NICE National Institute for Health and Care Excellence

NICE guidance

Rozanolixizumab 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 Recommendations

1.1 Rozanolixizumab, as an add-on to standard treatment, can be used as an option to treat generalised myasthenia gravis in adults who test positive for anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibodies. It can only be used if:

- the condition is classified as Myasthenia Gravis Foundation of America (MGFA) class 2 to 4a
- the condition is uncontrolled after 2 or more treatments, excluding acetylcholinesterase inhibitors, and
- intravenous immunoglobulin (IVIg) or plasma exchange (PLEX) would otherwise be offered, or has been tried and stopped because of side effects or because it did not work well enough.

Rozanolixizumab can only be used if the company provides it according to the commercial arrangement (see section 2).

1.2 This recommendation is not intended to affect treatment with rozanolixizumab 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 healthcare professional consider it appropriate to stop.

What this means in practice

Rozanolixizumab must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Early funding for rozanolixizumab is available through the Innovative Medicines Fund from 29 April 2026 until 90 days after final publication of this guidance. After that, rozanolixizumab must be funded through routine commissioning in England.

There is enough evidence to show that rozanolixizumab provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

Standard treatment for generalised myasthenia gravis in adults who test positive for anti-AChR or anti-MuSK antibodies includes:

- surgery
- acetylcholinesterase inhibitors
- corticosteroids
- non-steroidal immunosuppressants.

For some people whose condition does not improve with standard treatment, IVIg or PLEX may be added. But access to IVIg and PLEX varies, and they are not suitable for everyone. So, people who cannot have them continue to try standard treatments. Rozanolixizumab would be used as an add-on to corticosteroids or non-steroidal immunosuppressants.

For this evaluation, the company asked for rozanolixizumab to be considered for generalised myasthenia gravis if:

- it is classified as MGFA class 2 to 4a

- it is uncontrolled after 2 or more treatments, excluding acetylcholinesterase inhibitors, and
- IVIg or PLEX is being administered or considered (IVIg or PLEX would otherwise be offered).

This does not include everyone who rozanolixizumab is licensed for. Some people with generalised myasthenia gravis have IVIg or PLEX, or both, and have to stop treatment because of side effects or because it did not work well enough. This group of people is included in the recommendation.

Clinical trial evidence suggests that rozanolixizumab plus standard treatment reduces symptoms and improves people's ability to carry out their normal activities compared with standard treatment alone. But it is uncertain if this improvement lasts in the longer term. Indirect comparisons suggest that rozanolixizumab works better than IVIg or PLEX, but the extent of the benefit is uncertain.

There are uncertainties in the economic model and in the cost-effectiveness estimates for rozanolixizumab. But the most likely estimates are within the range that NICE considers an acceptable use of NHS resources. So, rozanolixizumab can be used.

2 Information about rozanolixizumab

Marketing authorisation indication

2.1 Rozanolixizumab (Rystiggo, UCB) is indicated 'as an add-on to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for rozanolixizumab.

Price

2.3 The list price of rozanolixizumab is £17,883.19 per 560 mg/4 ml vial of solution for injection (excluding VAT; BNF online accessed April 2026).

2.4 The company has a commercial arrangement. This makes rozanolixizumab available to the NHS with a discount. The size of the discount is commercial in confidence.

Sustainability

2.5 For information, the Carbon Reduction Plan for UK carbon emissions is published on UCB's webpage on sustainability.

3 Committee discussion

The evaluation committee considered evidence submitted by UCB, 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 (MG) is a rare autoimmune condition that can affect multiple muscle groups and causes muscle weakness and fatigue. At first, it usually only affects the eye muscles. But in around 80% of people it will affect other muscle groups and become generalised MG (gMG). Most people with gMG have anti-acetylcholine receptor (AChR) antibodies, but a small proportion have anti-muscle-specific tyrosine kinase (MuSK) antibodies. The patient experts explained that the condition can have substantial physical, emotional and financial impacts on both the person with gMG and their carers and family. They noted that the condition is highly variable and unpredictable, with symptoms typically including fatigue, and problems with breathing, speaking, seeing and concentrating. It substantially affects daily activities and the person's ability to work. The symptoms have a substantial impact on quality of life, and many people regularly need a high level of care. There is no cure for gMG. All current treatments for gMG aim to reduce symptoms. The patient experts noted that treatments for gMG are associated with side effects, and it is particularly difficult to manage the side effects of multiple treatments simultaneously. Many people with gMG take corticosteroids. But it can be difficult to optimise the lowest effective dose, to minimise side effects, without increasing the risk of exacerbations (an acute worsening of symptoms) or myasthenic crisis. A myasthenic crisis is a life-threatening complication of gMG which affects the muscles that are used for breathing and requires hospitalisation. The patient experts explained that there are limited options available for people whose condition does not improve with standard treatment (refractory gMG). Typically, people with refractory gMG will have intravenous immunoglobulin (IVIg) or plasma exchange (PLEX) or will try a different type of immunosuppressant. IVIg and PLEX both require regular hospital visits or stays. These can be difficult to fit around work and family commitments and place a substantial burden on carers. One patient expert explained that,

although PLEX had been effective, the permanent catheter line required had caused a blood clot, so this treatment had to be stopped. The patient experts highlighted the significant burden of side effects associated with some current treatments, and the unmet need for treatments for refractory gMG. The committee concluded that gMG is a debilitating condition with a high treatment burden.

Clinical management

Current treatment options for gMG

3.2 gMG is a long-term 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. Since consultation on the draft guidance, the ABN guidelines have been updated. The ABN guidelines on autoimmune myasthenia gravis management 2025 (from here, the 2025 ABN guidelines) recommend that people are first offered pyridostigmine (an acetylcholinesterase inhibitor) at the lowest effective dose. Surgery to remove the thymus gland (thymectomy) can be considered for people under 65 years with anti-AChR antibody-positive gMG. If symptoms continue, people are offered prednisolone. The clinical experts explained that corticosteroids such as prednisolone are associated with notable side effects, and so they aim to use minimal effective doses to reduce these. The 2025 ABN guidelines recommend non-steroidal immunosuppressants, such as azathioprine, if the condition does not go into remission with corticosteroids alone. They also now recommend rituximab early in the disease course, around the time of starting steroids. If response is not good enough on immunosuppressants or people have notable side effects on increasing corticosteroid doses, healthcare professionals should seek expert advice on the use of IVIg or PLEX. The NHS England commissioning criteria policy for the use of therapeutic immunoglobulin recommends IVIg should be used:

- when urgent inpatient treatment is needed and PLEX is not available, or
- in rare circumstances as a maintenance treatment when all standard treatments have failed, and the person is having treatment in a specialist

neuromuscular service.

Rescue treatments for a myasthenic exacerbation or crisis include IVIg or PLEX. The clinical experts explained that rozanolixizumab would be used as an alternative to long-term maintenance IVIg or PLEX but would not replace rescue use. They highlighted that IVIg and PLEX are time-consuming and resource-intensive treatments, and that access to IVIg and PLEX is highly variable across the NHS.

Target population

3.3 The marketing authorisation for rozanolixizumab is as an add-on to standard treatment for anti-AChR or anti-MuSK antibody-positive gMG. In its submission, the company positioned rozanolixizumab for a narrower population, people with refractory anti-AChR or anti-MuSK antibody-positive gMG, based on the following criteria:

- the disease is classified as Myasthenia Gravis Foundation of America (MGFA) class 2 to 4a
- the disease is uncontrolled after 2 or more treatments, excluding acetylcholinesterase inhibitors
- an additional treatment, such as IVIg or PLEX, is being administered or considered.

The clinical experts agreed that these criteria broadly describe the refractory population that rozanolixizumab would be used for in the NHS. The EAG commented that it might expect the definition of refractory gMG to include reference to a disease severity threshold score, such as the MG activities of daily living (MG-ADL) score. The clinical experts explained that MG-ADL is a 24-point score that assesses the following 8 domains:

- talking
- chewing
- swallowing

- breathing
- ability to brush teeth and hair
- ability to get up from a chair
- double vision
- ptosis (drooping eyelid).

A score of 0 means the person has almost no symptoms, although the clinical experts noted the person may still have some because MG-ADL does not capture all symptoms. If someone has a score of 1, it means, for example, they may have occasional double vision. A score of 2 or 3 means someone is affected in more than 1 of the domains on the scale or is affected in 1 domain but has the symptom all the time. The clinical experts explained that MG-ADL is routinely used, but it does not always reflect the level of disease severity. They also explained that a person's disease severity would likely be captured by their MGFA class, and that using other scores would not be expected to materially change who would be eligible for rozanolixizumab in the NHS. The committee agreed with the clinical experts that the population defined in the company submission was similar to the population that would have rozanolixizumab in the NHS.

The use of rituximab in the treatment pathway

3.4 At the first committee meeting, the committee understood that the treatment pathway and treatment options for gMG had been discussed by the committee for the NICE technology appraisal of zilucoplan for treating antibody-positive gMG. In that evaluation it was noted that rituximab is used earlier in the treatment pathway and is less widely used for refractory gMG. But the committee noted that the population in the evaluation for zilucoplan is people with gMG who test positive for anti-AChR antibodies only, whereas rozanolixizumab is indicated for people who test positive for anti-AChR or anti-MuSK antibodies. The committee noted that there are some minor differences in the treatment offered to people with anti-MuSK antibody-positive gMG. For the anti-MuSK antibody-positive gMG group, the clinical experts explained that rituximab can be offered after steroids

and non-steroidal immunosuppressants have been tried, but there is variation in practice. Healthcare professionals prefer to offer it earlier to people who test positive for anti-MuSK antibodies, before their condition becomes refractory. This is because it is more effective in this smaller subpopulation than in people who test positive for anti-AChR antibodies, who make up the majority of people with gMG. The clinical experts explained that if rituximab is not used earlier and is considered for refractory gMG, it is more likely to be offered as an option (in the same position as IVIg and PLEX) to people with anti-MuSK antibody-positive gMG. But the company added that it believed rituximab would be used after the targeted treatments (IVIg, PLEX and rozanolixizumab).

After consultation on the draft guidance, the company provided results from an expert elicitation survey of 11 specialist MG centres across the UK. These showed that rituximab is generally positioned earlier in the treatment pathway, around the time of starting corticosteroids, and not as an alternative to IVIg or PLEX. The EAG noted that this aligns with the 2025 ABN guidelines, which recommend rituximab earlier than targeted treatments such as neonatal fragment crystallisable receptor inhibitors or complement inhibitors. None of the respondents said they used rituximab as an alternative to IVIg or PLEX for treating refractory disease. Use as a subsequent treatment after targeted treatment varied between centres. The EAG agreed there was evidence that rituximab was not a direct comparator for rozanolixizumab. But it noted that rituximab should be considered as part of the standard-care basket (see section 3.5), which also includes immunosuppressants, IVIg and PLEX. Clinical experts at the second committee meeting said that it was not appropriate to consider rituximab in the same place in the treatment pathway as IVIg and PLEX (that is, as a comparator to rozanolixizumab). This is because it is less effective in this group of people, so if a healthcare professional is considering IVIg or PLEX, they would already have tried rituximab. The committee took into account the advice from clinical experts, and the 2025 ABN guidelines, and concluded that rituximab is likely to be offered early in the treatment pathway, before IVIg or PLEX. So, it is not a relevant comparator for rozanolixizumab (see section 3.5).

Comparators

3.5 The final scope issued by NICE listed the following comparators:

- efgartigimod (subject to NICE evaluation)
- zilucoplan (subject to NICE evaluation)
- ravulizumab (now terminated)
- standard care without rozanolixizumab (including immunosuppressive treatments [including rituximab] with or without IVIg or PLEX).

At the first committee meeting the company proposed the following comparators:

- efgartigimod
- zilucoplan
- IVIg and PLEX, excluding corticosteroids and non-steroidal immunosuppressants.

At the time of the first committee meeting (August 2024), the NICE technology appraisal of efgartigimod for treating antibody-positive gMG and the NICE technology appraisal of zilucoplan for treating antibody-positive gMG were both ongoing, so efgartigimod and zilucoplan could not be considered established NHS practice. At the time of the second and third committee meetings the appraisal of efgartigimod had concluded and it was not recommended; the zilucoplan appraisal remained ongoing. So, efgartigimod and zilucoplan were not comparators for this evaluation.

At the first committee meeting, the committee noted that rozanolixizumab is intended to be used as an add-on treatment to corticosteroids and non-steroidal immunosuppressants. So, corticosteroids and immunosuppressants should be included in both arms of the model. The clinical experts commented on the substantial variation in access to IVIg and PLEX across the NHS. Some centres exclusively use IVIg, some use a mixture of IVIg and PLEX, and some may not have access to either. So, some people are offered another type of immunosuppressant instead of IVIg or PLEX. To reflect this, the EAG preferred to use a 'basket' of standard care as the comparator. Within this blended comparator, some people have:

- IVIg (plus corticosteroids and immunosuppressants)
- PLEX (plus corticosteroids and immunosuppressants), or
- corticosteroids and immunosuppressants only.

The EAG explained that the company's consideration of IVIg and PLEX as standalone comparators did not reflect current treatment of refractory gMG in the NHS. The EAG also explained that data on the proportion of people having each treatment from the efgartigimod Early Access to Medicines Scheme (EAMS) would be relevant for this evaluation (Dionísio et al. 2024). The EAG noted that, although 'refractory' was defined slightly differently, people in the efgartigimod EAMS were comparable to the population who would have rozanolixizumab in the NHS. The EAMS cohort included 48 people with refractory gMG in the NHS. At the time of starting efgartigimod:

- 43.8% were having long-term IVIg (plus corticosteroids and immunosuppressants)
- 14.6% were having long-term PLEX (plus corticosteroids and immunosuppressants)
- 41.6% were having only corticosteroids and immunosuppressants.

After consultation on the draft guidance, the company said that the only relevant comparators were IVIg and PLEX. It said it did not agree that the standard-care basket was a relevant comparator for rozanolixizumab. It added that it had clinical expert advice that rozanolixizumab would replace IVIg and PLEX. The company also said that a freedom of information request, which 30 UK neuroscience centres responded to, showed that all of the centres had access to IVIg and 83% had access to PLEX. It said a pairwise comparison with IVIg or PLEX was the only appropriate analysis. The company provided a scenario analysis comparing rozanolixizumab with a standard-care basket but informed by a revised EAMS population. This is because it thought that the full EAMS population included some people who had non-refractory gMG, and did not entirely match the proposed target population for rozanolixizumab. The company also noted that the EAMS population did not include anyone with anti-MuSK antibody-positive gMG. To

address the issues it saw with the full EAMS population, the company revised the proportions of people having IVIg, PLEX, and corticosteroids and non-steroidal immunosuppressive therapy (NSIST) in the model. It did this by removing people from the EAMS cohort who:

- were not considered to have refractory gMG
- were not having treatment (so would not be eligible for rozanolixizumab because it is licensed as an add-on treatment), and
- were having corticosteroids only (who would likely try an NSIST before starting rozanolixizumab).

This left 35 people, so the company added 2 people who were on corticosteroids only to bring the number up to 37 (to match the number of people with refractory gMG). The company said this was a conservative assumption. Its revised EAMS cohort was a smaller population than the full EAMS cohort (n=48) and comprised:

- 56.7% having long-term IVIg (plus corticosteroids and NSIST)
- 18.9% having long-term PLEX (plus corticosteroids and NSIST)
- 24.4% having only corticosteroids and NSIST.

The EAG noted that the composition of the basket affected important parameters in the economic model. These included response rates, change from baseline in MG-ADL score, and treatment and administration costs, because these are calculated as weighted averages based on basket composition. The EAG preferred to use the standard-care basket, with proportions informed by the full EAMS population. This is in line with the committee's preference at the first committee meeting, and with the ongoing NICE technology appraisal of zilucoplan for treating antibody-positive gMG. Clinical experts said that rozanolixizumab would be offered to people who were having regular IVIg or PLEX, or for whom these treatments would be considered. They also noted that rozanolixizumab could be suitable for some people who could not have IVIg or PLEX because of side effects or because they were ineffective. A patient expert explained that PLEX had worked for them after IVIg had not worked, but PLEX had to be stopped after they

developed a life-threatening blood clot. The committee confirmed its decision from the first meeting that the standard-care basket was the most appropriate comparator. This was particularly because it did not want to exclude anyone with refractory gMG who would otherwise be considered for IVIg or PLEX but could not have them because of side effects or lack of efficacy. Having agreed that the standard-care basket was the appropriate comparator, the committee discussed which was the most appropriate EAMS population for the proportions in the standard-care basket. The clinical experts acknowledged that the criteria in EAMS were broader than those that would determine who would be offered rozanolixizumab. But they also noted that although only 77% of people in the full EAMS population gave refractory disease as a reason for starting targeted treatment, more than 1 reason could be given. So, this did not mean that the other people necessarily had non-refractory disease. The clinical experts noted that the broad consensus was that the EAMS should be for people who had uncontrolled disease after 2 standard treatments (average in the EAMS data, 2.6 NSIST). They said a small number (n=12) had had only 1 standard treatment and that this had been because of, for example, side effects. They also pointed out that most people in the study had had MG for more than 10 years and around 60% had had regular IVIg or PLEX. The clinical expert said that it was difficult to define refractory disease precisely. The committee noted the 2025 ABN guidelines defined refractory MG as 'highly active disease that has not responded to standard treatment with at least two steroid-sparing agents, or those ineligible/intolerant to these agents, those with frequent acute severe exacerbations and those who depend on regular IVIg/plasma exchange'.

The committee took account of the company's concerns about the comparability of the full EAMS population to the population that would have rozanolixizumab. But it noted the further reduced sample size of the revised EAMS cohort. The committee had concerns about the approach the company had used in its proposed revision of the EAMS cohort, which increased rather than decreased uncertainty. It also noted that the EAMS population was similar to the definition of refractory disease in the 2025 ABN guidelines. It recalled the question around rituximab's position in the treatment pathway for gMG (see section 3.4) noting the consensus that it would be used early in the pathway, before IVIg or PLEX. So, the committee concluded that the most appropriate comparator was a basket of standard care, excluding rituximab,

with proportions informed by the full EAMS cohort (n=48). The committee agreed to consider the uncertainty associated with the EAMS cohort proportions in its decision making.

Clinical effectiveness

MycarinG

3.6 MycarinG was a phase 3, randomised, multicentre, double-blind, placebo-controlled trial. It recruited adults with gMG who:

- had positive serology for anti-AChR or anti-MuSK antibodies
- had an MGFA class of 2 to 4a
- had an MG-ADL score of 3 or more
- had a Quantitative Myasthenia Gravis (QMG) score of 11 or more, and
- were being considered to have additional treatment (such as IVIg or PLEX).

The 200 people included in the trial were randomised as follows:

- 66 people to the licensed weight-based dose of around 7 mg/kg
- 67 people to the placebo arm
- 67 people to a higher unlicensed dose of around 10 mg/kg.

The 10 mg/kg dose is not relevant to this evaluation and only data from the 7 mg/kg arm informed the clinical effectiveness estimates for rozanolixizumab. People in the other 2 arms also continued to have standard treatment with corticosteroids and immunosuppressants. MycarinG consisted of a 6-week treatment phase, followed by an 8-week observation period in which people did not have rozanolixizumab. In the treatment phase, people had either 6 once-weekly subcutaneous infusions of rozanolixizumab or placebo as an add-on to standard care, which comprised 1 treatment cycle. The post-hoc refractory subgroup of relevance to this evaluation was defined

as uncontrolled disease despite standard treatment, specifically 2 or more previous gMG treatments, excluding acetylcholinesterase inhibitors. The primary outcome was change in MG-ADL score (a higher MG-ADL score shows more severe symptoms) from baseline to day 43. From baseline to day 43, rozanolixizumab was associated with a greater reduction in MG-ADL score compared with placebo in both the whole trial population and the refractory population. Compared with placebo, rozanolixizumab was also associated with a greater response rate, defined as 2.0 or more points change from baseline. The exact numbers for the refractory population are considered confidential by the company so cannot be reported here. The anti-AChR and anti-MuSK antibody-positive subgroups were prespecified. The EAG noted that the results for change in MG-ADL in these 2 prespecified subgroups were also generally consistent with those of the overall study population. The committee noted that evidence showed that rozanolixizumab was associated with a reduction in mean MG-ADL scores in people with gMG from baseline to day 43 within 1 treatment cycle. But it thought that the treatment effect may be overestimated because the chosen timing of outcomes assessment in MycarinG may have been the optimal time to assess the best response. Also, people in MycarinG only had 6 weeks of treatment, so the treatment effect of rozanolixizumab in the longer term is uncertain. The committee concluded that rozanolixizumab as an add-on to standard treatment is more effective at improving MG-ADL score than continuing standard treatment alone. But it said that the treatment effect may be overestimated and is uncertain in the longer term.

MG0007

3.7 MG0007 was an open-label extension trial that included people who had participated in other rozanolixizumab trials. People could enter MG0007 if they had entered or completed the observation period of MycarinG, and:

- required rescue therapy (limited to IVIg or PLEX) during the observation period of MycarinG, or
- had completed at least 6 visits in MG0004 (a discontinued extension study of MycarinG).

MG0007 had no placebo arm, so people were randomised to either the licensed dose of around 7 mg/kg or the unlicensed dose of around 10 mg/kg of rozanolixizumab. Rozanolixizumab was administered once-weekly in 6-week treatment cycles. The 6 once-weekly cycles were repeated as needed. There was a consistent and clinically meaningful reduction (more than 2.0) in MG-ADL score from baseline to day 43 in both arms within the treatment cycles assessed. The proportion of people with MG-ADL response at day 43 of each treatment cycle was also consistent in both rozanolixizumab trial arms within the treatment cycles reported. The exact results of this trial are considered confidential by the company so cannot be reported here. During consultation on the draft guidance, the company provided further data from the final results of the extension phase of MG0007. The EAG said that these results support the efficacy of rozanolixizumab and noted that no new safety concerns were raised. The committee concluded that MG0007 provided useful evidence of rozanolixizumab's long-term effectiveness but noted that this was uncertain because of the lack of a comparator arm.

Minimal symptom expression

3.8 During consultation on the draft guidance, the company provided additional data from MycarinG and MG0007 for minimal symptom expression (MSE). MSE was defined as an MG-ADL score of 0 or 1 and was reported for people who had an MG-ADL score of 0 or 1 in any (at least 1) treatment cycle. (The number of cycles in the trial is considered confidential by the company so cannot be reported here.) The clinical experts explained that MSE is a clinically relevant outcome and the best marker of a high-quality response because it means that people have few or almost no symptoms. But they said that not everyone has MSE and a response above MSE may still be a good outcome. A patient expert explained that every 1-point change in MG-ADL made a huge difference to quality of life. But they acknowledged that the MG-ADL did not reflect the variety of gMG symptoms well. The EAG noted uncertainty about how MSE was presented. It explained that reporting whether people had MSE at any point does not distinguish between brief and sustained MSE, or show if it occurred earlier or later in treatment. The EAG agreed MSE was clinically relevant, but it considered

that more detail on the timing and duration of MSE would help interpretation. The committee agreed that there was uncertainty about how MSE was reported. So, it requested further analyses about the distribution of MSE events among participants and treatment cycles.

After the second committee meeting, the company provided further data about the distribution of MSE events and other MG-ADL score ranges. The company provided the proportions of people having MSE from cycles 1 to 13 among:

- people who had MG-ADL response (2-point or more improvement in MG-ADL score) at day 43 of cycle 1, and
- all participants (safety set).

The EAG noted that the MSE rates were similar whether response was achieved during the first cycle or not. It also noted that the range of response rates appeared broad but that this was likely because of small sample sizes in later cycles. The committee noted that the proportion of people with MG-ADL response having MSE was consistent across cycles. But it also noted the uncertainty associated with the reduced sample sizes in later cycles. The committee questioned why some people who did not have MG-ADL response in the first cycle had MSE in subsequent cycles. The clinical experts explained that some people whose disease does not respond to treatment in the first cycle may go on to have response in subsequent cycles. For some people, it may take multiple cycles to have a response. The clinical experts also said that lack of response in the first cycle does not necessarily affect the depth of response in subsequent cycles. The committee noted the clinical and patient expert input about the clinical relevance of MSE and the relationship between MSE and MG-ADL response. The committee concluded that MSE is a clinically relevant outcome but noted that the data was uncertain because of the small sample sizes in later cycles. For the committee discussion on how MSE was incorporated into the model see section 3.11 and section 3.12.

Generalisability

3.9 In its submission, the company positioned rozanolixizumab for people with

refractory gMG who tested positive for either anti-AChR or anti-MuSK antibodies (see section 3.3). The EAG noted that people with refractory gMG were only a subgroup of the MycarinG population. It was concerned that the outcomes observed in the whole MycarinG population may not be generalisable to the refractory population that would have rozanolixizumab in the NHS. But clinical advice to the EAG suggested that the baseline characteristics of the whole MycarinG population approximated the baseline characteristics of the refractory population in the NHS that would be considered for IVIg or PLEX. This is because the MycarinG eligibility criteria included having or being considered for IVIg or PLEX, meaning that the overall trial population is likely to reflect a refractory population. The clinical experts also considered that refractory gMG is expected to respond to rozanolixizumab as well as non-refractory gMG. This is because treatments like rozanolixizumab have a novel mechanism of action, which people with refractory gMG will not have previously tried and to which their gMG may respond. The EAG explained that MycarinG mainly included people who tested positive for anti-AChR antibodies, with only a minority who tested positive for anti-MuSK antibodies (placebo, n=8, 11.9%; rozanolixizumab 7 mg/kg, n=5, 7.6%). The EAG explained that the overall trial population approximates the relative proportions of people who test positive for anti-AChR antibodies or anti-MuSK antibodies in the NHS. But it added that there is uncertainty about the efficacy outcomes for people who test positive for anti-MuSK antibodies because of the very small number of people in this subgroup. The clinical experts explained that there are some differences in the way that anti-AChR antibody-positive and anti-MuSK antibody-positive gMG responds to treatments. In particular, anti-MuSK antibody-positive gMG responds better to treatment with PLEX. The clinical experts also explained that it is reasonable to assume that anti-MuSK antibody-positive gMG might respond slightly better to rozanolixizumab than anti-AChR antibody-positive gMG. But this was uncertain because of the very small number of people who test positive for anti-MuSK antibodies. The committee concluded that the outcomes of the whole-trial population in MycarinG could be representative of the refractory gMG population in the NHS. It also concluded that the outcomes of the whole-trial populations in MycarinG could be generalised to those with anti-MuSK antibody-positive gMG. This is because it is reasonable to assume that rozanolixizumab is at least as effective in this group as in people with anti-AChR antibody-positive gMG.

Indirect treatment comparisons

3.10 For the first committee meeting, the company did network meta-analyses (NMAs) and matching-adjusted indirect comparisons (MAICs) to estimate the comparative effectiveness of rozanolixizumab. NMAs were provided for MG-ADL change from baseline and MG-ADL response (at least a 2-point reduction in MG-ADL score), but only for comparisons with zilucoplan and efgartigimod. These were not relevant comparators at the time of evaluation (see section 3.5). The company also did an unanchored MAIC for rozanolixizumab and IVIg. But this was limited because MG-ADL scores were not available and QMG scores were used instead, which did not inform the economic model. No indirect comparisons were provided for PLEX. The EAG thought that the unanchored MAIC for IVIg was not informative. It also noted that the company did not provide the requested systematic literature review to identify additional evidence, such as single-arm studies or phase 2 trials, for IVIg or PLEX. The clinical experts noted that there may be very few randomised controlled trials on IVIg or PLEX that could be used to inform the networks for indirect treatment comparisons. But it did agree with the EAG that it might be useful to include phase 2 trials or single-arm studies. The EAG suggested that it may also be possible to explore real-world evidence sources and cohort studies reporting outcomes for IVIg or PLEX. The EAG also noted that imputation techniques could be used to map the results from different reported outcomes to the MG-ADL outcomes relevant to this evaluation. The committee asked the company to provide more evidence on IVIg or PLEX and MG-ADL or other outcomes. It also asked the company to explore other indirect treatment comparison methods to inform relative treatment effects and adjust for potential placebo effects.

After consultation on the draft guidance, the company provided a new systematic literature review with 3 new observational studies on PLEX. The EAG identified several limitations of the 3 new observational studies included in the NMA, and disagreed with their inclusion. But it noted that the response results from the NMAs remained the same whether the studies were included or not. The EAG said that it believed the company had identified all relevant studies of IVIg and PLEX.

The company updated its indirect comparison analyses using bivariate NMAs and baseline risk-adjusted NMAs. The bivariate NMAs combined MG-ADL and QMG

outcomes to 'borrow' strength across correlated endpoints. This helped reduce uncertainty and informed initial response in the company's economic model (see section 3.13). But the EAG noted that the bivariate NMA did not adjust for heterogeneity in placebo responses across trials. It also could not fully account for differences in baseline risk between studies. As a result, while the bivariate NMA clarified the direction of effect and showed that rozanolixizumab (but not IVIg) was statistically significantly superior to placebo, the robustness of these estimates remained uncertain. The EAG also noted that no firm conclusions about PLEX could be drawn because of a lack of data.

The baseline risk-adjusted NMAs attempted to correct for placebo response heterogeneity by incorporating baseline risk into the model. But the EAG noted that the results were not statistically significant, suggesting limited ability to resolve uncertainty about the extent of placebo response heterogeneity. So there was still uncertainty about the importance of placebo response heterogeneity. But, the EAG said it believed the company had investigated this as thoroughly as possible. The committee noted that the credible intervals for the baseline risk-adjusted NMAs for MG-ADL response were very large. This was most likely because they were informed by implausibly large prior distributions. Because of this, it considered that the baseline risk-adjusted NMA did not sufficiently adjust for placebo response heterogeneity or baseline risk.

The committee considered that the bivariate NMA provided a clearer understanding of the outcome of interest (MG-ADL). It also showed that rozanolixizumab was an effective treatment for refractory gMG, although the size of the benefit was unclear. The committee was reassured by comments from patient experts explaining that treatment with targeted immunotherapy was a substantial improvement on treatment they had previously experienced. The committee concluded that the bivariate NMA results were acceptable for decision making. It noted that all relevant evidence had been included but that the results were uncertain.

Economic model

Company's modelling approach

3.11 The company used a cohort state transition model to estimate the cost effectiveness of rozanolixizumab against the comparators. The model included 7 health states. People start in the 'uncontrolled' health state. They then transition to the 'response' health state if they meet the treatment response criteria (a decrease of 2.0 or more in MG-ADL score) at the response assessment timepoint. People with MG-ADL response are further divided into 3 health substates:

- continued response (originally defined as an MG-ADL score that continues to improve after the response assessment, but in the company response to the draft guidance this was changed to people who had MSE)
- stable response (defined as an MG-ADL score that remains stable after the response assessment. The proportion of people in this health state was estimated as the proportion of responders who did not have MSE or loss of response)
- loss of response (the same rate was applied to all treatment arms based on the proportion of people who would be expected to lose response to treatment, according to clinical opinion).

  Within each health state (except death), people in the model can transition to the 'exacerbation', 'myasthenic crisis' or 'death' states. Once people reach a response health substate, they stay in that health state unless they experience an exacerbation or myasthenic crisis, or die. The model has a cycle length of 2 weeks and a time horizon of 52.5 years. The EAG said that the model structure was appropriate and reflective of the patient pathway. The committee accepted the model for decision making but identified the following limitations:

- People cannot move between response health states.
- The approach to modelling costs and benefits of all subsequent treatments is based on assumptions of what the next treatment would be after the initial

treatment for refractory gMG, not the full treatment sequence. That is, the proportion of people having PLEX, IVIg or corticosteroids and NSISTs alone as subsequent treatments remains the same, irrespective of how many subsequent treatments are tried (see section 3.13).

- The risk of transition to myasthenic crisis or exacerbation is the same regardless of quality of response to treatment (see section 3.18).

In future, the committee would prefer to see a model capturing the sequence of each subsequent treatment for refractory generalised myasthenia gravis that a person would have over the course of their life. The committee said that this could allow for more accurate modelling of the costs and benefits of subsequent treatments in the NHS (see section 3.13) and reflect methodological advances in modelling treatment sequences. But the committee accepted the model for decision making.

Treatment response rates

3.12 For the first committee meeting, the company estimated MG-ADL response rates for rozanolixizumab, zilucoplan and efgartigimod using results from the NMA. It adjusted for differences in placebo response by converting odds ratios to relative risks and applying these to a referent placebo response rate. The EAG thought that this approach was uncertain and noted that the referent response rate appeared implausible because placebo responses varied widely across trials. For IVIg and PLEX, the company used data from Barth et al. (2011), which reported QMG outcomes rather than MG-ADL and did not provide confidence intervals or standard errors. The EAG preferred to use trial arm data from MycarinG, RAISE and ADAPT for targeted treatments and clinical advice for IVIg and PLEX.

During consultation on the draft guidance, the company updated its economic model to include response rates for rozanolixizumab, IVIg, PLEX, and standard care only (corticosteroids and NSIST). It also incorporated MSE from MycarinG and MG0007 (see section 3.8). The rates of initial response (an improvement of 2.0 points or more in MG-ADL score) came directly from the bivariate NMA results (see section 3.10). The EAG also used the bivariate NMA to estimate response in its base case.

The proportions in the 3 response substates were determined as follows:

- continued response substate (rozanolixizumab and standard care only with corticosteroids and NSIST): MSE rate from MycarinG and MG0007 (for standard care only this was based on the placebo arm in MycarinG and for rozanolixizumab this was the mean proportion of people having MSE across all 13 cycles in MycarinG and MG0007)
- continued response substate (IVIg and PLEX): estimated from expert elicitation
- continued response substate (standard-care basket): weighted average of placebo MSE data from MycarinG and IVIg and PLEX from expert elicitation
- loss of response substate (all treatments): estimated from expert elicitation
- stable response substate (all treatments): the proportion not in either of the other 2 substates.

The company considers the response rates and the proportion of people in each response substate confidential so they cannot be reported here. The committee noted the uncertainty around using MSE to inform the continued response substate (see section 3.8). It also noted that that there was a substantial change in the proportions of people with continued response rates between models submitted for the first and second committee meetings (between which the definition of continued response changed). The committee noted uncertainty around how the response substates were modelled, including:

- The proportion of people having MSE in the rozanolixizumab arm was based on the average proportion who had MSE at any point across all cycles of MycarinG and MG0007. So, the model may not adequately capture when people have MSE or the extent to which MSE is sustained over time.
- Expert elicitation had been used to estimate that a lower proportion of people with MG-ADL response having IVIg or PLEX had MSE than people with MG-ADL response having rozanolixizumab. The clinical experts at the third committee meeting said that there was a lack of empirical evidence to support this assumption. But they explained that clinical experience of using

PLEX and IVIg indicated that more people would be expected to have MSE on rozanolixizumab than existing treatments. The committee concluded that it was plausible that there may be a difference in the proportion of people with MG-ADL response having MSE between the rozanolixizumab arm and the standard-care basket arm. But it added that the size of the difference was uncertain and may be overestimated. It also concluded that scenarios provided by the company showed that assuming an equal proportion of people with MG-ADL response having MSE across treatment arms had a moderate effect on the incremental cost-effectiveness ratio (ICER).

- Based on expert elicitation, a proportion of people were assumed to lose response, independent of treatment or the quality of the response. The clinical experts stated that people tend to have a maintained response with targeted treatments (like rozanolixizumab). They noted that having an infection may impact response to rozanolixizumab, but normally people have a maintained response to targeted treatments. The clinical experts also said that, in clinical practice, response is more likely to be lost with IVIg or PLEX treatment compared with targeted treatment (such as rozanolixizumab). The committee said that there was no empirical evidence presented to estimate differential rates of loss of response across treatment arms. But it concluded that assuming equal loss of response was likely to be a conservative modelling assumption.

The committee also concluded that:

- It was appropriate to use MSE to inform the continued response state because best clinical response should align with best modelled response.
- Given the available evidence, the company's approach to estimating MSE and loss of response was acceptable. But the committee noted the substantial uncertainty in using expert elicitation to inform the proportion having MSE for IVIg and PLEX, and to inform loss of response for all treatments.
- Although uncertain, it was plausible that people having MSE will have a disease course that corresponds to the continued response health state. It was also plausible that fewer people with MG-ADL response having IVIg and PLEX would have MSE than rozanolixizumab. But the estimated extent of benefit was uncertain and likely to be a favourable assumption to

rozanolixizumab.

Subsequent treatments

3.13 Over time, people in the model return to the 'uncontrolled' health state and have only corticosteroids and NSISTs. The company's original model, discussed at the first committee meeting, did not account for any future use of IVIg or PLEX for people who stop either rozanolixizumab or the comparator treatments. The EAG thought it likely that if gMG does not respond or loses response to a targeted treatment, people with the condition would change to an alternative treatment. At the first committee meeting, statements from the patient and clinical experts explained that gMG requires lifelong management. The clinical experts noted that they would consider IVIg or PLEX for people who stop rozanolixizumab. They explained that if someone's refractory gMG did not previously respond to a particular treatment they would not use it again. So, there may be differences in the choice and proportion of subsequent treatments in the rozanolixizumab and comparator arms. The committee noted that, if recommended, rozanolixuzumab would be an additional treatment option for refractory gMG. So, it recognised that there would be more subsequent treatment options available after recurrence of symptoms on rozanolixizumab than there are after recurrence on the current treatment options. The committee concluded that it would like to see the company include subsequent treatments in the economic model.

After consultation on the draft guidance, the company submitted an updated model that included costs and benefits from subsequent treatments, including IVIg, PLEX, and standard care (corticosteroids and NSISTs). It asked 9 clinical experts via a Delphi panel (a structured communication technique to get consensus from a group of experts) to say what treatments they would offer after IVIg and PLEX. It then applied the proportions from this survey to the revised EAMS population (see section 3.5) to estimate the proportions of people having IVIg, PLEX and standard care (corticosteroids and NSIST) as further subsequent treatments. The company preferred to use the same proportions (estimated from applying the survey estimates to the revised EAMS population) in both treatment arms. This was because it considered that these would become similar over a person's lifetime as people had repeated subsequent treatments. The company's preferred distribution of subsequent treatments for both the rozanolixizumab and

standard-care basket arms was:

- IVIg: 14.05%
- PLEX: 35.73%
- standard care only (corticosteroids and NSIST): 50.22%.

For modelling subsequent treatment in the standard-care basket arm, the EAG preferred to apply the treatment proportions for IVIg and PLEX from the Delphi panel to the proportions of the full EAMS cohort. The EAG noted that the company had assumed that a small proportion of people would have IVIg or PLEX retreatment. This was based on feedback from some clinical experts on the Delphi panel. The EAG noted that most clinical experts on the Delphi panel said that 0% of people would have IVIg or PLEX retreatment, so it preferred to exclude IVIg and PLEX retreatment. The EAG's preferred distribution of subsequent treatments for the standard-care basket arm was:

- IVIg: 8.2%
- PLEX: 27.16%
- standard care only (corticosteroids and NSIST): 64.64%.

For modelling subsequent treatments in the rozanolixizumab arm, the EAG preferred to use proportions of the full EAMS cohort. This was because it considered that this represents what people have without the availability of rozanolixizumab. The EAG's preferred distribution of subsequent treatments for the rozanolixizumab arm was:

- IVIg: 43.8%
- PLEX: 14.6%
- standard care only (corticosteroids and NSIST): 41.6%.

The committee considered the company's and EAG's approaches to modelling subsequent treatments. It noted that varying the proportion of people having IVIg or PLEX as subsequent treatments had a large impact on the ICER. It also noted the large amount of variation in responses from clinical

experts on the company's Delphi panel. At the third committee meeting, the clinical experts said that it was difficult to estimate the distribution of subsequent treatments after rozanolixizumab or standard care because of the rarity of the condition. They noted that the proportion of people having standard care only (corticosteroids or NSIST) as subsequent treatments seemed high in both the company's and EAG's approaches. This was because they would expect people to try IVIg or PLEX unless the condition did not respond to either of these. The clinical experts also noted that they expect the use of PLEX to increase, and the use of standard care only (corticosteroids or NSIST) to decrease in the future, citing the 2025 ABN guidelines. The clinical experts also explained that they may offer IVIg or PLEX retreatment if an exacerbation or a myasthenic crisis was not caused by the initial treatment failing. They may also offer retreatment to people who have had both IVIg and PLEX if there is a benefit in retrying the treatment that previously provided the best response.

The committee noted the substantial uncertainty associated with modelling subsequent treatments. It considered the clinical expert comments that the estimates of people having standard care only (corticosteroids and NSIST) seemed high, but that alternative evidence-informed estimates to the EAMS dataset or Delphi panel were not available. The committee was also aware that the company used the same proportions of subsequent treatments in the modelled standard care comparator basket and rozanolixizumab arms because it expected that the proportions would become similar over time. The committee noted that the proportions the company had used reflected the expected proportions after an initial treatment with the standard-care basket, not with repeated subsequent treatments. For consistency, the committee thought it was appropriate to use an estimate that represented the next treatment after rozanolixizumab. But the committee noted that it was a major limitation that a full treatment sequence could not be modelled. But, it would consider scenarios assuming equal proportions of subsequent treatments in both arms in its decision making. The committee noted that assuming the same proportions of subsequent treatments in both arms increased the ICER. The committee recalled the discussion about whether it was appropriate to use the full or revised EAMS population (see section 3.5) and concluded that the same population should be used for modelling subsequent treatments. For modelling subsequent treatments in the

standard-care basket arm, the committee preferred to apply the Delphi panel proportions to the full EAMS cohort and include IVIg and PLEX retreatment. The committee's preferred distribution of subsequent treatments in the standard-care basket arm was:

- IVIg: 10.8%
- PLEX: 27.74%
- standard care only (corticosteroids and NSIST): 61.46%.

For modelling subsequent treatments in the rozanolixizumab arm, the committee agreed with the EAG's approach of using the full EAMS cohort without applying the Delphi panel proportions. This was because the full EAMS cohort represents what people have without the availability of rozanolixizumab, and so is likely to represent what people have after rozanolixizumab. The committee's preferred distribution of subsequent treatments in the rozanolixizumab arm was:

- IVIg: 43.8%
- PLEX: 14.6%
- standard care only (corticosteroids and NSIST): 41.6%.

Response assessment timepoint

3.14 For the first committee meeting, the company selected the response assessment timepoints from the zilucoplan, efgartigimod and rozanolixizumab trials (12, 10 and 6 weeks, respectively) and used an assumption for IVIg and PLEX (6 weeks). The EAG noted that clinical advice suggested it would be reasonable to assess all interventions at 6 weeks. So it chose to use the response assessment timepoint of 6 weeks for all treatments in its analysis. The clinical experts explained that treatment response assessment for IVIg and PLEX is typically done much earlier than 6 weeks, usually at 2 or 3 weeks. So, they explained that 3 weeks would be more appropriate to assess for a response. The committee noted that there appeared to be inconsistencies in clinical opinion on the most appropriate timepoint for the response assessment of IVIg and PLEX. It concluded that a

response assessment timepoint of 3 weeks reflected NHS practice for IVIg and PLEX, but an assessment timepoint of 6 weeks was appropriate for rozanolixizumab.

After consultation on the draft guidance, the company updated its base case with response assessment timepoints of 6 weeks for rozanolixizumab and 3 weeks for IVIg and PLEX. But the EAG noted that the timepoint for the standard-care basket was 12 weeks. It changed this to 3 weeks for the standard-care basket in its base case, given that it includes IVIg and PLEX. The committee agreed and concluded that the response assessment timepoint for the standard-care basket should be 3 weeks.

Utility values

3.15 Health-related quality of life data was captured in MycarinG through the EQ-5D-5L. EQ-5D-5L scores were mapped to the EQ-5D-3L in line with the NICE reference case. Utility values based on EQ-5D scores from MycarinG were used in a regression model and fitted for everyone in the trial. Changes in utility depended on the person's baseline EQ-5D score and MG-ADL score. The model applied disutilities for exacerbations and myasthenic crises, sourced from REGAIN for eculizumab. The committee noted that the company's model did not apply disutilities for adverse events, because the company noted that there were no serious adverse events with an incidence of 5% or more in MycarinG. The model also did not apply disutilities for caregivers. The EAG noted that the company's approach to modelling utilities was appropriate. The committee thought that there may be uncaptured benefits on adverse events associated with rozanolixizumab and asked the company to provide scenarios that consider these.

After consultation on the draft guidance, the company used proxy data from lupus and asthma studies to estimate a utility decrement for corticosteroid-related adverse events. This was incorporated into the updated model to reflect the benefits of corticosteroid sparing. The EAG excluded this utility decrement in its base case, in line with the committee preference to account for this benefit qualitatively in the ongoing NICE technology appraisal of zilucoplan for treating antibody-positive gMG. The committee noted that the company's estimates used

in the model were based on lupus and asthma, a different condition to gMG. It concluded it would take account of any corticosteroid-sparing benefit qualitatively in its decision making (see section 3.22).

Costs

Treatment costs for IVIg and PLEX

3.16 At the first committee meeting, the company's model applied treatment costs for IVIg every 3 weeks and for PLEX every 4 weeks. The EAG received clinical advice that, in the NHS, IVIg and PLEX are typically given every 4 to 8 weeks. Sometimes the interval between treatments is extended to 12 weeks or, rarely, 16 weeks. The clinical experts at the committee meeting noted that treatment intervals of 8 weeks or longer are not common and that 4 weeks is more typical. The committee noted that IVIg and PLEX might be expected to be given every 6 weeks in the NHS and this is included in the EAG's base case. But it concluded that IVIg and PLEX costs should be applied every 4 weeks for consistency with the evaluation of zilucoplan.

After consultation on the draft guidance the company updated the dosing frequency so it was every 4 weeks for both IVIg and PLEX. The EAG tested how the ICER changed if people had fewer PLEX sessions per treatment cycle in a scenario analysis. This was to reflect that it might vary, based on individual people's needs and response to treatment. The EAG noted that people had 5 sessions of PLEX every 4 weeks in the company's base case, but the PLEX administration cost was set to £0 in the revised model. The EAG used the NHS reference cost SA44A – Single Plasma Exchange, Clinical Immunology Service (National Schedule of NHS Costs 2023 to 2024), applied 5 times every 4 weeks. After the third committee meeting, it was noted by the NICE team responsible for assessing budget and resource impact that the cost per administration may have been overestimated by the EAG. Multiple unit cost estimates for the administration of elective PLEX are available on the National Schedule of NHS Costs. There was uncertainty around the administration costs of PLEX. The committee concluded it was appropriate to apply IVIg and PLEX costs every 4 weeks, and to include administration costs for IVIg and PLEX. It took the

uncertainty around the administration costs of PLEX into account in its decision making.

Corticosteroid management

3.17 After consultation on the draft guidance, the company did a scenario analysis using costs of corticosteroids from Lee et al. (2018), while using Stirnadel-Farrant et al. (2023) to inform corticosteroid costs in its base case. It highlighted limitations with Lee et al., including that:

- there is no data on adverse events for people not having corticosteroids
- the severity of adverse events is not specified
- costs according to corticosteroid dose were not included.

The EAG preferred to use Lee et al. This is because it was in gMG (Stirnandel-Farrant et al. is in systemic lupus erythematosus) and it was accepted by the committee in the ongoing NICE technology appraisal of zilucoplan for treating antibody-positive gMG. So the EAG used Lee et al. data to inform the corticosteroid costs in its base case. The EAG also noted that the management costs in the continued response health states for IVIg and PLEX differed to those for rozanolixizumab. It preferred to use the same costs for all treatments in the continued response health state. The committee thought that the EAG's approach to add corticosteroid management costs to all treatments equally was appropriate. It concluded that corticosteroid costs informed by Lee et al. and applied equally for rozanolixizumab, IVIg and PLEX in the economic model was appropriate.

Exacerbation and myasthenic crisis costs

3.18 After the second committee meeting, the EAG noted that the cost of an exacerbation was lower in the rozanolixizumab arm than the standard-care basket arm. It also noted that the cost of a myasthenic crisis was slightly higher in the rozanolixizumab arm than the standard-care basket arm. Varying these costs had a large impact on the ICER. The committee requested clarification from

the company on the difference in these costs between treatment arms.

The company confirmed that the same rates of exacerbation and myasthenic crisis were applied to both treatment arms. It also confirmed that the same length of stay in hospital was assumed in both arms. But it clarified that costs for an exacerbation or a myasthenic crisis were different between treatment arms because of assumptions about the acute treatments used for an exacerbation or a myasthenic crisis. It said that these were dependent on the treatment people were having when these clinical events happened. The company had received clinical advice that PLEX would be used to treat an exacerbation or myasthenic crisis for people who were having IVIg, and vice versa. So, it assumed that 100% of people having IVIg would have PLEX as an acute treatment for an exacerbation or myasthenic crisis, and vice versa. But for people having rozanolixizumab or standard care only (corticosteroids and NSIST), it assumed that 73% would have IVIg and 27% would have PLEX for an exacerbation. For myasthenic crisis, it assumed 5% would have IVIg and 95% would have PLEX. This meant that the composition of acute treatments used for an exacerbation or myasthenic crisis differed between the rozanolixizumab and standard-care basket arms, which led to differing costs. The EAG said that it considered the company's approach to be appropriate. It noted that the clinical experts it had consulted did not highlight concerns with the company's assumptions for exacerbation and myasthenic crisis rescue treatment. The committee noted that in the model people are predicted to experience multiple exacerbations and that, once someone has an exacerbation, they move into the 'uncontrolled' health state. This means that people in the rozanolixizumab arm stop having rozanolixizumab after the first exacerbation. The committee noted that, although it was plausible that there may be a difference in cost between arms for the first exacerbation, it would expect the cost of subsequent exacerbations to be the same. So, the committee preferred to assume equal costs of an exacerbation or myasthenic crisis based on the assumed costs for rozanolixizumab in both treatment arms of the model.

Cost of IVIg

3.19 After the third committee meeting, the company noted that, since this evaluation had started, a new NHS framework for immunoglobulin products had been implemented by the Medicines Procurement and Supply Chain (MPSC). (See the

Immunodeficiency UK webpage on changes on immunoglobulin product supply in 2025.) This includes a number of formulations of IVIg. The committee noted that the cost of IVIg varied between products on the framework. The MPSC prices are confidential and cannot be reported here. The committee thought it was important that the cost of IVIg reflected the cost paid by the NHS through the MPSC. The committee also noted that the procurement of IVIg is done centrally, and that decisions on IVIg procurement are driven by factors including supply chain, availability and cost. In line with NICE's manual on technology appraisal and highly specialised technologies guidance, the committee agreed it was appropriate to consider cost-effectiveness results using the lowest price of IVIg, the highest price of IVIg and the midpoint value from the formulations available on the MPSC framework. The committee thought it was appropriate to use the midpoint MPSC cost for IVIg for decision making because it was likely to represent the cost of IVIg in the NHS.

Uncertainties and preferred assumptions

3.20 The committee noted the high level of uncertainty in the evidence and modelling, specifically that:

- The treatment effect of rozanolixizumab may be overestimated because of the chosen timing of outcomes assessment in the trial and uncertainty in the longer term (see section 3.6 and section 3.7).
- The comparative effectiveness of rozanolixizumab against IVIg and PLEX in terms of response is highly uncertain (see section 3.10 and section 3.12).
- The proportion of people having each treatment in the comparator basket is uncertain (see section 3.5). Increasing the proportion of people who have PLEX and decreasing the proportion of people who have corticosteroids or NSISTs increases the likelihood that rozanolixizumab is cost effective.
- The model structure may have limitations (see section 3.11).
- Using MSE to inform treatment response rates in the model is uncertain (see section 3.12).
- Using expert elicitation to inform MSE for IVIg and PLEX, and to inform loss of

response for all treatments, is uncertain (see section 3.12).

- The modelling of subsequent treatments is highly uncertain (see section 3.13). Assuming equal proportions of subsequent treatments in both modelled arms increased the ICER.
- The administration cost of PLEX was uncertain (see section 3.16).

The committee's preferred assumptions for the modelling were to:

- model the comparator as a basket of standard care, with the full EAMS population used to inform treatment proportions (see section 3.5)
- use the bivariate NMA to inform treatment response (see section 3.10)
- use the company's approach at the second and third committee meetings (based on MSE) to model the proportions of people in the continued response, stable response and loss of response substates (see section 3.12)
- in the rozanolixizumab arm, model subsequent treatments using the full EAMS cohort (see section 3.13)
- in the standard-care basket arm, model subsequent treatments by applying the Delphi panel proportions to the full EAMS cohort and include IVIg and PLEX retreatment (see section 3.13)
- use a response assessment timepoint of 6 weeks for rozanolixizumab and 3 weeks for the standard-care basket (see section 3.14)
- apply IVIg and PLEX administration costs every 4 weeks (see section 3.16)
- use corticosteroid costs informed by Lee et al. (2018) and applied equally for rozanolixizumab, IVIg and PLEX (see section 3.17)
- exclude the corticosteroid disutility but consider this qualitatively in decision making as an uncaptured benefit (see section 3.15 and section 3.22)
- assume equal exacerbation costs and myasthenic crisis costs in both the rozanolixizumab and standard-care basket arms (see section 3.18).
- use the midpoint value of the MPSC price range of IVIg (see section 3.19).

Other factors

Equality

3.21 The committee noted the variation in access to IVIg and PLEX across the NHS. It noted comments from patient and clinical experts on potential equality issues. They highlighted that to have IVIg or PLEX, people must either live near a hospital or have the means to travel to one regularly. The committee agreed that this was not an equality issue with regards to protected characteristics under the Equality Act 2010, and access to treatments or specialist centres cannot be addressed within technology appraisal recommendations. But it said that it is important to consider variability in access to PLEX and IVIg and potential uncaptured benefits of rozanolixizumab (see section 3.22). The committee considered that gMG may have a different burden on women than men. gMG is more prevalent in women, women are typically younger at disease onset, and women with gMG typically have higher mortality. The committee agreed that differences in the prevalence of a disease cannot normally be addressed in a technology appraisal recommendation. Also, pregnancy may contraindicate some types of treatment. The clinical experts said that women, trans men and non-binary people who are pregnant, or want to become pregnant, have limited options because current treatments are contraindicated, and steroids can affect fertility. They said that the improved disease control with rozanolixizumab may help people become healthy enough to be able to start a family. The summary of product characteristics for rozanolixizumab does not say that it is contraindicated in pregnancy but that it 'should only be considered if clinical benefit outweighs the risks'. Sex, maternity and pregnancy are protected characteristics under the Equality Act 2010. Because its recommendation does not restrict access to treatment for some people over others, the committee agreed these were not potential equality issues.

Uncaptured benefits

3.22 The committee considered whether there were any benefits of rozanolixizumab that were not captured in the quality-adjusted life year (QALY) calculation. The patient experts noted that treatment with IVIg or PLEX was time-consuming and

required regular hospital stays. They thought that rozanolixizumab, as a short-duration subcutaneous infusion, would be more convenient and could improve adherence. The committee heard from the company that it has a homecare service that helps people self-administer rozanolixizumab at home, which could reduce the need for people to travel to hospital for treatment. The patient expert stated that such a homecare service is an important benefit for people whose gMG is refractory, who may not live close to hospital and where there is variability in access to IVIg and PLEX. They also noted the negative impact on mental health of coming into hospital for current treatments for some people, and that the availability of a homecare service could improve mental health in this situation. The clinical experts noted how resource intensive IVIg and PLEX are to administer. They also explained that people who have rozanolixizumab may be able to reduce their corticosteroid dose. They said that this could lead to fewer corticosteroid-related adverse effects. The committee recalled its preference to take account of any corticosteroid-sparing benefit qualitatively in its decision making (see section 3.15). The committee noted that the patient experts said that people who cannot have PLEX or IVIg have a particular unmet need for treatments. They also noted that people with anti-MuSK antibodies have an unmet need for targeted treatments. The committee recalled comments from clinical and patient experts that gMG can have a substantial burden on carers of people with the condition. But it noted that the company did not provide sufficient evidence about the potential impact of rozanolixizumab on the health-related quality of life of carers. The committee recalled its preference in the ongoing NICE technology appraisal of zilucoplan for treating antibody-positive gMG to include a disutility for IVIg and PLEX, based on the mode of administration. But it noted that the company did not include this disutility in its base case or as a scenario analysis for this evaluation. The committee thought it was plausible that there may be an uncaptured benefit associated with subcutaneous administration compared with intravenous infusion. But evidence had not been presented to substantiate this. The committee concluded that some benefits of rozanolixizumab may not have been captured in the QALY calculation. These include the potential benefits of a treatment that could be delivered within a homecare service, the potential for corticosteroid sparing and the unmet need. The committee took account of these when deciding which ICER range would be a cost-effective use of NHS resources (see section 3.23).

Preferred ICER threshold

3.23 NICE's manual on technology appraisal and highly specialised technologies guidance notes that, above a most plausible ICER of £25,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects, including uncaptured health benefits. Because of confidential commercial arrangements for rozanolixizumab and some of the comparators, the exact cost-effectiveness results are confidential and cannot be reported here. The committee recalled the high level of uncertainty around the cost-effectiveness results (see section 3.20). But it also noted the high unmet need and the uncaptured benefits of rozanolixizumab (see section 3.22). NICE's manual on technology appraisal and highly specialised technologies guidance says that when evidence generation is particularly difficult because, for example, a medicine is for a rare disease, the committee may be able to accept a higher degree of uncertainty when making recommendations. The committee acknowledged the difficulty of generating evidence for gMG, taking into account the uncertainties in the company's clinical evidence and model assumptions. It decided that an acceptable ICER would be towards the upper end of the range NICE considers a cost-effective use of NHS resources (£25,000 to £35,000 per QALY gained). Using the committee's preferred assumptions (see section 3.20), the most likely cost-effectiveness estimates were within the range that NICE considers value for money.

Conclusion

Recommendation

3.24 The committee considered that the cost-effectiveness estimates presented by the company and the EAG were highly uncertain. But the committee considered that, given its preferred assumptions and based on the analysis it had seen, the cost-effectiveness estimates were likely to be within the range that NICE considers a cost-effective use of NHS resources. The committee concluded that

rozanolixizumab, as an add-on to standard treatment, can be used for treating refractory gMG in adults who test positive for anti-AChR or anti-MuSK antibodies if:

- the condition is classified as MGFA class 2 to 4a, and
- the condition is uncontrolled after 2 or more treatments, excluding acetylcholinesterase inhibitors, and
- IVIg or PLEX would otherwise be offered or has been tried and stopped because of side effects or because it did not work well enough.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 Section 4f of The Innovative Medicines Fund Principles states that a discretionary source of early funding (from the overall Innovative Medicines Fund budget) is available for certain medicines recommended by NICE. In this instance, interim funding has been agreed for rozanolixizumab. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has generalised myasthenia gravis that is positive for anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibodies, and the healthcare professional responsible for their care thinks that rozanolixizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 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 B.

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.

Chair

Charles Crawley
Chair, technology appraisal committee B

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, a project manager and an associate director.

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Technical leads

Yelan Guo, Caron Jones and Mary Hughes
Technical advisers

Jeremy Powell

Project manager

Emily Crowe
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