myasthenia gravis, QMG: quantitative myasthenia gravis score

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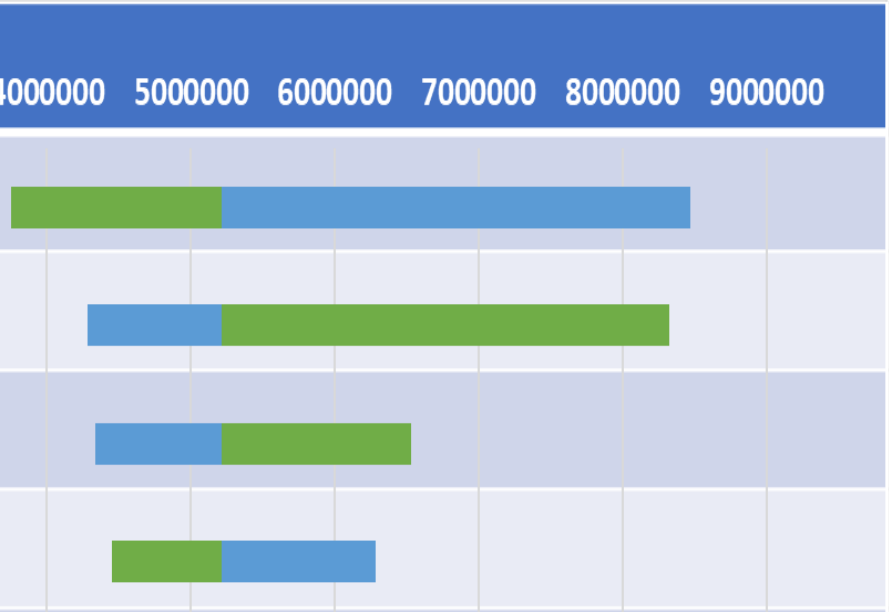

CT: conventional therapy, MG: myasthenia gravis, QMG: quantitative myasthenia gravis score

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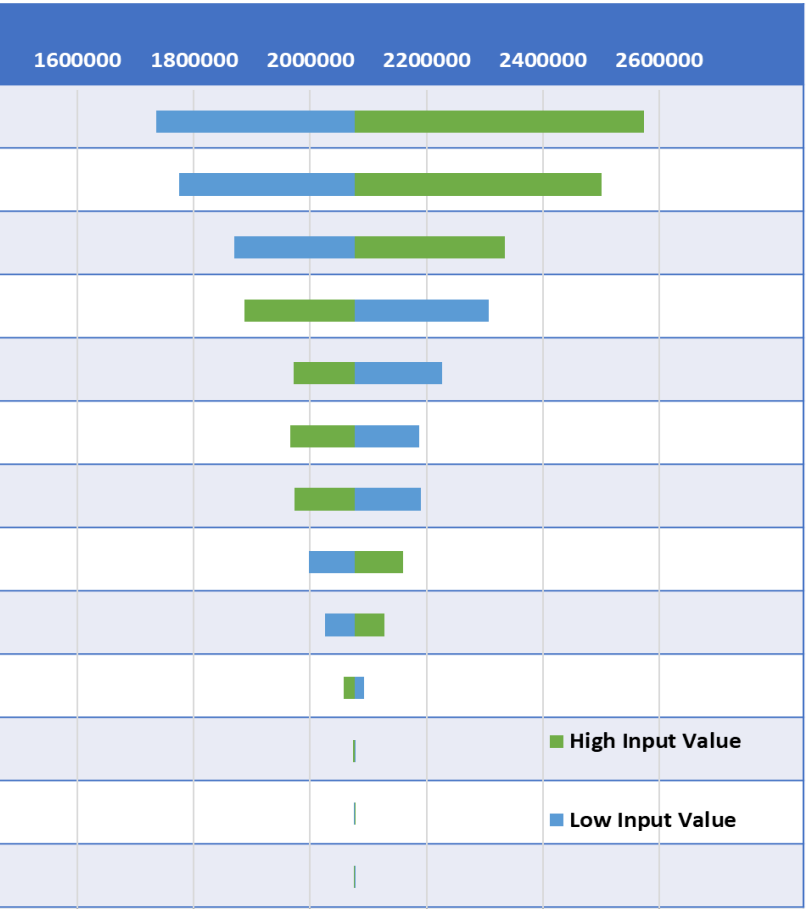
One Way Sensitivity Analyses: Efgartigimod* plus Conventional Therapy versus Conventional Therapy in Patients with gMG

Parameter	Low input Value	High Input Value
Proportion of patients achieving 3 point or more reduction in QMG at week 4	0.28	0.49
Slope of the linear regression between QMG and EQ-5D	-0.036	-0.026
Mean Change in QMG of improved MG at week 4	-9.69	-8.19
Mean Change in QMG of unimproved MG at week 4	1.05	2.64
Proportion of patients achieving 3 point or more reduction in QMG at week 4	0.63	0.82
Hospitalization rate in unimproved MG per month	0.01	0.07
Mean Change in QMG of improved MG at week 4	-7.61	-6.27
Mean Change in QMG of unimproved MG at week 4	-0.38	1.00
Hospitalization rate in improved MG per month	0.01	0.04
Cost per hospitalization	$74,500	$151,400
Emergency Care visit rate in unimproved MG per month	0.01	0.08
Emergency Care visit rate in improved MG per month	0.01	0.04
Cost per ED visit	$280	$2,252



CT: conventional therapy, MG: myasthenia gravis, QMG: quantitative myasthenia gravis score
*Efgartigimod evaluated using a placeholder price

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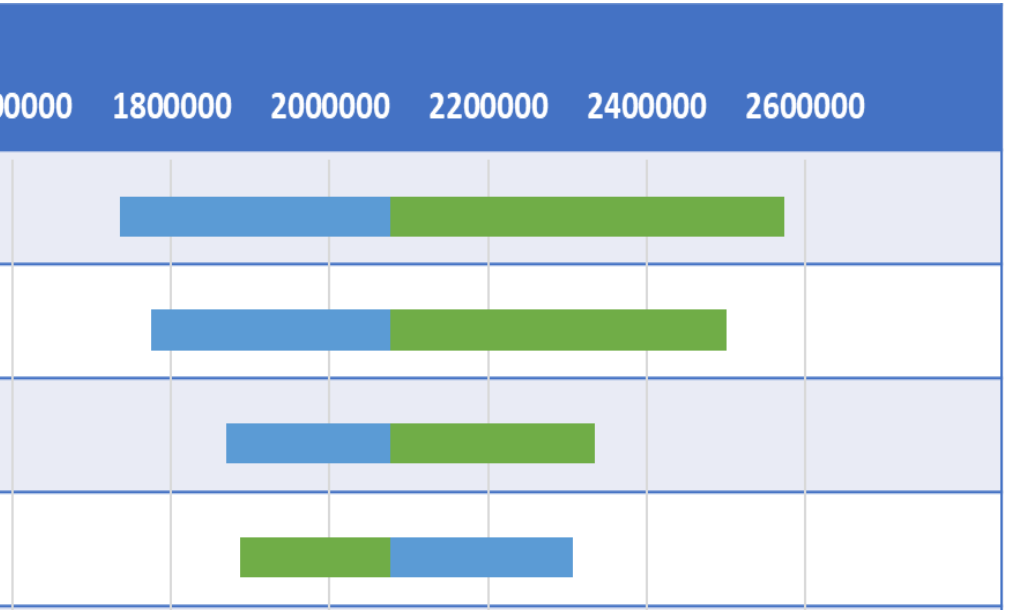
One Way Sensitivity Analyses: Efgartigimod plus Conventional Therapy versus Conventional Therapy in Patients with gMG

Parameter	Low input Value	High Input Value
Proportion of patients achieving 3 point or more reduction in QMG at week 4	0.28	0.49
Slope of the linear regression between QMG and EQ-5D	-0.036	-0.026
Mean Change in QMG of improved MG at week 4	-9.69	-8.19
Mean Change in QMG of unimproved MG at week 4	1.05	2.64



CT: conventional therapy, MG: myasthenia gravis, QMG: quantitative myasthenia gravis score
*Efgartigimod evaluated using a placeholder price

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Probabilistic Sensitivity Analysis

Drug	Cost-Effective at $50,000 per QALY	Cost-Effective at $100,000 per QALY	Cost-Effective at $150,000 per QALY	Cost-Effective at $200,000 per QALY
Eculizumab plus CT	0%	0%	0%	0%
Efgartigimod plus CT*	0%	0%	0%	0%

CT = Conventional therapy, QALY: quality-adjusted life year

*Efgartigimod evaluated using a placeholder price

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Limitations

- Efgartigimod dosing frequency not known; effectiveness not known at different dosing frequencies
- Small sample sizes resulted in greater uncertainty of the treatment effectiveness
  - More pronounced in subgroup analyses
- Bootstrapped results were needed for key study inputs (treatment response rate and change in QMG in improved), might not precisely replicate the study's results
- Lack of controlled results in long-term studies (open label, post-marketing)
- Data regarding impact of treatment on productivity, caregiver burden, or other societal costs or benefits is lacking
  - Unable to conduct analysis from societal perspective

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Comments Received

- Two-year time horizon used in the model did not sufficiently capture long-term outcomes
  - Impact of long-term steroid use on patient health was not evaluated in the model
- Mean/median dosing frequency of efgartigimod in open-label trial was longer than what was modeled
- Utilities were obtained in ADAPT trial
- Hospitalization cost was too low

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Conclusions

- The cost effectiveness of **eculizumab**, at its current price, is well beyond typical thresholds
- The cost effectiveness of **efgartigimod** will depend on its price
- The cost effectiveness of **IVIG** and **rituximab** were also above commonly used thresholds
- Access to effective treatments for MG in patients not receiving sufficient benefit or experiencing intolerable adverse events from conventional treatments may be limited by their prices

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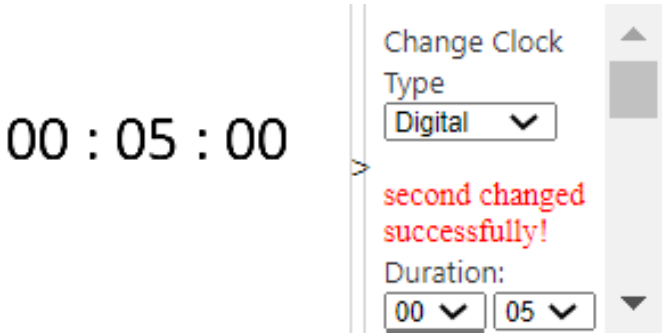
Questions?

Manufacturer Public Comment and Discussion

Glenn Phillips, PhD
Senior Director, Health Economics and Outcomes Research, argenx

Conflicts of Interest:

- *Dr. Glenn Phillips is a full-time employee of argenx.*



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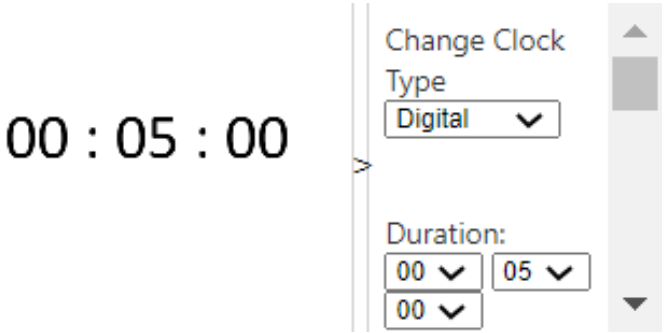
Public Comment and Discussion

Tammy Boyd
Chief Policy Officer and Counsel, Black Women's Health Imperative

Conflicts of Interest:

- *BWHI receives <2% of it's funding from Alexion through the Rare Disease Diversity Coalition*



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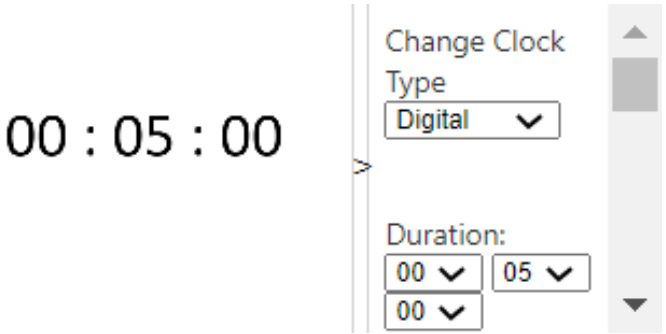
Wendi Huff
Vice President of Programs & Clinical Care, Myasthenia Gravis Foundation of America

Conflicts of Interest:

- *The MGFA receives >25% of its funding from health care companies, including Alexion and argenx*



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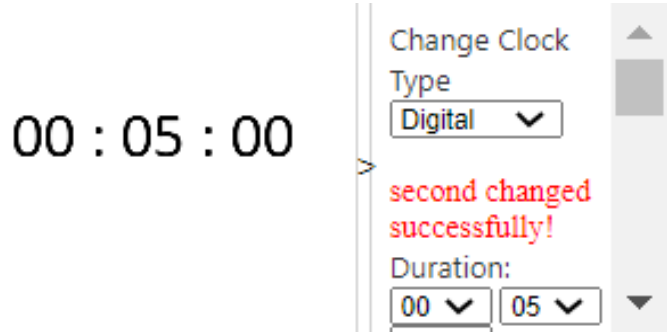
Kevin B. Kimble, Esq
Executive Director Southern Christian Leadership Global Policy Initiative

Kevin Kimble collaborated with BWHI in the composition of his public comments.

Conflicts of Interest:

- *No financial conflicts to disclose.*



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Lunch

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Voting Questions

Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

1. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of eculizumab added to conventional therapy is superior to that provided by conventional therapy alone?

A. Yes

B. No

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

2. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of efgartigimod added to conventional therapy is superior to that provided by conventional therapy alone?

A. Yes

B. No

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

3. Given the currently available evidence, is the evidence adequate to distinguish the net health benefit of eculizumab from that of efgartigimod?

A. Yes

B. No

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

3a. If the answer to question 3 is yes, which therapy has the greater net health benefit?

A. Eculizumab

B. Efgartigimod

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

4. Given the currently available evidence, is the evidence adequate to distinguish the net health benefit of IVIG from that of eculizumab and efgartigimod?

A. Yes

B. No

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

4a. If the answer to 4 is yes, which therapy has the greater net health benefit?

A. IVIG

B. Eculizumab and efgartigimod

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

5. Given the currently available evidence, is the evidence adequate to distinguish the net health benefit of rituximab from that of eculizumab and efgartigimod?

A. Yes

B. No

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

5a. If the answer to 5 is yes, which therapy has the greater net health benefit?

A. Rituximab

B. Eculizumab and efgartigimod

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody negative.

6. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of efgartigimod added to conventional therapy is superior to that provided by conventional therapy alone?

A. Yes

B. No

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Contextual Considerations and Potential Other Benefits or Disadvantages

7. When making judgments of overall long-term value for money, what is the relative priority that should be given to <u>any</u> effective treatment for gMG, on the basis of the following contextual considerations:

Acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability

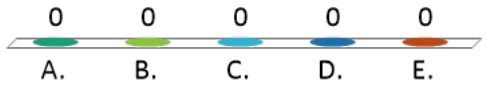
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



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8. When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective treatment for gMG, on the basis of the following contextual considerations:

Magnitude of the lifetime impact on individual patients of the condition being treated

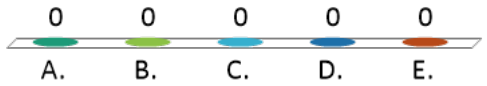
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



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9. What are the relative effects of eculizumab versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of eculizumab?

Patients' ability to achieve major life goals related to education, work, or family life

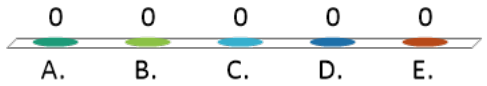
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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10. What are the relative effects of eculizumab versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of eculizumab?

Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

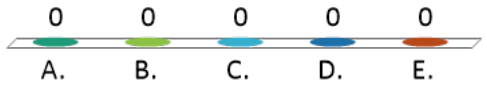
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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11. What are the relative effects of eculizumab versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of eculizumab?

Patients' ability to manage and sustain treatment given the complexity of regimen

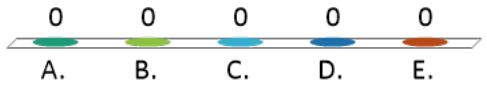
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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12. What are the relative effects of eculizumab versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of eculizumab?

Society's goal of reducing health inequities

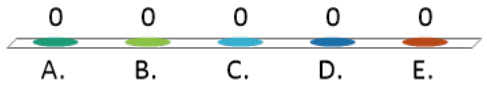
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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13. What are the relative effects of efgartigimod versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of efgartigimod?

Patients' ability to achieve major life goals related to education, work, or family life

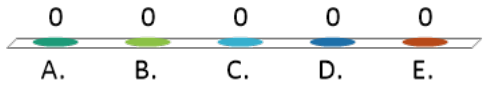
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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14. What are the relative effects of efgartigimod versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of efgartigimod?

Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

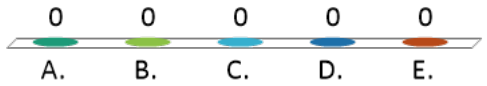
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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15. What are the relative effects of efgartigimod versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of efgartigimod?

Patients' ability to manage and sustain treatment given the complexity of regimen

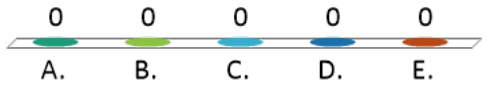
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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16. What are the relative effects of efgartigimod versus conventional therapy on the following outcomes that inform judgment of the overall long-term value for money of efgartigimod?

Society's goal of reducing health inequities

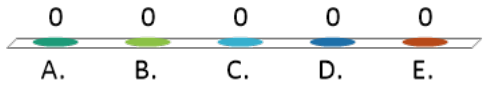
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



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Long-term Value for Money

Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

17. 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 at current pricing with eculizumab added to conventional therapy versus conventional therapy alone?

A. Low long-term value for money at current pricing

B. Intermediate long-term value for money at current pricing

C. High long-term value for money at current pricing

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Patient population: Adults with gMG, defined by MGFA clinical classes of II to IV for whom conventional immunosuppressive therapies have not been effective or have not been tolerated, and who are anti-AChR antibody positive.

18. 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 at assumed pricing with efgartigimod added to conventional therapy versus conventional therapy alone?

A. Low long-term value for money at assumed pricing

B. Intermediate long-term value for money at assumed pricing

C. High long-term value for money at assumed pricing

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Break

Meeting will resume at 2:10 pm EST

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Adrejia Boutté, JD, LLM, Patient Expert	No financial conflicts to disclose.
Marcia Lorimer, MSN, CPNP, Board Chair Emerita, Myasthenia Gravis Foundation of America	The MGFA receives >25% of its funding from health care companies, including Alexion and argenx.
Kimberly Grant, PharmD, Clinical Pharmacist, IPD Analytics	Dr. Grant is a full-time employee of IPD Analytics.
Pushpa Narayanaswami, MD, Vice-Chair, Clinical Operations, Beth Israel Deaconess Medical Center; Associate Professor of Neurology, Harvard Medical School	Dr. Narayanaswami has received funding in excess of $5,000 from Alexion, argenx, and UCB, and has received research support from Momenta/Janssen, Alexion, and UCB.
Glenn A. Phillips, PhD, Senior Director, Health Economics and Outcomes Research, argenx	Dr. Phillips is a full-time employee of argenx.
A. Gordon Smith, **MD,** Professor and Chair of Neurology, Virginia Commonwealth University	Dr. Smith has received funding in excess of $5,000 from Alexion, argenx, Eidos, and Lexicon.
Emily Tsiao, **PharmD,** Clinical Pharmacist, Premera Blue Cross	Dr. Tsiao is a full-time employee of Premera Blue Cross.

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New England CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around October 20th
  - Includes description of New England CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/myasthenia-gravis/#timeline

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Adjourn

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