Slides for the public – contains no ACIC or CPAS information

Efgartigimod for treating generalised myasthenia gravis [ID4003]

Technology appraisal committee D [10th August 2023]

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Background on generalised myasthenia gravis (gMG)

Causes

- Myasthenia Gravis (MG) is an autoimmune disorder caused by Immunoglobulin G autoantibodies targeting acetylcholine receptors (AChRs) and other parts of the neuromuscular junction which impairs neuromuscular transmission → When muscle groups other than the eye muscles are affected, the condition is known as generalised MG (gMG)

Epidemiology

- MG affects about 15 in every 100,000 people in the UK → Around 80% progress to gMG
- About 80% of people with gMG have detectable antibodies against AChRs
- In women incidence peaks between 30 and 50 and in men increases with age

Diagnosis, symptoms and prognosis of gMG

- Diagnosis via physical examination, blood tests and MRI and CT scans
- Symptoms include difficulties with swallowing, vision, speech, breathing, mobility, and fatigue
- Up to 20% of people with gMG experience a myasthenic crisis at least once, where the muscles that control breathing are affected, which requires intensive care support and is the main cause of MG-related deaths

Abbreviations: AChR, Acetylcholine receptor; CT, Computerised tomography; gMG, Generalised Myasthenia Gravis; IgG, Immunoglobulin G; MG, Myasthenia Gravis; MRI, Magnetic resonance imaging; NMJ, neuromuscular junction;

Patient perspectives

Joint submission from Muscular Dystrophy UK and Myaware & submissions from 2 patient experts

- Surveyed 551 people living with Myasthenia Gravis, and a further 7 people currently receiving efgartigimod
- People suffer from fatigue, and problems with breathing, speaking, seeing and concentrating - 37% said it led to them changing or stopping work
- Survey data showed that MG not only affects individuals physically, but also impacts them emotionally, socially and financially
- People with gMG struggle to balance treatments, symptom management and undertaking their day-to-day activities

"Due to fatigue and embarrassment with my slurry speech, I don't feel comfortable going out too much. I also can't walk for long … changed me as a person"

"gMG has affected every aspect of my daily life for 40 years. My ability to work, study, care for the needs of my family has been severely impacted. My symptoms include weakness of legs ..., arms…, facial muscles…, mouth…, eyes…, neck…, and lungs. I have had crisis periods in ICU on a ventilator."

 Abbreviations: gMG, Generalised Myasthenia Gravis; ICU, Intensive care unit;

Patient perspectives

Joint submission from Muscular Dystrophy UK and Myaware & submissions from 2 patient experts

Benefits of efgartigimod:

- Efgartigimod could manage symptoms without the side effects of steroids, although several people suffered from tiredness and headaches
- Almost all of the people surveyed who had had efgartigimod said it improved their ability to engage in family and social life, plan activities with more certainty, and have greater confidence in managing their MG

"Since starting efgartigimod I have felt better than I have in a very long time. I am still on prednisolone but feel that if I can reduce this right down to around 5mg or even remove it completely then efgartigimod will look after my MG 100%."

"I have been treated with Efgartigimod since February 2023, and the improvement has been positive and life altering. I am now able to take daily walks, cook for the family, help with housework, and importantly for my dignity, dress and bathe myself. My quality of life has improved immensely"

Abbreviations: MG, Myasthenia Gravis

Clinical perspectives

Submissions from 2 clinical experts with experience treating gMG in both specialist and non-specialist centres

Unmet need

- Disease-modifying drugs available have changed little over decades
- Available drugs are accompanied by short- and/or long-term side-effects

Benefits of efgartigimod

- Could provide a treatment option for people that are refractory to treatment or with inadequately-controlled disease
- The infusion time is much shorter than for existing treatments and home care treatment should greatly reduce the burden of treatment

"I would hope that [efgartigimod] will improve symptom control and hence quality of life by reducing the burden of other medications that may shorten life through treatment-related complications."

 Abbreviations: gMG, Generalised Myasthenia Gravis;

Other considerations

Equality considerations

Potential issues identified by patient experts

- It could be difficult for patients that do not live close to specialist centres to access efgartigimod
- The need for regular hospital visits may make it difficult for people on a low income to access efgartigimod

Potential issues identified by clinical experts

- Initially pregnant people may not be able to access efgartigimod until additional information is available because pregnant and lactating people were excluded from the main study (see SmPC).

Innovation

- Clinical experts stated that efgartigimod was innovative…

↳ It has a novel mode of action → It specifically targets the underlying cause of gMG

↳ It works rapidly and can be had at home

Are there any relevant equality or health inequality issues for decision making?

Abbreviations: gMG, Generalised Myasthenia Gravis; SmPC, Summary of product characteristics;

Efgartigimod (Vyvgart, Argenx)

Table: Technology details

Marketing authorisation	• Efgartigimod is indicated as an add-on to standard therapy for the treatment of adult patients with gMG who are AChR antibody positive. • MHRA MA received March 2023
Mechanism of action	• Efgartigimod is a human IgG1 antibody fragment that binds to the neonatal Fc Receptor, resulting in a reduction in the levels of circulating IgG including pathogenic IgG autoantibodies
Administration	• Efgartigimod is provided as a concentrate for IV infusion • The recommended dose is 10 mg/kg as a 1-hour IV infusion administered in cycles of once weekly infusions for 4 weeks • Subsequent treatment cycles are administered according to clinical evaluation → The frequency of treatment cycles may vary by patient • Company anticipate MHRA MA decision for SC formulation in [redacted]
Price	• List price: £6,569.73 per 400 mg vial - Treatment cycle: [redacted] • A simple PAS discount has been agreed for efgartigimod

Abbreviations: AChRs, Acetylcholine receptor; gMG, Generalised Myasthenia Gravis; IgG, Immunoglobulin G; IV, Intravenous; MA, Marketing authorisation; MHRA, Medicines and Healthcare products Regulatory Agency; PAS, Patient access scheme; SC, Subcutaneous;

Key issues

Table: Key issues not resolved during technical engagement for discussion

Key issue	ICER impact
Maintenance IVIg: • Should IVIg be included as a maintenance therapy? • If yes in which health states and for what proportion of people?	Largest 
Caregiver disutilities: • Should caregivers' utility be included in the QALY calculation? • If yes are the company's caregiver utility decrements appropriate?	Large 
Costs of corticosteroid use complications: • Which source should be used for decision making?	Large 

Table: Key issues resolved during technical engagement

Key issue	Conclusion
Permanent treatment discontinuation transition probabilities	• EAG & Company assume 15% of patients remain in the MG-ADL<5 health state 6 months after discontinuation of therapy. • Company provide scenarios that use different %s

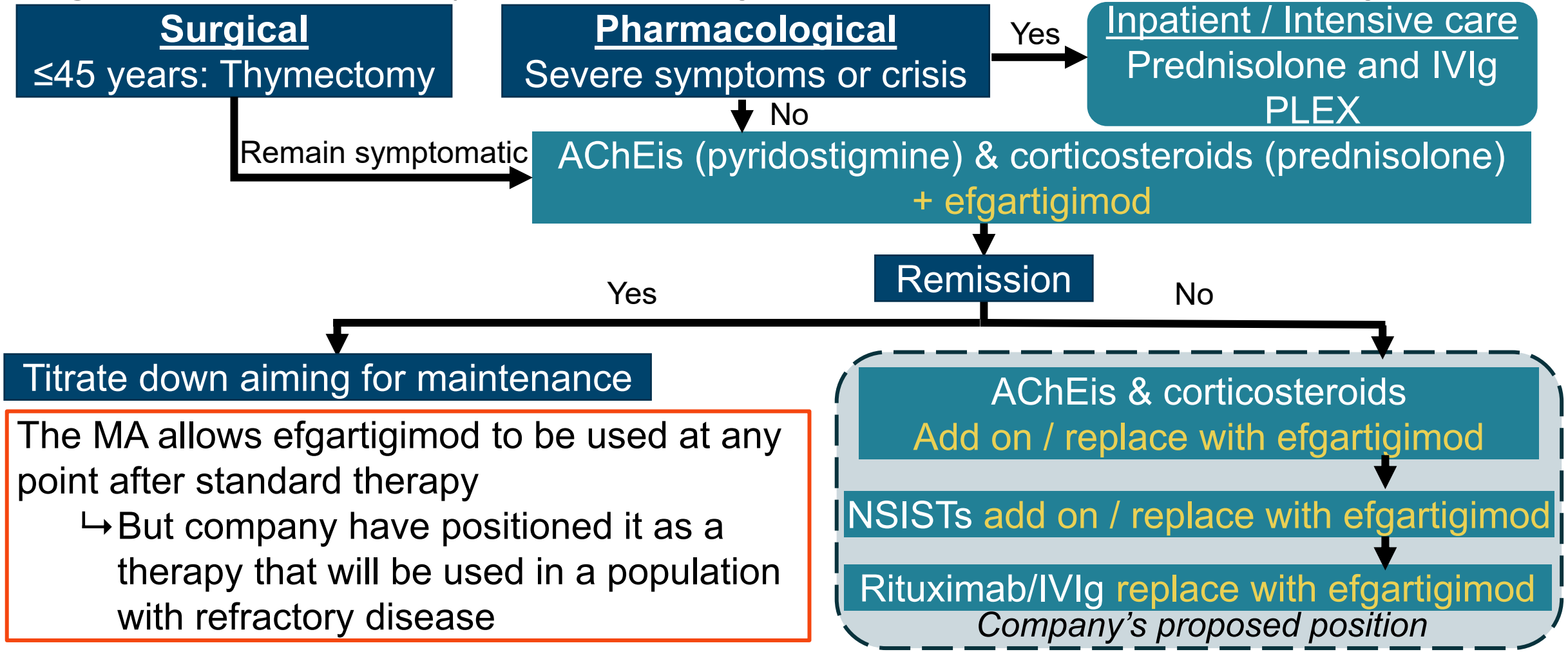
NICE

Abbreviations: EAG, External assessment group; ICER, Incremental cost-effectiveness ratio; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; QALY, Quality-adjusted life year;

Treatment Pathway

There is no single universally accepted treatment pathway for gMG

Figure: Potential pathway based on ABN guidelines and national commissioning policies



The MA allows efgartigimod to be used at any point after standard therapy

↳ But company have positioned it as a therapy that will be used in a population with refractory disease

Abbreviations: ABN, Association of British Neurologists; AChEi, Acetylcholinesterase inhibitors; gMG, Generalised Myasthenia Gravis; IVIg, Intravenous immunoglobulin; MA, Marketing authorisation; NSIST, Nonsteroidal immunosuppressive therapy; PLEX, Plasma exchange;

Decision problem

	Final Scope	Company	EAG
Population	Adults with gMG who are AChR Ab+	Consistent with scope	Scope, company, and the SmPC do not specify when efgartigimod would be used
Intervention	Efgartigimod	Consistent with scope	
Comparators	ECM without efgartigimod including corticosteroids and immunosuppressive therapies, with or without IVIg or PLEX	PLEX not a comparator	Clinical expert estimates the proportion receiving PLEX as a maintenance therapy is small (about 5%)
Outcomes	Improvement in MG, time to clinically meaningful improvement, mortality, hospitalisations, AEs and HRQoL	Consistent with scope	

Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor; AE, Adverse events; EAG, External assessment group; ECM, Established clinical management; gMG, Generalised Myasthenia Gravis; HRQoL, Health-related quality of life; IVIg, Intravenous immunoglobulin; MG, Myasthenia Gravis; PLEX, Plasma exchange; SmPC, Summary of product characteristics;

Population covered by committee recommendation

Background:

- MA: "*add-on to standard therapy for the treatment of adults with gMG who are AChR Ab+*"
- ADAPT Key inclusion criteria:
  - ↳A total MG-ADL score ≥5 at screening and on a stable dose of ≥1 therapy for gMG
- Model assumptions: In the MD-ADL<5 & crisis health state efgartigimod is not received

Clinical experts

- The place of efgartigimod in real-world UK use is under review
- Efgartigimod is expected to be used exclusively in specialist centres initially → treating those who have significant residual symptoms despite current optimal therapies
- In time efgartigimod could be used in other groups
  - ↳Could include "explosive-onset" severely affected patients in intensive care
  - ↳Could also be used earlier in the pathway to minimise the steroid burden

Patient experts

- Selective usage in severe, refractory, hard to treat MG, could be lifesaving & life changing

What population should be included in any potential recommendation?

Abbreviations: Ab+, Antibody positive; AChR, Anti-acetylcholine receptor; gMG, Generalised Myasthenia Gravis; MA, Marketing authorisation; MG, Myasthenia Gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Clinical effectiveness

NICE National Institute for Health and Care Excellence

Key clinical trial

	ADAPT (Phase 3, n=167)	ADAPT+ (Phase 3, n=151)
Design	Randomised, double-blind, placebo-controlled	Extension of ADAPT, single-arm, open-label
Population	Adults with gMG 129 (77%) were AChR Ab+	Previously enrolled in ADAPT 111 (74%) were AChR Ab+
Intervention	Efgartigimod 10 mg/kg (IV formulation)	Efgartigimod 10 mg/kg (IV formulation)
Comparator	Placebo	N/A
Duration	26-week	156-week
Key outcomes	Proportion of AChR Ab+ patients who were MG-ADL responders in the 1st cycle	Safety and tolerability in the ACHR Ab+ population
Locations	56 sites in 15 countries	-

n.b. Key exclusion criteria included pregnant and lactating people and people with known seropositivity or who tested positive for an active viral infection

NICE Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor; gMG, Generalised Myasthenia Gravis; IV, Intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Trial results ADAPT

ADAPT Primary outcome - MG-ADL responders in cycle 1

MG-ADL is a patient-reported scale developed to assess MG symptoms and their effects on daily activities

- It has an eight-item scale where each item is given a value from 0 (normal) to 3 (severe) → total score can range from 0 to 24 (higher = more severe)

MG-ADL is used to define model health states that capture disease activity levels

Primary outcome: Proportion who were MG-ADL responders in the first treatment cycle

- ≥2-point improvement (reduction) in total MG-ADL score → sustained for ≥4 consecutive weeks → first improvement occurring by week 4 of the cycle

Table: Proportion of MG-ADL responders, AChR Ab+ population

	Efgartigimod (n=65)	Placebo (n=64)
Responders % (n)	68% (44)	30% (19)
OR / p value	4.95 (95% CI 2.21, 11.53); p<0.0001	

NICE

Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor; CI, Confidence interval; MG, Myasthenia Gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; OR, Odds ratio;

Trial results ADAPT+

ADAPT+ efficacy outcome: MG-ADL total score

Mean MG-ADL change from cycle baseline was measured at week 3 of each cycle

- CMIs (≥2-point improvement (reduction) in MG-ADL score) were made in each of cycles 1 to 14 → For all cycles, [redacted] of people with AChR-Ab+ had an improvement of ≥2 points while [redacted] had an improvement of ≥3 points

Figure: Mean change from cycle baseline MG-ADL total score (AChR Ab+)

Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor; CMI, Clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Other sources of evidence

Early access to medicines scheme (EAMS)

- Efgartigimod was granted promising innovative medicine status in November 2021 and a positive scientific opinion by the MHRA under EAMS in May 2022
  - ↳EAMS made efgartigimod available in the UK from May 2022 until the MHRA MA was granted (March 2023)
  - ↳EAMS+ makes efgartigimod available for existing and new patients from the point the MA was granted until a recommendation is made by NICE about routine commissioning
- According to the company EAMS/EAMS+ aims to…
  - ↳Provide access to patients with high unmet medical need
  - ↳Generate real-world evidence to support HTA discussions and address uncertainty
- <u>EAMS indication:</u> Adults with AChR Ab+ gMG, including patients with refractory gMG who have failed, not tolerated or are ineligible for licensed treatment
- EAMS/EAMS+ data is available for [redacted] patients from [redacted] specialist gMG centres in England

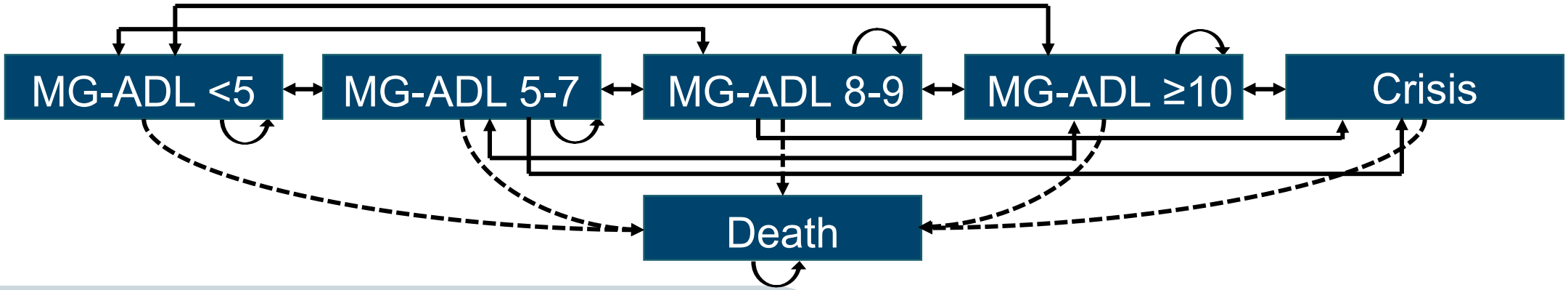
Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor, EAMS, Early access to medicines scheme; gMG, Generalised Myasthenia Gravis; HTA, Health technology assessment; MA, Marketing authorisation; MHRA, Medicines and Healthcare products Regulatory Agency;

Cost effectiveness

NICE National Institute for Health and Care Excellence

Company's model overview (1)

Figure: Model structure



- State transition model with a lifetime time-horizon and 28-day cycle length
- Treatment effect modelled through transition probabilities and utility values
- After a treatment cycle, patients will have at least one cycle with no efgartigimod
- Patients in the MG-ADL<5 and Crisis health states do not receive efgartigimod

Health states with lower MG-ADL scores are associated with:

- Lower probability of crisis
- Lower corticosteroid and IVIg use
- Lower monitoring costs
- Better QoL
- Lower caregiver disutility

Abbreviations: ECM, Established clinical management; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; Qol, Quality of life;

Company's model overview (2)

Inputs and assumptions affecting costs and QALYs

Technology affects costs by:

- Increased drug costs due to efgartigimod use as an add-on to standard therapy
- Lower costs from reduced;
  - maintenance IVIg (both acquisition + administration costs)
  - disease monitoring and corticosteroid related chronic complications
  - exacerbation, crises and end of life costs

Technology affects QALYs by:

- More time spent in less severe health states
- Higher utility than established clinical management alone
- Lower mortality from decrease in corticosteroid use and time spent in crisis health state

Assumptions with the greatest ICER effect:

- Exclusion/Inclusion of costs for maintenance IVIg
- Inclusion of disutilities for caregivers

Abbreviations: ICER, Incremental cost-effectiveness ratio; IVIg, Intravenous immunoglobulin; QALY, Quality-adjusted life year;

Company's model overview (3)

Benefits not captured in the QALY calculation

Company

- The utility decrement associated with gMG may be underestimated because of the fluctuating nature of the disease and the fact that people adapt to manage their symptoms
- The economic impact of gMG due to its impact on a person's ability to work and pursue educational activities are not captured

Note: The NICE reference-case perspective on costs is that of the NHS and PSS

↳ *Productivity costs should not be included*

Clinical experts

- Treatments can improve aspects of a person's QoL that are not captured using regular measures of HRQoL
- Efgartigimod can be administered at home

Patient experts

- One patient expert explained that since receiving efgartigimod they no longer experience falls due to weakness in their legs

Abbreviations: gMG, Generalised Myasthenia Gravis; HRQoL, Health-related quality of life; PSS, personal social services; QALY, Quality-adjusted life year; Qol, Quality of life;

How company incorporated evidence into the model (1)

Input	Source
Baseline characteristics and health state distribution at model entry	ADAPT and MyRealWorld MG study
Transitions between MG-ADL health-states	ADAPT and ADAPT+
Percentage of non-responders	ADAPT
Rate of MG exacerbations	ADAPT
Transitions into the crisis health state	Literature *(Ramos-Fransi et al)*
Incidence of treatment emergent AE's	ADAPT
Mortality	MG-ADL health-states: General population Crisis health-state: Literature *(7 studies)* Chronic corticosteroid use: Literature *(3 studies)*
Health state utilities	MG-ADL health states: ADAPT Crisis health state: MyRealWorld MG study

Abbreviations: AE, Adverse events; MG, Myasthenia Gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

How company incorporated evidence into the model (2)

Input	Source
Disutility and duration of exacerbation	Literature *(Van Wilder et al, and 4 studies)*
Caregiver disutilities	Literature *(Acaster et al,)*
Discontinuation	ADAPT and ADAPT+
ECM components and conventional therapy use	ADAPT / MyRealWorld MG / Clinical experts
Maintenance IVIg utilisation	EAMS/EAMS+
Monitoring resource use by health state	MyRealWorld MG study / Survey of clinicians
Exacerbation and crisis resource use	Survey of clinicians
Costs of corticosteroid use complications	Literature *(Bexelius et al)*
Costs	BNF, PSSRU, NHS Cost Collection

Key Issue

Abbreviations: BNF, British National Formulary; EAMS, Early access to medicines scheme; ECM, Established clinical management; IVIg, Intravenous immunoglobulin; MG, Myasthenia Gravis; PSSRU, Personal Social Services Research Unit;

Key model inputs (1)

Table: Baseline distribution and IVIg utilisation by health state

Health-state	Distribution of the cohort at model entry, %	Maintenance IVIg utilisation*,**, %			
		Company	EAG	Commissioning expert:	
MG-ADL <5	0.0	[redacted]	0	-	-
MG-ADL 5–7	26.4	[redacted]	0	-	-
MG-ADL 8–9	41.9	[redacted]	0	-	-
MG-ADL ≥10	31.8	[redacted]	0	-	-
Crisis	0.0	63.3	63.3	-	-
Overall	-	[redacted]	0	[redacted]	[redacted]
Source	*ADAPT*	*EAMS/ EAMS+*	-	*MDSAS database*	*Clinical view*

*IVIg can also be used as a rescue therapy to manage exacerbations and crisis
**Model assumes the same maintenance IVIg utilisation per health state for both intervention and comparator

NICE Abbreviations: EAG, External assessment group; EAMS, Early access to medicines scheme; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Key issue: Maintenance IVIg (1)

Company and EAG disagree on the inclusion of maintenance IVIg in the model

Background

- IVIg can be used to treat exacerbations and crisis but can also be a maintenance therapy
  - ↳commissioned in line with the NHSE commissioning criteria

Company

- Received clinical expert advice supporting inclusion of maintenance IVIg
- Use data collected from EAMS/EAMS+ to inform use of maintenance IVIg assumptions
- NHS IGD data shows the number of people receiving IVIg has only reduced slightly
  - ↳unlikely that maintenance IVIg use has dropped to zero since March 2022

EAG

- Received clinical expert advice that does not support the inclusion of maintenance IVIg
  - ↳IVIg is no longer regularly used as a maintenance therapy due to a shortage of IVIg
  - ↳EAG acknowledged uncertainty due to the limited clinical expert opinion available to it
- Believe that IVIg is not commissioned in this population as a maintenance therapy
- Uncertain if data informing the company's assumptions is representative of all of England

Abbreviations: EAG, External assessment group; EAMS, Early access to medicines scheme; HS, Health state; IGD, Immunoglobulin database; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; NHSE, NHS England;

Key issue: Maintenance IVIg (2)

Company and EAG disagree on the inclusion of maintenance IVIg in the model

Clinical experts

- People on maintenance therapies will be treated mainly in specialist centres
- National Ig database data may not be complete due to differences in the people entering the data and how categories are used
- Database may underestimate maintenance use by not capturing…
  - ↳People that started receiving IVIg before the commissioning process was introduced
  - ↳People receiving IVIg for a secondary indication
- Efgartigimod use may lead to a reduction in maintenance IVIg use

Patient expert

- Described finding it difficult to access IVIg
- One patient expert stated that IVIg had no positive impact on their condition

Abbreviations: EAG, External assessment group; Ig, Immunoglobulin; IVIg, Intravenous immunoglobulin

Key issue: Maintenance IVIg (3)

NHSE commissioning guidance restricts the use of maintenance IVIg

Commissioning expert:

- NHSE Commissioning Criteria for the use of therapeutic Ig recommends:
  - ↳ Short-term use in crisis, weakness requiring hospital admission or prior to surgery/thymectomy
  - ↳ Maintenance therapy may be considered "*In rare circumstances where a patient has failed all standard treatments (including steroids and immunosuppression) and where authorised by a specialist in MG from a centre with a specialist neuromuscular service*,"
- Maintenance use is limited in people with gMG who are AChR-Ab+ with refractory disease
- Maintenance use likely higher in the EAMS data because that population urgently required treatment

- Should IVIg be included as a maintenance therapy?
- If yes in which health states and for what proportion of people?

NICE

Abbreviations: Ab+, Antibody positive; AChR, Acetylcholine receptor; EAMS, Early access to medicines scheme; gMG, Generalised Myasthenia Gravis; IVIg, Intravenous immunoglobulin; MG, Myasthenia Gravis; NHSE, NHS England;

Key model inputs (2)

- Company use utility values collected from the AChR Ab+ population in ADAPT
- EQ-5D-5L data was captured and mapped to EQ-5D-3L values
- Health state specific utility values were estimated using a regression model with a treatment effect coefficient
  - ↳ The CS states that the treatment effect is a statistically significant variable, indicating that MG-ADL is not fully capturing the effect of efgartigimod

Table: Utility and caregiver disutility values by health state

Health state	Efgartigimod	ECM	Caregiver disutility
MG-ADL <5	0.828	0.723	-0.002
MG-ADL 5–7	0.769	0.664	-0.045
MG-ADL 8–9	0.696	0.591	-0.142
MG-ADL ≥10	0.618	0.513	-0.160
Crisis	0.463	0.463	-0.180
Source	*MG-ADL: ADAPT, Crisis: MyRealWorld MG*		*Acaster et al,*

Abbreviations: CS, Company submission, ECM, Established clinical management; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Key issue: Caregiver disutility (1)

Company believe the impact on caregiver's utility should be included in the model

Background

- Company include caregiver utility decrements in the model → Increases inc QALYs
  - ↳ Use proxy values from a published MS study (*Acaster et al)* that used the PDDS scale
  - ↳ Decrement increases with more severe health states

Company

- Using data from a MS study as a proxy for gMG is appropriate
  - ↳ Both are chronic, autoimmune conditions that disturb the neuromuscular system, affect similar populations and have similar symptoms and treatments
- Developed a survey to assess caregiver disutility (21 caregivers)
  - ↳ [redacted] of those employed reported working fewer hours because of caregiving responsibilities
  - ↳ [redacted] reported an impact on their usual activities
  - ↳ [redacted] reported an impact on their mobility
  - ↳ [redacted] reported an impact on their personal care activities
  - ↳ [redacted] reported that their QoL was affected to some degree

Abbreviations: gMG, Generalised Myasthenia Gravis; Inc, Incremental; MS, Multiple sclerosis; PDDS, Patient Determined Disease Steps; QALY, Quality adjusted life years; Qol, Quality of life;

Key issue: Caregiver disutility (2)

EAG believe caregiver's utility should not be included in the base case analysis

EAG

- Received clinical advice that most people are independent and do not require a caregiver
- Acknowledge similarities between MS and gMG but note typical symptoms are not similar, so the values estimated are likely not representative
- NICE methods manual states "*evidence should be provided to show that the condition is associated with a substantial effect on carer's HRQoL*"
  - ↳Believe company has not provided evidence to show a substantial effect on carers
- DSU paper *(Pennington & Wong, 2019)* states "*there is no generic approach to estimating caregiver HRQoL across disease areas*" and "*that it is unclear to what extent carer HRQoL estimates are transferable between disease areas*"
- Company's survey has several limitations and is descriptive so does not provide utility values that can be used in the model
- People in company's survey appear to have more severe disease so the impact on these caregivers may be greater

Abbreviations: DSU, Decision Support Unit; EAG, External assessment group; gMG, Generalised Myasthenia Gravis; HRQoL, Health-related quality of life; MS, Multiple sclerosis;

Key issue: Caregiver disutility (3)

Patient experts believe gMG has an impact on carer's HRQoL

Patient experts

- Caregiver burden is caused by the physical, emotional and financial impact of gMG
- It is often partners and family members that take on caregiving responsibilities
- Improvements in symptoms can improve caregivers' mental health and mean that caregivers need to provide less assistance
- Provided results from a survey (156 participants)
  - ↳82% receive carer support from family all week
  - ↳80% strongly agreed and 17% agreed that the support they receive from family, a partner, or friends positively impacts them
  - ↳72% strongly agreed and 22% agreed that supporting them has an impact on their family members, partner, or friends

- Should caregivers' utility be included in the QALY calculation?
- If yes are the company's caregiver utility decrements appropriate for decision making?

Abbreviations: gMG, Generalised Myasthenia Gravis; HRQoL, Health-related quality of life; QALY, Quality-adjusted life year;

Key issue: Costs of corticosteroid use complications (1)

Company and EAG disagree on the most appropriate source for costs

Background

- Company conducted a SLR for evidence on burden of chronic corticosteroid use
- Three studies identified
  - ↳Asthma - Voorham et al. (9,413 patients, UK) and Janson et al (223 patients, Sweden).
  - ↳SLE - Bexelius et al. (190 patients, Sweden)

Company

- Bexelius et al. should be used to provide costs of managing corticosteroid complications
- SLE is a better comparator than asthma because like gMG it is an autoimmune disorder
- The socioeconomic status of the UK and Sweden are not significantly different
  - ↳healthcare costs can be assumed to be comparable between the countries
- Alternative approach may be to use the average of Voorham et al and Bexelius et al.
  - ↳Costs of corticosteroid use complications would be based on two proxy diseases

Abbreviations: EAG, External assessment group; gMG, Generalised Myasthenia Gravis; SLE, Systemic lupus erythematosus; SLR, Systematic literature review;

Key issue: Costs of corticosteroid use complications (2)

Company and EAG disagree on the most appropriate source for costs

EAG

- Voorham et al. should be used to estimate costs of managing corticosteroid complications
  - ↳ It has more patients in each arm, and it is more representative of UK costs
- Weekly costs in Bexelius et al. are far higher compared to the other two studies

Table: Sources of costs for corticosteroid-related chronic complications

Author	High dose threshold	Cost per week		Disease, country, n	Base case
		High dose	Low dose		
Bexelius et al. 2013	7.5mg/day	£233.74	£110.13	Lupus, Sweden, 190	Company
Voorham et al. 2019	7.5mg/day	£43.99	£6.16	Asthma, UK, 9413	EAG
Janson et al. 2018	5mg/day	£71.46	£19.03	Asthma, Sweden, 223	-

Which source should be used for decision making?

Abbreviations: EAG, External assessment group; gMG, Generalised Myasthenia Gravis

Summary of company and EAG base case assumptions

Table: Difference in assumptions in company and EAG base cases

Assumption	Company base case	EAG base case
Maintenance IVIg	Included *(EAMS England data - weighted by MG-ADL states)*	Not Included
Caregiver disutilities	Included *(Acaster et al. 2013)*	Not Included
Costs of corticosteroid use complications	Costs from Bexelius et al. 2013	Costs from Voorham et al. 2019

Abbreviations: EAG, External assessment group; EAMS, Early access to medicines scheme; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale;

Cost-effectiveness results

All ICERs are reported in PART 2 slides

because they include confidential

comparator CMU prices

- When the company and EAG base case ICERs are calculated using mid-point CMU prices only the company's base case ICER is within the range normally considered as an effective use of NHS resources
- The criteria for the severity decision modifier were not met

NICE Abbreviations: CMU; Commercial Medicines Unit; EAG, External assessment group; ICER, Incremental cost-effectiveness ratio;

Key issues

Table: Key issues not resolved during technical engagement for discussion

Key issue	ICER impact
Maintenance IVIg: • Should IVIg be included as a maintenance therapy? • If yes in which health states and for what proportion of people?	Largest 
Caregiver disutilities: • Should caregivers' utility be included in the QALY calculation? • If yes are the company's caregiver utility decrements appropriate?	Large 
Costs of corticosteroid use complications: • Which source should be used for decision making?	Large 

Table: Key issues resolved during technical engagement

Key issue	Conclusion
Permanent treatment discontinuation transition probabilities:	• EAG & Company assume 15% of patients remain in the MG-ADL<5 health state 6 months after discontinuing efgartigimod • Company provide scenarios that assume different %s

NICE

Abbreviations: ICER, Incremental cost-effectiveness ratio; IVIg, Intravenous immunoglobulin; QALY, Quality-adjusted life year;

Key questions for committee to answer in Part 2

Parameter	Key Question	Scenarios	ICER impact
Maintenance IVIg	Should IVIg be included as a maintenance therapy?	Not included	Largest
		EAMS/EAMS+ estimates	
		Company's original estimates (Pre TE)	
		↳50% reduction / 75% reduction	
Caregiver disutilities	Should caregivers' utility be included in the QALY calculation?	Not included	Large
		Included (*Acaster et al.*)	
		↳Proportion that needed a caregiver in MyRealWorldMG	
Costs of corticosteroid complications	Which source should be used for decision making?	*Voorham et al.*	Large
		Bexelius et al.	
		Average of *the two studies*	
Other considerations	Method of administration (IV) - does SC provide similar results? Proportion of patients remaining in MG-ADL <5 after permanent discontinuation from efgartigimod (1%,5%,10%,15%)		

NICE Abbreviations: EAMS, Early access to medicines scheme; IV, Intravenous; IVIg, Intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; QALY, Quality-adjusted life year; SC, Subcutaneous; TE, Technical engagement;