NICE National Institute for Health and Care Excellence

NICE guidance

Efgartigimod for treating antibody-positive generalised myasthenia gravis

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendation

1.1 Efgartigimod is not recommended, within its marketing authorisation, as an add-on to standard treatment for generalised myasthenia gravis in adults who test positive for anti-acetylcholine receptor antibodies.

1.2 This recommendation is not intended to affect treatment with efgartigimod that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Standard treatment for generalised myasthenia gravis in adults who test positive for anti-acetylcholine receptor antibodies includes surgery, acetylcholinesterase inhibitors, immunosuppressants, intravenous immunoglobulin or plasma exchange. Efgartigimod would be used as an add-on to standard treatment.

Clinical trial evidence suggests that efgartigimod plus standard treatment improves symptoms and people's ability to carry out their normal activities compared with standard treatment alone. But it is uncertain if the people in the trial reflect the people who would have efgartigimod in the NHS because the company has proposed a target population with more severe disease.

The economic model does not accurately capture how efgartigimod would be used in the NHS; that is, as an additional treatment in the treatment pathway. The most likely cost-effectiveness estimates are substantially above what NICE considers an acceptable use of NHS resources. This is because while the company's model suggests there is a modest gain in quality-adjusted life years, this is at a substantial additional cost, since efgartigimod is an additional treatment in the treatment pathway. So, efgartigimod is not recommended.

2 Information about efgartigimod

Marketing authorisation indication

2.1 Efgartigimod (Vyvgart, Argenx) is indicated as 'an add-on to standard therapy for the treatment of adult patients with generalised Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive'.

Dosage in the marketing authorisation

2.2 The dosage schedules are available in the summary of product characteristics for efgartigimod (concentrate for solution for infusion and solution for injection).

Price

2.3 The list price of efgartigimod is £6,569.73 per 400-mg solution for infusion vial and £15,307.47 per 1,000-mg solution for injection vial (excluding VAT, company submission).

2.4 The company has a commercial arrangement, which would have applied if efgartigimod had been recommended.

3 Committee discussion

The evaluation committee considered evidence submitted by Argenx, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

3.1 Myasthenia gravis is an autoimmune condition that can affect multiple muscle groups, and causes muscle weakness and fatigue. At first, it usually affects only the eye muscles. But, in about 80% of people, it will affect other muscle groups and become generalised myasthenia gravis (gMG). Most people with gMG have anti-acetylcholine receptor (AChR) antibodies. The patient experts explained that symptoms of gMG can vary and their impact can change from day to day. They explained the condition can have substantial physical, emotional and financial impacts on the person with gMG, as well as their family. There is currently no cure for gMG. The patient experts noted that treatments for gMG have side effects that need managing and there is a high unmet need for effective treatments. They explained that many people with gMG take corticosteroids, but finding a dose that manages symptoms while minimising the risk of side effects is challenging. They also said that strict treatment schedules can impact daily life and that managing these and side effects of multiple treatments together is difficult. The patient experts explained that people with gMG and their carers spend their life fearing a myasthenic crisis. Myasthenic crisis is the most common cause of gMG-related deaths and occurs when the muscles that control breathing stop working. The committee concluded that gMG is a debilitating condition with a high treatment burden.

Clinical management

Treatment options

3.2 gMG is a chronic condition and most people need lifelong treatment. The clinical

experts explained that people would usually have treatments outlined in the Association of British Neurologists (ABN) guidelines. But they added that, at the time of this evaluation, the ABN guidelines are being updated. The ABN (2015) guidelines recommend that people are first offered pyridostigmine at the lowest effective dose and that surgery to remove the thymus gland can be considered for people under 45 years. If symptoms continue, people should be offered prednisolone (a corticosteroid). The clinical experts explained that corticosteroids have notable side effects, so the aim is to use minimal doses to minimise these effects. But a significant proportion of people will need high doses of corticosteroids. The ABN guidelines recommend offering people a non-steroidal immunosuppressant, such as azathioprine, if remission is not achieved on corticosteroids alone. If their condition does not respond to immunosuppressants or they experience notable side effects on increasing corticosteroid doses, expert advice should be sought on the use of plasma exchange or intravenous immunoglobulin (IVIg). The NHS England commissioning criteria policy for the use of therapeutic immunoglobulin recommends IVIg should be used:

- when urgent inpatient treatment is needed and plasma exchange is not available
- in rare circumstances as a maintenance treatment when all standard treatments have failed and the person is having treatment in a specialist neuromuscular service.

NHS England's clinical commissioning policy statement on rituximab bio-similar for the treatment of myasthenia gravis states it could be considered for several populations. The patient experts explained that existing treatments are not only associated with notable side effects but can be slow to take effect. The committee concluded that an effective and fast-acting treatment option would be welcomed by people with gMG and clinicians.

Treatment population

3.3 Efgartigimod has a marketing authorisation as an add-on to standard treatment for gMG. The company positioned efgartigimod as a treatment for gMG in people with uncontrolled symptoms despite established clinical management. The

clinical experts advised that efgartigimod could be positioned at several points in the clinical pathway. They added that, initially, in the NHS it would be offered in specialist centres for gMG in people with substantial symptoms despite optimal standard treatment. But they explained that, in time, the treatment could be used in the much larger population whose symptoms remain suboptimally controlled despite standard treatment. The clinical experts explained that this is because gMG worsens over time, so they aim to offer the most effective treatments as early as possible. They stated that efgartigimod could potentially reduce the corticosteroid dose needed. The committee noted that the marketing authorisation indication for efgartigimod positions it at any point after standard treatment has started. The committee also noted that the company used efficacy data from the ADAPT trial in its model (see section 3.10). The committee noted that the inclusion criteria for ADAPT may not reflect the population that could have efgartigimod in NHS clinical practice if it were recommended by NICE within its marketing authorisation. The committee also noted that the clinical and cost effectiveness of efgartigimod would change for different populations. It stated that the characteristics of this population should be clearly defined to enable efgartigimod's use in the NHS.

Target population

3.4 As part of its response to draft guidance consultation, the company held a Delphi panel involving 6 experts from neuromuscular specialist centres to identify a target population description. The company explained that its proposed description closely aligns with the Early Access to Medicines Scheme (EAMS) eligibility criteria (see section 3.11). It proposed that the target population should be people:

- with active, refractory disease with a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of 5 or more (over 50% of MG-ADL score from non-ocular symptoms) and
- who cannot tolerate or are ineligible for standard treatment, or in whom standard treatment has failed. Standard treatment was defined as a maximal dose of corticosteroids, and at least 2 additional treatments, such as non-steroidal immunosuppressants and rituximab, for an adequate period of time, at an adequate dose.

The company stated that this population has few alternative treatment options and high unmet need and could be identified in specialist centres. The committee understood the difficulties of identifying a target population for a condition with no single universally accepted treatment pathway. The committee concluded that the company's target population description broadly described the most suitable population to have add-on treatment with efgartigimod, and acknowledged the high unmet need in this population, but some uncertainty remained. In response to the second consultation the company stated that, if recommended, efgartigimod would only be used in specialist centres. This would help ensure efgartigimod was given only to people in the proposed target population. The EAG agreed the proposed target population closely aligned with the EAMS eligibility criteria, which would allow clinicians to identify people who should be offered efgartigimod in the NHS. The clinical experts explained that the clinical community believe that the population with refractory disease have the most to benefit from efgartigimod. So, they agreed with the company's proposed target population. A clinical expert also stated that efgartigimod should only be approved for use in specialist centres. The committee noted that the company's target population appeared appropriate although it differed from the population reflected in the evidence from the clinical trial (see section 3.11). The committee concluded that it would evaluate efgartigimod in the population proposed by the company.

Maintenance IVIg

3.5 The company stated that maintenance IVIg is part of established clinical management in the NHS and is used by a sizeable proportion of the people who would be offered efgartigimod. The EAG explained that it had received clinical advice that IVIg is not regularly used as a maintenance treatment because of a lack of availability and because an NHS England commissioning policy restricts how it should be used (see section 3.2). The EAG excluded maintenance IVIg from its original base case. At technical engagement (before the first committee meeting), the company updated the proportion of people that have maintenance IVIg in its base case based on data collected as part of the EAMS for efgartigimod (see section 3.11). Also at technical engagement, an NHS

commissioning expert provided an estimate of the proportion of people with gMG who have maintenance IVIg (this data is confidential so cannot be reported here), which was substantially lower than the proportion the company used in its base case. The commissioning expert said that the larger proportion of people having maintenance IVIg in the EAMS data may be because people who had efgartigimod through the EAMS were people who urgently needed treatment. At the first committee meeting, the clinical experts provided estimates of the proportion of people with gMG that would likely have maintenance IVIg, for overall use and by model health state. These estimates were substantially lower than the proportion the company assumed in its base case. The clinical experts said that the proportion of people having maintenance IVIg varies between treatment centres, noting higher use in specialist centres, and highlighted that IVIg is more frequently used for severe disease. They also explained that maintenance IVIg use can be continuous or intermittent. The committee decided that the difference in estimates of IVIg use was likely because different populations were being considered. It concluded that IVIg was part of the treatment pathway for gMG but its use across the NHS varies.

Maintenance IVIg in the target population

3.6 In response to the first draft guidance consultation, the company used a Delphi panel to directly estimate the proportion of people eligible for maintenance IVIg in its new target population (see section 3.4). The company updated its base case and assumed maintenance IVIg use of 69.17%, distributed between the MG-ADL 5 to 7, 8 to 9, and 10 or above health states based on clinical expert opinion and weighted by the baseline cohort distribution in the model (see section 3.22). The EAG thought the evidence from the Delphi panel was appropriate for the proposed target population, but it noted that the model remained sensitive to maintenance IVIg use assumptions.

In response to the first draft guidance consultation, NICE received a comment from a clinical expert stating there is regional variation but maintenance IVIg is a relatively uncommon treatment. The committee noted that the panellists recruited to the company's Delphi panel were all from specialist centres. It noted the panellists were asked to estimate the proportion of people who would be eligible for IVIg, but this was different from asking about the proportion of people

who would actually have maintenance IVIg. It also noted that the panellists were asked to assume there were no issues around the supply of IVIg and were not asked about IVIg use by MG-ADL health state. The clinical experts explained that not everyone who was eligible for maintenance IVIg would have it. A patient expert noted that although they might be considered eligible for maintenance IVIg they have not had it. Another patient expert noted that they would not be able to access maintenance IVIg at their current treatment centre. The committee concluded that the evidence from the Delphi panel substantially overestimated the use of maintenance IVIg. It noted that the IVIg estimates and modelling used by the company also impacted other issues, such as placebo effect (see section 3.14) and treatment effect after discontinuation (see section 3.13). This caused them to have greater impact on the cost-effectiveness results.

At the third committee meeting, the company updated its base case and assumed maintenance IVIg use of 43.8%. This was based on data from a study of the EAMS cohort (Dionisio et al. 2024), which reported that 43.8% of people in the cohort were having IVIg just before they started efgartigimod treatment. The EAG advised that data from the study of the EAMS cohort provided evidence of the likely maintenance IVIg use in a population similar to the proposed target population. The committee recalled comments from the clinical experts that the population in the EAMS cohort may have more severe disease than those who would have efgartigimod if it were recommended for routine commissioning in the proposed target population. It also recalled comments from clinical experts that maintenance IVIg use differs according to location. But the committee decided that data from the EAMS cohort provided the most reliable estimate of maintenance IVIg use in the proposed target population it had seen. So, the committee concluded that assuming maintenance IVIg use of 43.8% was acceptable despite being associated with high uncertainty.

Maintenance IVIg clinical benefit

3.7 At the first committee meeting, the committee noted that the company's model included the cost of maintenance IVIg but assumed no clinical benefits. The committee decided that this was implausible. It noted that this biases the cost-effectiveness results in favour of efgartigimod because the company model assumed substantially more IVIg use in the established clinical management arm.

For the third committee meeting the company updated its modelling using a network meta-analysis (NMA) to include clinical benefits associated with IVIg. The company also did 2 matching-adjusted indirect comparisons (MAICs) comparing efgartigimod with IVIg using the 2 IVIg trials that were included in the NMA. The EAG explained it was not possible to compare baseline characteristics across studies and there were differences in outcomes reported for the studies. The EAG also explained that the company did not explicitly discuss potential treatment effect modifiers and prognostic factors. So, the EAG stated that the indirect comparisons were subject to a high degree of uncertainty and the assumed IVIg clinical benefit should be considered illustrative. The committee noted that there was uncertainty in the modelling of IVIg clinical benefit. But it also noted that the results using the MAICs and NMA were relatively similar. The committee decided that the similar results support the use of the NMA estimate. The committee concluded that the company's approach to including the clinical benefits associated with IVIg was acceptable for use in decision making despite the uncertainty associated with it.

Maintenance IVIg response rate, dosing and discontinuation

3.8 At the second meeting, the committee noted that the company's approach to modelling IVIg use did not account for a proportion of people whose disease did not respond to IVIg. Another important limitation in the company's modelling of IVIg was that it did not account for people who would stop IVIg over the lifetime of the model (which is over 50 years in length). The committee noted that IVIg may be stopped because of side effects, patient choice or a loss of efficacy. Also, few people, if any, would remain on IVIg for such long periods of time as implied by the company's modelling. The committee also noted that the company's model assumed the maximum dosing frequency for IVIg, which may also overestimate IVIg use. The clinical experts noted that IVIg would usually be a last-line treatment and some people may continue it for some time, but they could not advise on how long IVIg might be used.

The committee noted that in the company's base case, undiscounted IVIg acquisition and administration costs accounted for substantially over £1 million per person in the established clinical management arm. The committee also noted that there was uncertainty around using MG-ADL scores to estimate IVIg

use. This was because other clinical details, alongside MG-ADL score, would probably be used in the NHS when deciding whether to offer IVIg. The committee concluded that the company's approach to modelling IVIg use substantially overestimated the use of maintenance IVIg. It also concluded that because of how IVIg use was estimated and modelled, it could not have confidence in any estimate of IVIg use provided by the company's model.

For the third committee meeting the company updated its modelling of IVIg to account for people whose disease did not respond to IVIg or who stop IVIg. The company estimated that 19.5% of people would stop IVIg because their disease did not respond to IVIg based on pooled data from 2 studies (Hellman et al. 2014 and Bril et al. 2023). The company also estimated a constant annual rate of long-term IVIg discontinuation based on data from published studies. The estimated rate is considered confidential by the company and cannot be reported here. The company stated that the UK ABN guidelines suggest that the duration of efficacy of IVIg is 3 to 4 weeks. So, it considered that assuming IVIg was given every 4 weeks was appropriate. The EAG thought that the company's dosing regimen and updated discontinuation assumptions were reasonable.

The company stated that it had aligned IVIg discontinuation with how discontinuations were considered in the efgartigimod arm of the model. But the estimated time on treatment for IVIg was substantially higher than for efgartigimod. The committee decided that this lacked face validity given the easier administration and improved clinical benefit associated with efgartigimod, and the fact that efgartigimod is licensed for this condition. The clinical experts explained that because efgartigimod is a new treatment they could not definitively state the likely time on treatment for efgartigimod compared with IVIg. The company explained that time on treatment for IVIg may be longer because treatment options are limited after stopping IVIg, whereas people could have IVIg after stopping efgartigimod.

At the fourth committee meeting the company produced a scenario modelling the same time on treatment for IVIg and efgartigimod, in line with the committee's preference. But the company stated this was not representative of discontinuations from maintenance IVIg treatment. It noted that some discontinuations observed for efgartigimod were in people with an MG-ADL score less than 5, which it believed was related to improvement in the condition. The

company stated there was no evidence that discontinuation because of improvement of symptoms would happen for people having IVIg. So, the company produced an analysis that extrapolated time on treatment for IVIg from the efgartigimod data but censored people who stopped with an MG-ADL score less than 5. This resulted in a time on treatment for IVIg that was significantly longer than for efgartigimod (the company considers the time on treatment for both IVIg and efgartigimod to be confidential so cannot be reported here). The EAG noted that, although it was reasonable that people with an MG-ADL score less than 5 would not have maintenance IVIg, censoring had a high impact on the incremental cost-effective ratio (ICER) and evidence for IVIg time on treatment was poor. At the fourth committee meeting, the clinical experts again explained that they would expect time on treatment for IVIg and efgartigimod to be similar, acknowledging the limitations of the evidence base available. The clinical experts also stated that a 65% to 70% response rate for IVIg would be expected, which was lower than that estimated by the company. The committee was aware that this range was consistent with the response rates that were used in the modelling in other ongoing NICE evaluations addressing the same condition. The patient experts explained that, in their experience, people had poor responses and more complications when using IVIg and plasma exchange, and people would be less likely to stop efgartigimod than IVIg or plasma exchange. The committee noted that the company's censoring analysis was based on a very small number of people who had stopped efgartigimod treatment with an MG-ADL score of less than 5 and that the length of follow up was short for these people. The committee decided that the statements from the clinical and patient experts also suggested that the company's analysis including censoring was implausible. The committee decided that IVIg inputs in the model had a substantial impact on cost effectiveness, which created very high uncertainty in the cost-effectiveness results. The committee concluded that the most appropriate time on treatment for IVIg was the same as that estimated for efgartigimod, but noted that this was highly uncertain. The committee recalled that NICE aims to promote consistency across evaluations when appropriate. So, the committee also concluded that a 70% response rate, as used in the modelling in other ongoing evaluations in the same condition, and 4-weekly 1 g per kg dosing was the most appropriate base-case assumption for IVIg in the model, although this was highly uncertain.

Maintenance IVIg after efgartigimod

3.9 The EAG noted that for the third committee meeting the company had updated its modelling to remove maintenance IVIg from the efgartigimod arm. The EAG thought that people would have maintenance IVIg after stopping efgartigimod. So, it reinstated IVIg costs and quality-adjusted life-year (QALY) gains after stopping efgartigimod into the model and included them in its base case. The EAG explained that it had to approximate the clinical benefit associated with maintenance IVIg after efgartigimod because of time constraints. At the third committee meeting, the company explained that because the committee had asked that the clinical benefit associated with IVIg be included in the model it thought that maintenance IVIg was being considered as an active comparator. So, it assumed that after stopping efgartigimod and maintenance IVIg people would have conventional therapy alone. The company also stated concerns about how the EAG modelled maintenance IVIg after efgartigimod discontinuation and the assumptions it used. NICE's technical team noted that section 2.2.16 of NICE's health technology evaluations manual states that the care pathway is an important consideration for evaluating effectiveness and costs (see section 3.15). The committee recalled that the company model at the second committee meeting had included maintenance IVIg costs in the efgartigimod arm. The committee was not convinced that maintenance IVIg should be removed from the efgartigimod arm. But it recognised that there might be issues associated with using the EAG's modelling approach and assumptions. The committee concluded that IVIg maintenance costs should be included in the efgartigimod arm.

Clinical effectiveness

ADAPT and ADAPT+

3.10 The clinical evidence for efgartigimod came from the ADAPT trial and ADAPT extension (ADAPT+) study. ADAPT was a phase 3, multicentre, double-blind, placebo-controlled trial. It recruited adults with an MG-ADL total score of 5 points or more with over 50% of the total score attributed to non-ocular symptoms and who were on a stable dose of established clinical treatment. Of the 167 people recruited, 129 (77%) tested positive for AChR antibodies. The primary endpoint was proportion of AChR antibody-positive patients who were MG-ADL

'responders' (at least 2-points MG-ADL improvement sustained for 4 or more weeks) in the first treatment cycle. After the first treatment cycle, 68% of the AChR antibody-positive population who were randomised to the efgartigimod arm had a reduction of at least 2 points on the MG-ADL scale (clinically meaningful improvement) compared with 30% of people who had placebo. ADAPT+ is an ongoing, open-label, single-arm, multicentre, 3-year extension of the ADAPT trial. Of the 151 people who 'rolled over' from ADAPT to ADAPT+, 111 (74%) tested positive for AChR antibodies. Data from the January 2022 data cut showed that, on average, a clinically meaningful improvement was achieved in cycles 1 to 14. The committee concluded that efgartigimod as an add-on to established clinical management is more effective at improving MG-ADL score than established clinical management alone.

Data sources and generalisability

3.11 Efgartigimod was available in the NHS through the EAMS from May 2022 until its marketing authorisation was granted in March 2023, and since then it has been available through the EAMS+ programme. At the first meeting, the committee noted that the EAMS data was used only to inform the proportion of people who have maintenance IVIg in the company's base case. In response to the first draft guidance consultation, the company updated the description of its anticipated target population (see section 3.4). The company said that evidence from ADAPT showed that the efficacy observed in the AChR antibody-positive population is generalisable to its updated target population. So, it did not make any changes to the modelling of clinical effectiveness. The EAG stated that there was uncertainty around the evidence supporting the generalisability of the clinical-effectiveness estimates. The EAG also thought that age and gender distribution of people enrolled in EAMS should be used in the model. It noted that the company's proposed target population aligned closely with the EAMS cohort. That cohort was larger than the UK cohort in the MyRealWorld MG study used by the company to inform the baseline age and gender distribution in its revised base case. The company stated that the baseline characteristics of the UK cohort in MyRealWorld MG (a prospective, observational, longitudinal study that aimed to capture the impact of myasthenia gravis from the perspective of people with the condition) were similar to those of the EAMS cohort. So, it did not update its base case. The committee noted that no alternative approaches to the modelling of

clinical effectiveness were presented to overcome the uncertainty. The committee concluded that using clinical-effectiveness results from a population broader than the updated target population was a source of uncertainty.

The committee decided that baseline characteristics used in the model should align with other inputs such as quality of life (see section 3.17), dosing of efgartigimod (see section 3.22) and clinical-effectiveness estimates. For the third committee meeting the company updated its modelling to use age and gender distribution captured in ADAPT. The company presented results from a post-hoc analysis that compared baseline characteristics in the AChR antibody-positive population in ADAPT, the AChR antibody-positive refractory subgroup in ADAPT and the EAMS cohort. The company said that the analyses showed alignment of baseline characteristics. The company also presented results from the analysis that compared efficacy outcomes and considered previous lines of therapy used and whether or not people in the subgroups had refractory disease. The company said the analyses showed that efgartigimod had similar clinical efficacy regardless of the subgroup considered or previous lines of therapy. The company stated that these observations showed that evidence from ADAPT is generalisable to the updated target population. The EAG agreed that population characteristics appeared relatively similar between the ADAPT subgroup and EAMS cohort. It also agreed that the results from the company analyses of efficacy outcomes also support the generalisability of the evidence from ADAPT to the updated target population. The committee noted that the EAMS data came from a population that was more generalisable to the company's target population. The committee concluded that the clinical evidence from ADAPT could be generalised to the proposed target population but other model inputs should be based on EAMS data, such as baseline MG-ADL scores and dosing frequency of efgartigimod (see section 3.22), because this more closely represented the population likely to have efgartigimod in the NHS.

Economic model

Company's modelling approach

3.12 The company used a state transition model to estimate the cost effectiveness of

efgartigimod plus established clinical management compared with established clinical management alone. It included 4 health states based on the MG-ADL total score (MG-ADL below 5, MG-ADL 5 to 7, MG-ADL 8 to 9, and MG-ADL 10 or more) to capture disease severity, as well as crisis and death health states. The clinical experts explained that the MG-ADL health states used in the model should broadly capture differences in costs and quality of life. But they also explained that there may be rare circumstances when they do not. They suggested, for example, that someone with the most severe score for a single activity while the other activities are unaffected would have a score of 3, so would be included in the least severe health state. But a person who scores 1 for all 8 activities would be included in the second-worst health state. The clinical experts also noted that MG-ADL score would not be used on its own to decide whether IVIg should be offered. gMG exacerbations needing hospitalisation were included in the model as an acute event that could occur in any of the MG-ADL health states and that was associated with an additional cost and a utility decrement. The EAG thought that the company's model health states were reasonable. The committee recalled that in the company's model people did not have a subsequent cycle of treatment with efgartigimod if they remained in the MG-ADL below 5 health state. The clinical experts explained that in clinical practice they would not offer efgartigimod to people with an MG-ADL score below 5 and would stop treatment if a person's MG-ADL score falls below 5. The committee concluded that the company's modelled health states were generally appropriate for decision making. But there was uncertainty about how closely MG-ADL scores inform disease severity, and significant limitations to some aspects of the modelling (see section 3.6, section 3.9 and section 3.11).

Treatment effect after stopping efgartigimod permanently

3.13 The EAG highlighted that in the company's original base case, the transition probabilities for people who had permanently stopped efgartigimod resulted in a notable proportion of people remaining in the MG-ADL below 5 health state after 6 months. The EAG also highlighted that the company had stated in its clarification response that it was not aware of any evidence of a residual (ongoing) treatment effect for efgartigimod. So, the EAG provided updated transition probabilities assuming that 1% of people remain in the MG-ADL below 5 health state after stopping efgartigimod permanently. At technical engagement,

the company provided an additional analysis of ADAPT and ADAPT+ data, real-world evidence from the US and evidence on efgartigimod in other indications that it believed supported a residual treatment effect for efgartigimod after treatment had stopped permanently. It updated its base case to assume that 15% of people remain in the MG-ADL below 5 health state after stopping treatment with efgartigimod. The EAG thought the company's assumption was reasonable and updated its base case to match the company's. The committee noted that this assumption substantially affected the cost-effectiveness results and accounted for about 50% of incremental QALY gains for efgartigimod in the EAG's base case. It noted that the data provided by the company was based on a small number of people and a short duration of follow up. At the first meeting, it concluded that a residual treatment effect after treatment stops was plausible but highly uncertain. The committee stated it would have preferred more evidence about the possible residual treatment effect, which should include clinical expert input. At the second meeting the company maintained its base-case position, assuming that 15% of people that stopped efgartigimod with a MG-ADL score below 5 remain in the MG-ADL below 5 health state after permanently stopping treatment with efgartigimod. It provided a statement from a clinical expert who, after reviewing the additional evidence provided at technical engagement, believed a 15% residual effect is plausible. But the clinical expert stated that this assumption was based on the limited data available at the time and that it would have to be further investigated. One of the clinical experts at the meeting stated that they could not comment on the plausibility of such an effect. The EAG noted that the population in ADAPT and ADAPT+ was broader than the company's proposed target population (see section 3.4). It explained that it was uncertain if the company's proposed target population and the ADAPT populations would have a similar proportion of people with a residual treatment effect after stopping efgartigimod.

In response to the first draft guidance consultation, NICE received a comment from a clinical expert that stated they were unaware of evidence that some people can stop efgartigimod without a relapse. They also stated that most people seem to need 7- to 8-week cycles and become rapidly symptomatic once treatment is stopped or postponed. The committee decided that the company's approach to modelling a residual treatment effect after treatment stops was plausible but highly uncertain. The committee noted that the available evidence was limited with short follow up. It also noted that it had not been presented with

the reasons for discontinuation in those who maintained an MG-ADL score of below 5 after permanently stopping efgartigimod. The committee recalled that varying the percentage (from 15% to 1%) of people who remain in the MG-ADL below 5 health state after permanently stopping efgartigimod had a substantial effect on the cost-effectiveness results. The committee also noted that treatment effect after permanent discontinuation may be linked to the placebo effect (see section 3.14). But the committee noted the EAG's comments that the company's model could not adjust the assumptions related to the treatment effect after permanent discontinuation, while also retaining the placebo effect in the established clinical management arm. The committee wanted to see more input on this issue (see section 3.25). It concluded that it would consider the company's assumption alongside other scenarios, but noted the high uncertainty associated with these assumptions. For the third committee meeting the company updated its modelling to include the benefit observed in the placebo arm of ADAPT (see section 3.14). It stated that because the assumption of a maintained placebo effect is not compatible with a residual treatment effect assumption, the residual treatment effect was removed from its base case. The EAG did not include a maintained placebo effect assumption in its base case, so it was able to include a residual treatment effect assumption. The EAG found it reasonable to assume that 7.5% of people who stopped efgartigimod with an MG-ADL score below 5 remain in the MG-ADL below 5 health state. The committee concluded that the evidence supporting any treatment effect after discontinuation was highly uncertain and this assumption was removed to account for the placebo response rate in ADAPT. So, it did not include a treatment effect after discontinuation assumption in its preferred analysis.

Placebo effect

3.14 In the company's model, the transition probabilities for the first 4 model cycles in the established clinical management arm were derived from observations over the first 16 weeks in the placebo arm of ADAPT. After the fifth model cycle, people in the established clinical management arm were assumed to return to baseline health state distribution and remain in the same health state unless a crisis or death occurred. The company stated that this assumption was conservative because it meant that the condition would not get worse. After the first meeting, NICE's technical team asked the company to explain:

- why the observed effect in the established clinical management arm would not persist in the long term
- if it believed the observed effect was because of any of the following mechanisms:
  - regression to the mean (a tendency for extreme values to move closer to the mean when measures are repeated over time)
  - a trial effect (benefit from being in the trial that would apply to both arms but not in routine practice)
  - a 'true placebo' effect (benefit from the expectation that treatment may lead to improvement, which would apply to both arms and may apply in practice).

    The company noted that the average duration of established clinical management from disease diagnosis was 9.3 years in the AChR antibody-positive population in ADAPT. It also noted that the ADAPT inclusion criteria required people to have an MG-ADL score of at least 5, despite treatment with established clinical management. The company stated this suggested that established clinical management would be unlikely to reduce disease activity. The company explained that no long-term data from the placebo arm of ADAPT is available. The company believed that regression to the mean, a trial effect and a placebo effect all likely played a role in the observed response. But it stated that these mechanisms are specific to a trial setting. The company recalled that in ADAPT, 30% of the established clinical management arm had an MG-ADL response. It suggested that a response of this size could probably only be attributed to a placebo effect. The company stated that, in its model, the efgartigimod cohort are assumed to worsen during the off-treatment period after each treatment cycle and after permanent treatment discontinuation. The EAG agreed the company's approach to modelling the established clinical management arm was reasonable. The committee noted that randomised controlled trials, such as ADAPT, provide evidence for relative treatment effects. It decided that by assuming the observed effect in the established clinical management arm does not persist in the company's model, the model artificially inflated the

treatment effect. This problem was compounded when assuming a treatment effect for efgartigimod persists after permanently stopping treatment (see section 3.13). The committee noted the size of the response observed in the placebo arm. But it decided it was unlikely that a true placebo effect would have such a response and instead it was most likely a statistical consequence of regression to the mean. The committee agreed that in the model the efgartigimod cohort should be assumed to worsen during the off-treatment period. But it did not agree that this justified removing the observed treatment effect from the established clinical management arm. The committee concluded that the benefit observed in the placebo arm of ADAPT should be maintained over the time horizon of the model. For the third committee meeting the company updated its modelling so that the benefit observed in the placebo arm of ADAPT was maintained equally in both treatment arms. They explained that this required the removal of a treatment effect after treatment discontinuation (see section 3.13). The EAG thought the company had correctly implemented the benefit observed in the placebo arm of ADAPT into the model. But it maintained that the company's original approach to modelling the established clinical management arm was reasonable and retained it in its base case. The committee concluded that the company's approach to incorporating the benefit observed in the placebo arm of ADAPT was suitable for decision making.

Modelling of treatment pathway

3.15 At the fourth committee meeting the company included plasma exchange as part of the treatment pathway in the model, having previously omitted it because of a lack of quality data. The company stated that the treatment pathway, clinical opinion and data from EAMS suggested that plasma exchange should be included in the pathway. The company included plasma exchange after IVIg in the established clinical management arm but as an alternative to IVIg in the efgartigimod arm. The company modelled 43.8% of people to have IVIg in both arms. In the established clinical management arm all people who had IVIg also had plasma exchange (43.8%), but in the efgartigimod arm only 6% of people had plasma exchange. The clinical experts explained that plasma exchange is used in NHS practice for people who would be eligible for efgartigimod. They advised

that IVIg or plasma exchange were given at the same point in the pathway, with the other treatment (IVIg or plasma exchange) potentially being used if the original stopped being effective. The clinical experts also explained that people could have IVIg or plasma exchange even if the disease was refractory to other treatments. The clinical experts disagreed with the company's assumption in the efgartigimod arm that, after stopping IVIg or plasma exchange, people would not have the other treatment. Because the company did not model IVIg followed by plasma exchange (or vice versa) in the efgartigimod arm, the introduction of plasma exchange increased drug costs by around 2% in the efgartigimod arm but by 29% in the established clinical management arm. Because the company's modelling approach biased in favour of efgartigimod, the EAG excluded plasma exchange from its base case. The committee agreed with the clinical experts that plasma exchange was part of the treatment pathway for gMG. But it did not agree with the company's approach to including plasma exchange in the model. The committee agreed the most reasonable approach would model the same proportions of people having plasma exchange and IVIg in both arms. That would mean that people who stop efgartigimod would have the same sequence of IVIg and plasma exchange as the comparator arm. So, the overall net effect of adding plasma exchange to the model would have a similar effect on costs in both arms. Neither the company nor EAG's approach accurately reflected this sequence. But the committee decided the EAG's approach of removing plasma exchange was less biased than the company's approach and achieved a net effect more similar to what would be expected under the committee's preferred approach. So, it would consider this in decision making.

Utility values

Source of utility values

3.16 Health-related quality of life data was collected in ADAPT using the EQ-5D-5L and was mapped to the EQ-5D-3L by the company. At the first meeting, the company's model used utility values 0.105 higher in the efgartigimod arm than in the established clinical management arm. The company stated that MG-ADL does not fully capture the effect of efgartigimod, so the benefit of efgartigimod would be underestimated if it were only captured in the model using the transition

probabilities. The EAG thought that the method the company used to derive utility values and using higher utility values in the efgartigimod arm were both reasonable. It explained that clinical advice it had received suggested some of the difference in utility values between the 2 arms may be because of differences in corticosteroid use. The committee noted the magnitude of the difference in utility values between the 2 arms and that it was greater than the utility benefit associated with transitioning to the next less-severe MG-ADL health state. The committee also noted that the company's model used higher utility values in the efgartigimod arm for the MG-ADL below 5 health state, in which the model assumed people would not have efgartigimod, which did not appear valid. The committee noted it had not seen evidence to support the higher utility values used in the efgartigimod arm, for example, because of differences in corticosteroid use between arms. It thought that corticosteroid use in specific MG-ADL health states might not differ substantially between the 2 arms. It noted that in the model it was assumed people in the MG-ADL below 5 health state would not use corticosteroids. It highlighted that in the more severe MG-ADL health states, corticosteroid use would be optimised regardless of whether or not efgartigimod was used. The committee concluded that the same utility values should be used for the 2 arms. In response to the first draft guidance consultation, the company revised its base case to use the same utility values from the MyRealWorld MG study for the 2 arms. It noted that data from MyRealWorld MG was more accurate than data collected in ADAPT. The company proposed that because data from ADAPT was collected in a clinical trial setting, in which people were monitored closely, this may have resulted in overvaluation of health state utility. It stated that using pooled data from ADAPT would include some of the effect of efgartigimod. It highlighted that data from MyRealWorld MG is representative of people having established clinical management, including immunoglobulins and rituximab. The EAG noted that the populations included in both ADAPT and MyRealWorld MG are different from the new proposed target population (see section 3.4). It also advised that the MyRealWorld MG study is at high risk of bias. The EAG thought there remained significant uncertainty around the source of health state utility values, but utilities from the EAMS or the subgroup in ADAPT that meets the new target population description would be more appropriate. The committee noted NICE's health technology evaluations manual states that EQ-5D data can be sourced from the literature when it is not available in the relevant clinical trials. It recalled that EQ-5D data was available from ADAPT. The committee decided that utility values used in the model should

align with other inputs, such as the baseline characteristics (see section 3.11) and clinical-effectiveness estimates. The committee concluded that pooled utility values from ADAPT should be used in decision making.

Carer quality of life

3.17 The company said that the symptoms people with gMG experience and their need for support has a substantial impact on carers. Carers' health-related quality of life was not measured in ADAPT. Instead, in its original base case, the company used a published study that reported carer disutility at different severity stages of multiple sclerosis, measured using the Patient-Determined Disease Steps (PDDS) scale, to map to the MG-ADL and crisis health states. The company said that multiple sclerosis data was chosen because multiple sclerosis and gMG are both chronic, autoimmune conditions with similar symptoms that mainly affect young women. The EAG acknowledged that there are some similarities between multiple sclerosis and gMG. But it noted that the conditions have different characteristics that could have an impact on carer health-related quality of life, such as the impact on a person's mobility, which limit the generalisability of the 2 conditions. At technical engagement, the company provided the results of a survey it did exploring the impact of gMG on carers. It said that the survey showed that caregiver responsibilities constitute a large burden on carers. The EAG noted that the survey results should be interpreted with caution. It explained that the survey was descriptive and did not provide values that could be used directly in the model. The EAG also explained that the population that completed the survey may not be generalisable to the overall population of people with gMG in England. The EAG's base case did not include carer disutilities because it decided that the company had not provided robust evidence for their inclusion. The EAG also received clinical expert advice that most people with gMG are independent and would not need lots of caregiver time. The patient experts explained how gMG has a notable impact on carers and how carers often spend a substantial amount of time providing care. The patient experts noted that carers will sometimes need to help prevent choking and this can have a substantial impact on their mental health and prevent carers going out and leading independent lives. The committee recognised that, depending on the severity of the condition, gMG can have a substantial impact on carers' lives. But it also noted that MG-ADL examines a range of symptoms, whereas the PDDS focuses

on a person's ability to walk, so the committee decided that mapping between MG-ADL and PDDS was not appropriate. The committee noted that carer disutilities contributed substantially to the overall QALY gain associated with efgartigimod in the company's model. The committee thought the carer disutilities used appeared large and it had not seen evidence to suggest that a person with gMG and their carer would experience a similar level of disutility. The committee concluded that, depending on the severity of the condition, gMG could have a substantial impact on carers' lives, which it would take into account qualitatively. But it agreed that the disutilities used in the company's model were not appropriate for decision making without more evidence.

Updated carer disutilities

3.18 In response to the first draft guidance consultation, the company updated its base case to include disutilities obtained from 2 unpublished studies. The company noted that in these studies the utility values of the carers generally declined with the severity of the condition but no linear relationship was found. The EAG explained that the lack of linear relationship could result from the small sample size. It also explained that these studies did not include a matched control group, so it could not determine if the utility decrements were only from caregiving. The EAG noted that the 2 studies were observational and potentially subject to selection bias because people taking part were self-selecting. In response to the first draft guidance consultation, NICE received a comment from the ABN stating that comparison of carer support is not appropriate in a population of people with myasthenia gravis. The committee thought that because the disutilities presented at the second meeting were collected from carers of people with gMG they were potentially more appropriate and relevant than the disutilities presented at the first meeting. The committee recognised that the availability of carer disutilities data sources are often limited. But it noted the limitations identified by the EAG and that some of the values lacked face validity. The committee concluded that it would continue to take into account the impact on carers' lives qualitatively in its preferred assumptions for decision making.

Costs

Corticosteroid complications

3.19 The company said that the published literature shows that higher doses of corticosteroids are associated with higher costs from treating complications. In its original submission, the company identified 3 studies that estimated the costs for corticosteroid-related chronic complications with low- and high-dose corticosteroid use. The company's base case used corticosteroid complication costs from a study in people with systemic lupus erythematosus (SLE) done in Sweden (Bexelius et al. 2013). The company explained that it selected this study because SLE and gMG are both autoimmune conditions. It said that it could also be assumed that costs were comparable between the UK and Sweden because the 2 countries have similar socioeconomic conditions. The EAG used corticosteroid complication costs from the second study identified by the company, which was in people with asthma in the UK (Voorham et al. 2019). The EAG advised that this study was more representative of costs in the UK. The clinical experts explained that the costs from the Voorham et al. study are unlikely to be generalisable to gMG because asthma does not have similar characteristics. The committee noted that the third study identified by the company (Janson et al. 2018) had similarities with the other 2 studies because it was done in Sweden and included people with asthma. But the clinical experts explained that, in all 3 studies, the doses of corticosteroids and the threshold used in the company's model to define high-dose corticosteroids were notably lower than what they would expect for people with gMG. The clinical experts noted that higher doses of corticosteroids could result in different complications and therefore costs. The committee noted that the Voorham et al. study excluded key weight-related adverse events, such as sleep apnoea. The committee noted that the company had not provided evidence that resource use and costs from Sweden are generalisable to the NHS. It also noted that costs from the Bexelius et al. study were notably higher than costs from the other studies. The committee was unsure whether SLE was directly generalisable to gMG. It decided that the costs from Bexelius et al. lacked face validity and may be confounded, because the study did not account for condition severity or exclude condition-related costs. The committee concluded that none of the studies identified by the company were suitable for decision making. It also concluded that corticosteroid complication costs should be generalisable to NHS clinical practice, applicable to

gMG and valued using prices relevant to the NHS.

Updated corticosteroid complication costs

3.20 In response to the first draft guidance consultation, the company updated its base case to use corticosteroid complication costs derived from NHS reference costs and the frequency of corticosteroid-related adverse events from a US study in people with myasthenia gravis (Lee et al. 2018). The company's updated base case applied the same costs for both low- and high-dose corticosteroid use. The EAG advised that the company's estimates of complication costs were not fit for purpose and lacked face and methodological validity. It explained that it had concerns related to the use of adverse-event frequencies reported by Lee et al. and the approach taken by the company to assign costs. The EAG provided a scenario in which it applied corticosteroid complication costs only for people in Lee et al. who found the side effects intolerable. In response to the first draft guidance consultation, NICE received a comment from a clinical expert who suggested that most people with refractory disease will have stopped taking corticosteroids because they were not effective. In response to the second draft guidance consultation, a separate clinical expert disagreed and stated that evidence from clinical trials in refractory populations found that most people continued to have corticosteroids. The committee recognised that the corticosteroid complication costs used in the company's revised base case used data from a study in people with myasthenia gravis. But it decided that the costs lacked face validity. The committee thought that some of the costs used were not appropriate and some of the complications would be treated as part of ongoing routine care. The committee recalled the clinical expert's comment received during draft guidance consultation. It thought it was likely that some of the people captured in the company's proposed target population description would have stopped having corticosteroids. The committee concluded that the EAG's scenario, in which costs were only applied for people in Lee et al. who found their side effects intolerable, was appropriate for decision making. The company's updated submission for the third committee meeting only applied corticosteroid complication costs for people in Lee et al. who found the side effects intolerable. But the company stated that this approach did not fully capture the burden associated with the use of corticosteroids.

Subcutaneous formulation of efgartigimod

3.21 In response to the first draft guidance consultation, the company stated that both subcutaneous and intravenous formulations of efgartigimod will soon be licensed. The company provided a scenario analysis that assumed 80% of people had the subcutaneous formulation and 20% had the intravenous formulation. Acquisition and administration costs were adjusted accordingly but it was assumed that all other costs and outcomes were unchanged. The company stated that the subcutaneous formulation would enable faster administration, reducing the burden on people with gMG, their carers and healthcare providers, because treatment could be taken at home. The clinical experts explained that it is difficult to estimate the exact proportion of people who would have the subcutaneous formulation, but 80% was a reasonable assumption because of the potential additional benefits. The committee concluded that a scenario in which 80% of people have the subcutaneous formulation was appropriate for decision making. It would also consider the additional potential uncaptured benefits of a subcutaneous formulation (see section 3.27).

Efgartigimod dosing

3.22 The company modelled dosing for efgartigimod based on the amount of dosing used in ADAPT (see section 3.11). People in ADAPT had an initial 4-week treatment cycle of efgartigimod, followed by a minimum of 4 weeks off treatment. Starting cycles beyond the first was dependent on response, including having an MG-ADL score greater than 5. NICE's technical team noted that dosing in EAMS was more frequent than in ADAPT, as seen in Dionisio et al. (2024). The EAG noted that the minimum time between doses in EAMS was 3 weeks, which suggested that the ADAPT dosing schedule was not strictly followed. It also noted that the time between treatment cycles decreased over time. NICE's technical team noted that if efgartigimod was used more frequently, or if people with an MG-ADL score less than 5 had efgartigimod, the costs in the efgartigimod arm would increase, and potentially by a substantial amount. At the fourth committee meeting, a clinical expert stated that they were not aware of efgartigimod use in EAMS in people with an MG-ADL score less than 5. The expert explained that the minimum time between dosing of 3 weeks in EAMS was related to 1 person, who was anxious about their condition severely worsening.

The committee recognised that dosing in EAMS was more frequent on average than in ADAPT. It decided that dosing in EAMS was more generalisable to the population in NHS practice that would have efgartigimod if recommended, compared with the ADAPT population (see section 3.11). The committee also noted that the baseline MG-ADL score was significantly higher for people in the EAMS data than those in the ADAPT study. It noted that this may explain the more frequent dosing of efgartigimod in EAMS than in ADAPT, as people needed to achieve a higher reduction in MG-ADL score to achieve a score below 5. The committee noted that although no analysis had been done using the EAMS dosing schedule, it would very likely increase costs in the efgartigimod arm. The company noted that both costs and outcomes were based on ADAPT, and increased dosing should also be associated with increased efficacy. The committee noted that the cost of efgartigimod was a key driver of the cost-effectiveness estimates. The committee concluded that dosing of efgartigimod should be based on EAMS data.

Cost-effectiveness estimates

3.23 Because of confidential commercial arrangements for efgartigimod and some of the established clinical management treatments, the exact cost-effectiveness results are confidential and cannot be reported here. The company's base-case ICER was above the range usually considered a cost-effective use of NHS resources. The EAG's base-case ICER was substantially above this range.

Acceptable ICER

3.24 NICE's health technology evaluations manual notes that, above a most plausible ICER of £20,000 per QALY gained, decisions about the acceptability of the technology as an effective use of NHS resources will consider the degree of uncertainty around the ICER and any benefits of the technology that were not captured in the QALY calculations. The committee will be more cautious about recommending a technology if it is less certain about the evidence presented. The committee noted the high amount of uncertainty across many points in the appraisal. But the committee noted the high unmet need in the company's target population (see section 3.4). The committee also noted that gMG could have a

substantial impact on carers' lives (see section 3.17). The committee also recognised that evidence in rare disease areas is more likely to be uncertain. So the committee agreed that despite the uncertainties, the maximum acceptable ICER would be at the upper end of the £20,000 to £30,000 per QALY gained range that NICE considers a cost-effective use of NHS resources.

The committee's preferred assumptions

3.25 The committee's preferred assumptions included:

- using population characteristics from EAMS (see section 3.11)
- maintaining the benefit observed in the placebo arm of ADAPT over the time horizon of the model (see section 3.14)
- using the same pooled utility values from ADAPT for both the efgartigimod and established clinical management arms (see section 3.15)
- considering carer disutilities qualitatively (see section 3.18)
- including corticosteroid complication costs only for people in the Lee et al. study who found their side effects intolerable (see section 3.20)
- 80% of people having the subcutaneous formulation and 20% having the intravenous formulation (see section 3.21)
- equal time on treatment for IVIg and efgartigimod (see section 3.8)
- 70% response rate for IVIg (see section 3.8)
- appropriate modelling of plasma exchange and IVIg in the treatment pathway (see section 3.15)
- dosing of efgartigimod, and baseline MG-ADL scores, based on EAMS data (see section 3.22).

  The committee decided that its preferences most closely aligned with the EAG's base case, noting the concerns about its approach to modelling plasma exchange (see section 3.15). Combining the EAG's base case with equal time

on treatment for IVIg and efgartigimod resulted in an ICER exceeding £300,000 per QALY gained. This ICER increases further if the dosing of efgartigimod was based on the EAMS data. The committee noted the company argument that this scenario should also use clinical data from EAMS. But it decided that even if efgartigimod were more effective in EAMS than ADAPT, it would not be to such an extent that it would reduce the ICER to the range normally considered cost effective. The ICER is so high because the company's model estimates a modest QALY benefit but, because efgartigimod is an addition to the treatment pathway, this is associated with substantial additional costs. The committee recognised that the ICER reflecting all of its preferred assumptions was uncertain, but it was confident that it would be substantially above the top of the range usually considered a cost-effective use of NHS resources.

Other factors

Equality

3.26 The committee noted the patient experts' comments that a person's socioeconomic status and how close they live to a gMG specialist centre may impact their ability to access efgartigimod. The committee also noted the clinical experts' comment that efgartigimod may not be used during pregnancy until additional information is available. But the committee noted that access to specialist centres is an implementation issue that cannot be addressed by a NICE technology appraisal recommendation. The committee agreed that if efgartigimod was recommended, the decision to use efgartigimod during pregnancy should be made by the person and their clinician if the clinical benefit outweighs the risks. No other potential equalities issues were identified.

Uncaptured benefits

3.27 The committee took the following uncaptured benefits into account in its decision making:

- The company and clinical experts thought efgartigimod was innovative, stating that it had a novel mechanism of action that specifically targets the underlying cause of gMG. The clinical experts also noted that efgartigimod can be used at home and works rapidly. This is more convenient than treatment with IVIg or plasma exchange, which require hospital visits.
- The committee considered the qualitative benefits of efgartigimod on carers (see section 3.18).

  The committee reflected these uncaptured benefits in its decision about an acceptable ICER threshold (see section 3.24).

Conclusion

3.28 The committee concluded that given its preferred assumptions, and based on the analysis it had seen, the cost-effectiveness estimates were highly likely to be substantially above the top end of the range that NICE considers a cost-effective use of NHS resources. The committee noted there were some uncaptured benefits but, given the magnitude of the most likely ICER, these were not sufficient to offset this. The committee concluded that efgartigimod could not be recommended for treating gMG in adults who test positive for AChR antibodies.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chairs

Megan John and Raju Reddy
Chairs, technology appraisal committee D

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

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