NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Efgartigimod for treating chronic inflammatory demyelinating polyneuropathy

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using efgartigimod in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: April 2026

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using efgartigimod in the NHS in England.

For further details, see NICE’s technology appraisal and highly specialised technologies guidance manual.

The key dates for this evaluation are:

- Closing date for comments: 18 May 2026
- Second evaluation committee meeting: 23 July 2026
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Efgartigimod should not be used to treat progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) in adults after corticosteroids or immunoglobulins.

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 healthcare professional consider it appropriate to stop.

What this means in practice

These are NICE's draft recommendations. If these recommendations become final, efgartigimod would not be required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because there is not enough evidence to determine whether efgartigimod is value for money in this population.

Why the committee made these recommendations

Usual maintenance treatment for CIDP is immunoglobulins, after treatment is started with either corticosteroids or another immunoglobulin.

Clinical trial evidence suggests that efgartigimod reduces the risk of relapse compared with placebo. But it is uncertain how well efgartigimod may work in clinical practice because the trial population does not reflect the population that would have efgartigimod in the NHS. Indirect treatment comparisons with immunoglobulins are highly uncertain but suggest that efgartigimod might work as well as these.

There are uncertainties in the economic model, including:

- the assumptions on:
  - how immunoglobulins are used in NHS clinical practice
  - how often people would take efgartigimod
- a key assumption that efgartigimod works as well as immunoglobulins is not included.

Because of the uncertainties in the economic model, it is not possible to determine the most likely cost-effectiveness estimates for efgartigimod. So, efgartigimod should not be used.

2 Information about efgartigimod

Marketing authorisation indication

2.1 Efgartigimod (Vyvgart, Argenx) is indicated for 'the treatment of adult patients with progressive or relapsing active chronic inflammatory demyelinating polyneuropathy (CIDP) after prior treatment with corticosteroids or immunoglobulins'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of efgartigimod is £15,307.47 for a pre-filled 5-ml syringe containing 1,000 mg of efgartigimod (200 mg per ml; excluding VAT, sourced from company submission).

2.4 The company has a commercial arrangement. This makes efgartigimod available to the NHS with a discount and it would have also applied to this indication if efgartigimod had been recommended. The size of the discount is commercial in confidence.

Sustainability

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for Argenx will be included here when guidance is published.

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 Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare, debilitating acquired neurological disorder that causes muscle weakness and sensory disturbances, resulting in fatigue, pain and disability. The exact causes of CIDP are unknown, but it involves the immune system damaging the myelin sheath of peripheral nerves. It is a clinically heterogeneous disease, with typical and variant types. Common symptoms depend on the type but often include motor and sensory deficits, causing problems in mobility, numbness, paraesthesia (pins and needles) and pain, which can impact quality of life. The patient experts explained that their experience of living with CIDP varies. They mentioned that CIDP impacts all aspects of their life, causing physical and emotional issues. They explained that people with CIDP having immunoglobulins go through a cycle with fluctuating symptoms. They have treatment and start to feel better, but the effects of treatment can wear off and symptoms can return until the next treatment is given. They noted that even though CIDP does not usually shorten an individual’s life, it has a large impact on how they live day to day. They also highlighted that current treatments can be stressful and emotionally challenging, particularly because of their administration, such as intravenous treatments. They added that it can be hard to plan their lives and some struggle to have stable relationships because of constant ups and downs. They also explained that carers, who are often the family members of people with CIDP, also feel the impact of the condition themselves. The clinical experts explained that around 20% to 25% of people with CIDP have “brain fog” as a side effect of current treatment. The patient and clinical experts explained that the current treatments do not work for all and that some people have no treatment because of side effects or lack of response. They explained that existing treatments (see section 3.2) need repeated hospital visits, intravenous access, frequent blood monitoring, and prolonged periods away from work and family. The patient and clinical experts highlighted that because efgartigimod can be administered at home, it may be more convenient than other treatment options. The committee concluded that people with CIDP, their carers and healthcare professionals would welcome a new treatment option. The committee noted that living with CIDP is physically, mentally and emotionally challenging. It concluded that CIDP is a highly heterogeneous condition with debilitating symptoms and there is a substantial unmet need for effective treatment for this condition.

The treatment pathway

3.2 There are no NICE-recommended treatments for CIDP. Usual care is treatments to improve function, maintain stability, prevent relapse and enable independence. These include corticosteroids, immunoglobulins and plasma exchange (PLEX). Treatment decisions are informed by the European Academy of Neurology and Peripheral Nerve Society (EAN/PNS) guideline on diagnosis and treatment of CIDP. Treatment initially involves induction treatment, aimed at gaining rapid control over disease activity. Either intravenous immunoglobulin (IVIg) or corticosteroids are recommended as an induction treatment for most people with CIDP, while IVIg is often recommended for motor CIDP. If the CIDP responds to induction treatment, maintenance treatment is used to maintain stable levels of disease control, avoid relapse and optimise long-term function. These include IVIg, subcutaneous immunoglobulin (SCIg), corticosteroids and PLEX. The choice of maintenance treatment is based on disease severity, comorbidities and availability of the treatment. Immunoglobulins are the most used maintenance treatment and are usually favoured over corticosteroids because of a faster treatment response and fewer long-term adverse effects. IVIg is the most common form of immunoglobulin administration, but SCIg is more suitable for people who need only low-dose or low-frequency immunoglobulins to achieve stable disease control. But the availability of SCIg is limited in many centres at present. The clinical experts explained that corticosteroids and PLEX are rarely used for maintenance treatment. Corticosteroids are associated with risks, such as adverse events and lack of long-term benefits. PLEX is associated with adverse events, often followed by relapse, and is only available in specialised units. The clinical experts explained that treatments are chosen according to individual risk profile, disease severity, local infrastructure availability and patient preference. They explained that not all treatments are available at every centre and there is variation in practice. Only some centres have access to SCIg or PLEX, or both. The EAG also explained that most people in clinical practice have immunoglobulins for maintenance treatment and that corticosteroids and PLEX are rarely used. The committee acknowledged that several treatments are available for CIDP. These involve induction then maintenance treatments, and the choice of treatments is based on multiple factors. It noted that immunoglobulins are the treatment option that is used most often.

Clinical evidence

3.3 The company's submission included evidence from 2 clinical trials, ADHERE and ADHERE+. ADHERE was a multistage, phase 2, open-label, randomised-withdrawal, double-blind, placebo-controlled trial. It included people who had pulsed or oral corticosteroids and IVIg or SCIg, or IVIg or SCIg only, within the previous 6 months and who were willing to stop this treatment. It used a randomised withdrawal method and comprised 2 stages:

- Stage A was an open-label, single-arm treatment phase with efgartigimod. Before entering ADHERE, people had a screening period for up to 4 weeks, during which their CIDP was assessed as definite or probable. During the run-in period, people stopped their previous CIDP treatment and those who had a clinically meaningful deterioration were eligible to progress to stage A. Clinically meaningful deterioration was defined as a 1 or more point increase on the adjusted Inflammatory Neuropathy Cause and Treatment score (aINCAT) scale, a decrease of 4 points or more on the Inflammatory Rasch-built Overall Disability Scale (I-RODS), or a decrease in mean grip strength (MGS) of 8 kilopascal or more. After screening and the run-in period, eligible people entered stage A and had efgartigimod for up to 12 weeks. People needed to have at least 4 doses of efgartigimod and have evidence of clinical improvement (ECI) at 2 subsequent consecutive weekly visits in stage A to be eligible for stage B.

- Stage B was a double-blind, randomised withdrawal phase. Only people with confirmed ECI in stage A were eligible to enter stage B. In stage B, people were randomised to have weekly efgartigimod or placebo for up to 48 weeks or until relapse.

ADHERE+ is an ongoing, single-arm, open-label, phase 2 extension study for people from ADHERE. People were eligible if they had completed week 48 of the double-blind stage B of ADHERE, had clinical deterioration during stage B or discontinued early once sufficient events for the primary endpoint in ADHERE were reached and the trial had concluded. The committee noted that only people who had ECI with efgartigimod in stage A were eligible to progress to stage B of ADHERE. It also noted that the results of stage B of ADHERE reflected only people whose disease responded to efgartigimod, rather than the wider CIDP population. It thought this may have resulted in an overestimation of treatment effects and an underestimation of adverse events with efgartigimod compared with placebo (see section 3.6). It concluded that these were key clinical uncertainties that it would take into account in its decision making.

Population

3.4 The marketing authorisation for efgartigimod is for treatment of progressive or relapsing active CIDP after prior treatment with corticosteroids or immunoglobulins. But in its submission, the company positioned efgartigimod for a narrower population, which included people who have had prior unsatisfactory treatment with immunoglobulins. It defined unsatisfactory as people who:

- have a high burden of immunoglobulin treatment, defined as:
  - having had at least 6 months of treatment with either IVIg or SCIg, which has had a significant impact on their daily life, work or caregiving responsibilities and who remain symptomatic, or
  - needing high doses or a high frequency of immunoglobulins to continue to have treatment benefits and avoid variation in symptoms between doses; or
- are intolerant or refractory to immunoglobulins, defined as being unable to continue immunoglobulin treatment because of comorbidities, adverse events or safety concerns, such as the risk of developing thromboembolism or heart failure. (The company notified NICE ahead of the first committee meeting that it is no longer seeking a recommendation for this subgroup.)

The EAG stated that the company's proposed population was not clearly represented by the ADHERE population (see section 3.6). It noted that ADHERE included people who pulsed corticosteroids, oral corticosteroids, IVIg or SCIg within the previous 6 months. It explained that only 51.2% of people in stage A and 43.4% in stage B had prior IVIg, SCIg or corticosteroids. It explained that it was unclear how many people met the company's high burden criteria, because, for example, they did not have a full 6 months of IVIg or SCIg treatment before having efgartigimod. The company acknowledged that there are some differences between ADHERE and its proposed population. It explained that the subgroup with prior IVIg or SCIg is generalisable to NHS clinical practice because this population meets NHS England’s immunoglobulin commissioning policy. It also stated that all people who entered ADHERE were symptomatic despite having immunoglobulin or corticosteroid treatment. The committee questioned how the ADHERE inclusion criteria relate to the company’s proposed population. The company clarified that, although the ADHERE population and the company’s population were different, there was a substantial overlap in their clinical characteristics. It explained that it had validated the proposed population with 5 UK clinical experts in its structured expert elicitation. The clinical experts stated that they are generally able to identify the population that has a high treatment burden and other comorbidities that prevent high doses of immunoglobulins. They explained that this population represents only a small proportion of the wider CIDP population. They explained that this population is likely to have a high aINCAT score and high disease impact. The clinical experts estimated that this would be around 10% of the overall CIDP population. The committee noted that there were several ‘or’ criteria in the company’s proposed population and was concerned that a large proportion of the CIDP population could be eligible, which may not be representative of the population modelled in the comparator arm. The committee was also concerned that some of the descriptions in the company’s proposed population were subjective, such as the definition of caregiving responsibilities. The committee also noted that the company’s proposed population stated ‘prior unsatisfactory treatment with immunoglobulins’, but this should state that the population should be having current treatment with immunoglobulins (because this was the population in the comparator arm of the company’s economic model). The committee noted that the population included in the clinical and economic evidence does not closely reflect the population that would be seen in NHS clinical practice. The committee also noted that the clinical and cost effectiveness of efgartigimod would depend on which population was considered in the economic model. It stated that the characteristics of this population should be clearly defined to enable efgartigimod’s use in the NHS. The committee requested that the company should refine its target population to make it easier to identify, less subjective and more reflective of the population included in the comparator arm. The committee noted that the company was no longer seeking a recommendation for people whose disease is intolerant or refractory to immunoglobulin. So, the committee concluded that immunoglobulins are the most relevant comparator for efgartigimod.

Outcomes

3.5 The EAG explained that the during the run-in period, people stopped efgartigimod and clinical deterioration was assessed using a range of outcomes. This included an increase in aINCAT score of 1 point or more, a decrease in I-RODS score of 4 points or more, and a decrease in MGS of 8 kilopascal or more. It explained that, during stage A, established clinical improvement was assessed using the same measures as those used during the run-in period. But relapse in stage B was assessed solely on the change in aINCAT score. The clinical opinion to the EAG suggested that aINCAT, I-RODS and MGS are used in combination rather than relying on 1 outcome alone. The EAG highlighted that, by using only the aINCAT score in stage B, some people may not have been classed as having relapse if they showed a decline in I-RODS score or MGS, but not in aINCAT. So, the EAG thought that using only aINCAT in stage B may have underestimated or overestimated the number of people who had relapse. The committee was aware that the clinical experts' statements highlighted that NHS England's immunoglobulin commissioning policy recommend clinical monitoring in CIDP with at least 3 disease-specific clinical outcome measures. The committee concluded that using only a change in aINCAT score was uncertain because it may have overestimated the treatment effect of efgartigimod or placebo in ADHERE. This was an uncertainty that it would take into account in its decision making.

Clinical trial results

3.6 The primary outcome of stage A was the percentage of people with confirmed ECI and the primary outcome of stage B was time to first aINCAT deterioration. The stage A results suggested that 66% of people had ECI with efgartigimod at the end of stage A. The stage B results suggested that efgartigimod significantly reduced the risk of relapse by 61% at week 48 compared with placebo. The EAG explained that of people having efgartigimod who had previously had IVIg or SCIg (the company's proposed population), 41% did not achieve ECI in stage B. It explained that CIDP will relapse in some people when they switch from immunoglobulin maintenance to efgartigimod, but this was not captured in the company's economic model. It also explained that, in ADHERE, only people with ECI with efgartigimod in stage A were allowed to enter stage B, rather than the wider CIDP population (see section 3.4). It noted that the company's model includes only people whose condition responded to efgartigimod in stage A and were randomised to stage B. The EAG highlighted that this may have overestimated the efgartigimod treatment effect and underestimated the adverse events. The clinical experts explained that, in clinical practice, people with CIDP having first-line treatment are assessed for evidence of clinically meaningful deterioration first and only people whose condition responds to the induction treatment have maintenance treatment. They explained that if people are symptomatic, they are treated accordingly (see section 3.2). People whose condition does not respond in a meaningful way are offered alternative treatments and response is assessed. The clinical experts agreed that ADHERE generally captures how induction and maintenance treatments are used in clinical practice. The committee noted that relapses occurred for some people having efgartigimod after switching from immunoglobulin maintenance in ADHERE. It was aware that the company included costs but not outcomes for this population. The committee thought that the relative treatment effect of efgartigimod came only from people whose condition responded to efgartigimod in stage A. It concluded that ADHERE may have overestimated efgartigimod's treatment effect. This was a key clinical uncertainty that it would consider in its decision making. The committee also noted it would also like to see a scenario which included costs and outcomes, for people who relapse during switching from immunoglobulin maintenance to efgartigimod.

Indirect treatment comparisons

3.7 There was no head-to-head evidence comparing efgartigimod with immunoglobulins, so the company did an indirect treatment comparison (ITC) using an anchored MAIC. The ITC was done for the outcome change in aINCAT score only. The company identified 4 trials (ADVANCE-CIDP 1, PATH, PIMPA and Katzberg [2013]) that reported a change in aINCAT score. After assessing study design, randomisation methods, concomitant treatment, and eligibility and discontinuation criteria, the company concluded that only ADVANCE-CIDP-1 was suitable for comparison with data from stage B of ADHERE. After population adjustment and matching for treatment effect modifiers and prognostic factors between ADHERE and ADVANCED-CIDP 1, the company's ITC results suggested the change in aINCAT from baseline was statistically significantly more favourable for efgartigimod than for SCIg. The EAG noted that an additional trial comparing IVIg with placebo (ICE), was identified in the company's literature searches. The EAG explained that ICE was included in the sensitivity analyses for the ITCs. It added that ADVANCE-CIDP 1 differed from ADHERE in trial design and placebo response, and had limited reporting of treatment effect modifiers. It thought that there was a lack of clear differentiation between prognostic factors and treatment effect modifiers in the company's ITC, and that a number of treatment effect modifiers (such as typical or atypical CIDP) could not be adjusted for. After weighting adjustment, the change from baseline in aINCAT score was greater in the placebo arm of ADHERE than in ADVANCE-CIDP 1. The EAG outlined that, for these reasons, the company's ITC was highly uncertain and may have overestimated the treatment effect of efgartigimod. The clinical expert statements submitted to NICE also noted that the ADHERE results suggested comparable efficacy to first-line standard care within a well-defined population of people with active, treatment-responsive CIDP. The committee was aware that the company also provided results of ITCs with ICE and PATH. It noted that some of the ITC results suggested non-statistically significant benefits of efgartigimod over both SCIg and IVIg. The committee understood there were challenges in evidence generation, given the limited trial data available for the proposed population. After considering the substantial key limitations associated with each comparison and the very high uncertainty in the evidence, it concluded that the ITC results were not robust and could not be used in decision making. The committee thought that a better approach would be to assume equal efficacy between efgartigimod and immunoglobulins, which would mitigate overestimation of efgartigimod treatment effect (see sections 3.5 and 3.6). So, it concluded that the economic model should assume equal efficacy between efgartigimod and immunoglobulins. It requested that the company update its economic model to provide an equal efficacy comparison between efgartigimod and immunoglobulins.

The company's model

3.8 The company presented a Markov model with time-varying transition probabilities. The health states were defined based on both disease severity and whether the disease was active or in remission. The health states were aggregated by aINCAT score into 5 categories: very limited impairment (aINCAT score of 0 or 1), mild impairment (aINCAT score of 2 or 3), moderate impairment (aINCAT score of 4 to 6), severe impairment (aINCAT score of 7 or 8), and very severe impairment (aINCAT score of 9 or 10). The active disease health states included all aINCAT categories, while the remission health states included very limited, mild and moderate impairment states. People could move between any 2 active disease health states based on transition probabilities specific to their current treatment. People could also move between active disease and the corresponding remission health state at the same rate for very limited, mild and moderate impairment, and independently of the treatment used. People entered the model in the active disease health states. The company's model had a lifetime horizon (45 years) and a 6-monthly cycle. The EAG thought the company's model structure, including health states, active disease, remission and relapse, was broadly appropriate. The baseline distributions of health states were informed by the ADHERE run-in period. The committee noted that people having efgartigimod were modelled to potentially enter remission after having maintenance treatment for at least 1 year. People having immunoglobulin were modelled to potentially enter remission health states from baseline. The per-cycle probabilities for remission and relapse were assumed to be the same, regardless of disease severity and treatment. The 6-month probability of relapse was estimated using the proportions of people:

- on a stable dose of immunoglobulin at any given time
- on a stable dose of immunoglobulin and who were willing and eligible to have a dependency test
- who successfully stopped immunoglobulin treatment after a dependency test and remained clinically stable for the next 6 months.

The committee was aware that when a person entered remission in the model, temporary withdrawal of treatment is assumed and treatment restarts when the condition relapses. The transition probabilities for remission and subsequent relapse were calculated based on Koay et al. (2025) and the company's structured expert elicitation. The committee noted that the proportion of people on a stable immunoglobulin dose was based on Koay et al. But, the proportions of people on a stable dose of immunoglobulin who were willing and eligible to have a dependency test and who successfully stopped immunoglobulin after a dependency test and remain clinically stable for the following 6 months was based on the company's structured expert elicitation. The committee noted that Koay et al. was a small study from 1 UK centre, in which only 12 out of 45 people met these criteria. Of

12 people who discontinued, 8 remained stable off-treatment for at least 12 months. The committee was also aware of the limitations of the company's structured expert elicitation (see section 3.10). It concluded that it would accept the company's inclusion of remission health states in the model, but it was uncertain what percentage of people would temporarily withdraw active treatment and for how long. It would like to see further evidence informing this.

Model cycle length

3.9 The company's base case used a 6-month model cycle length for the entire time horizon. It explained that the cycle length duration aligns with the standard intervals of assessing dose adjustments of immunoglobulin, while remaining short enough to capture changes in the aINCAT score from ADHERE. The EAG thought that a 6-month cycle would be too long to capture rapid changes in disease severity after starting a new treatment. It explained that using a 6-month cycle was incompatible with most of the ADHERE data used to inform the model. This was because of misalignment between the model and the timing of observations. The company explained that calculating transition probabilities when using the 3-month cycle approach results in less robust transition probabilities, because fewer data points were available to inform each transition probability matrix. It stated that it was not possible to model transitions to the remission health state from baseline in the comparator arm using the 3-month cycle length, and this could underestimate the benefits in the comparator arm. The clinical experts clarified that they would like to see people every 3 months if they were starting a new treatment. They agreed that they usually see people whose condition is stable or who are having maintenance treatment less frequently, around every 12 months. The committee noted that the choice of cycle length had a large impact on the EAG's base case. The EAG noted that when using a 6-month cycle length, a small change at the beginning of the model can result in larger impacts on cost effectiveness, particularly because of the limited movements between the health states. The committee concluded that the

EAG's choice of using a 3-month cycle for the first 2 years was more appropriate.

Use of immunoglobulin in clinical practice

3.10 There are several immunoglobulin products available in the UK, and dosing of these treatments can vary between people with CIDP. In the company's model, the proportions of people having IVIg and SCIg products were informed by an interim analysis from a UK chart review study that was sponsored by the company. This retrospective study collected the details of healthcare resource use of 69 people with CIDP across 4 NHS secondary care sites in England. It reported a split of 95% IVIg and 5% SCIg. The proportion of people on each dose of immunoglobulin was based on the company's structured expert elicitation. The EAG noted the company did not give any justification for using the interim analysis when the final analysis was also available. It thought that the split between IVIg and SCIg that was informed by the Immunoglobulin Database annual report and the final data-cut analysis was more appropriate (76.7% IVIg and 23.3% SCIg). The clinical experts explained that there is variation in the UK and that not all centres have consistent access to SCIg or are equipped to provide training for home administration. They mentioned that if SCIg is available, it is usually preferred but this involves more injections than IVIg administration. They explained that only around 30% of centres have the capacity to deliver SCIg. They mentioned that a survey on the use of immunoglobulin is ongoing with 33 centres in the UK. They highlighted that 66% of these centres have SCIg availability. The survey also shows that around 10% of people with CIDP have SCIg in clinical practice. They explained that the average immunoglobulin dose in clinical practice varies between 1.2 g per kg and 1.4 g per kg, with a median dosing frequency of every 4 weeks. The committee noted that the company used its structured expert elicitation to inform immunoglobulin dosing, whereas the EAG used the company's chart review dosing data. The clinical experts explained that an ongoing dose and frequency study is not yet complete but may be available soon. The committee noted that the chart review study had around 50% missing data, which may increase uncertainty in the results, but heard that missing data is common in NHS data collection. The committee concluded that the chart review better reflects clinical practice nationally than the structured expert elicitation, which had a wide range of clinical opinion. It also concluded that using a 90% IVIg and 10% SCIg split, and the chart review, was the most appropriate source to inform dosing. The committee would welcome further data from an updated analysis of the chart review, and other sources, for inputs in the model related to immunoglobulin use.

Treatment effectiveness data for severe health states

3.11 The company only used data for the first 96 weeks because data beyond this point was informed by fewer than 10 people. The transition probabilities were derived for 24-week time periods (approximately 6 months), in line with model cycles. The EAG explained that there were very few data points informing 24-week transition probabilities. It highlighted that there was no data to inform transitions out of a very severe health state and very limited data informed transitions out of the severe impairment health state. So, it preferred to assume that all people in the severe and very severe impairment health states remain in these health states indefinitely, regardless of whether they are having efgartigimod or immunoglobulin. The clinical experts explained that severe or very severe impairment health states are very rare in clinical practice and usually the disease at that severity level is resolved quickly. The committee concluded that the EAG's approach of assuming all people in severe and very severe impairment health states remain in these health states indefinitely was more appropriate, but it would consider alternative scenarios in an updated company model.

Treatment pathway after stopping efgartigimod

3.12 The proportions of people having each treatment after stopping efgartigimod were informed by the company's structured expert elicitation.

Some people who stopped efgartigimod and returned to immunoglobulin maintenance treatment were also assumed to stop this treatment during the first 18 months on treatment and were then assumed to proceed to the basket of alternative treatments. The EAG thought that the proportion of people restarting immunoglobulin treatment in the company's model after efgartigimod was implausibly low (31%). The EAG and NICE technical team also noted that the questions asked in the company's structured expert elicitation did not match the company's proposed population for efgartigimod and the model structure, therefore the results of the study were not reliable. The clinical opinion received by the EAG suggested that almost everyone would restart immunoglobulin after stopping efgartigimod, because it had been effective to some degree before switching to efgartigimod. So, the EAG assumed that 95% of people would restart immunoglobulin after efgartigimod. The company stated that, because its proposed population had a high burden of immunoglobulin use, they are unlikely to have immunoglobulin again for clinical or other reasons. The committee concluded that the economic model should assume that 100% of people return to immunoglobulin after stopping efgartigimod, which aligns with the population in the comparator arm of the model.

Comparator treatment effectiveness

3.13 In the company's model, the transition probabilities for immunoglobulin treatment were derived by combining the data for efgartigimod with the outcomes of the company's ITC comparing efgartigimod and immunoglobulin based on the ADHERE and ADVANCE-CIDP 1 trials. Based on these ITC results, the company assumed that 88% of people had a 1 point or more improvement in aINCAT score if they had efgartigimod, whereas the rest had the same response to efgartigimod and immunoglobulin. The company generated data for people who had a 1 point or more change in aINCAT from baseline if they had efgartigimod. The EAG thought that the company's ITC was not an appropriate source for model inputs. This was because the methodology was not robust, assumptions were flawed and the results of the ITC were highly uncertain (see section 3.7). It explained that a small number of data points were used to derive the transition probabilities, which contributes to the uncertainty of this approach. It also explained that the company's approach to deriving transition probabilities for comparator treatments relied on the assumption that the difference in change from baseline is the same, regardless of a person's aINCAT score. It thought this was clinically implausible, because it may be expected that efgartigimod would have a greater incremental effect for people with a greater disease severity at baseline than those with relatively mild disease. It explained that the company's approach was inappropriate because people entering the model in immunoglobulin maintenance (comparator arm) were already stable on treatment. Therefore, the company's modelling of early changes in severity and then long-term stability would not be consistent. So, it preferred to assume that people having immunoglobulin treatment from baseline would remain in the same aINCAT categories for the entire duration of the model's time horizon. The committee was aware that most people in the model having immunoglobulin maintenance treatment were stable. It concluded that it was not appropriate to model changes in a person's disease severity for a short period of time at the start of the time horizon and then assume that people do not move between aINCAT categories in the long term because of the assumed stability of treatment. It concluded that the EAG's approach that people having immunoglobulin maintenance treatments from baseline remain in the same aINCAT categories for the entire duration of the model time horizon more appropriate. The committee also recalled that it preferred to assume equal efficacy for efgartigimod and immunoglobulins, and this should be reflected in an updated company model.

Comparator discontinuation

3.14 The company's model implemented permanent discontinuation for efgartigimod and immunoglobulins in the first 18 months from baseline for reasons other than non-response. It then assumed that people did not permanently discontinue either treatment. Treatment discontinuation data for efgartigimod was sourced from ADHERE and ADHERE+. For people having immunoglobulin it included separate inputs for the probability of discontinuation from baseline to 6 months, and for 6 months to 18 months. The EAG thought it was not logically coherent to assume that people could stop immunoglobulin in the first few model cycles when they are having maintenance treatment, but not stop it after maintenance treatment. So, it thought that it was more appropriate to exclude all treatment discontinuation for immunoglobulin in the model. The clinical experts explained that if the condition responds to treatment and remains stable for 12 months, people will usually have a cessation trial in clinical practice. They explained that immunoglobulin is generally well tolerated but they would expect around 20% of people to have minor side effects, such as headache or rash. They explained that older people with additional risk factors, such as cardiovascular risks, are more likely to stop using IVIg. The committee noted that some people may stop immunoglobulin permanently because of adverse events or comorbidities. The committee concluded that the EAG's approach of excluding permanent discontinuation may be appropriate, but it would like to see scenarios in which a proportion of people stop immunoglobulin treatment over time. This is because this may more closely reflect clinical practice.

Adverse events

3.15 The company's model informed the duration of adverse events based on NICE's technology appraisal guidance on ozanimod for treating relapsing–remitting multiple sclerosis (TA706). If the duration of adverse events was not available, it assumed an average duration of 21.6 days based on an average of the durations of adverse events reported in TA706. The model also included complications related to intravenous administration for people having IVIg and PLEX based on a budget impact analysis of SCIg compared with IVIg in people with CIDP in the US (Mallick et al. 2023). The EAG noted that there was limited data to inform the frequency, costs and health-related quality of life impact of adverse events for any treatment included in the model. It explained that the durations of most of the adverse events were based on an average of all adverse events and did not reflect how long the event lasts or whether it is clinically plausible. It thought that the definitions were not consistent across treatments, mainly because of how data were reported for comparators and because the company used different inclusion criteria in the model. It also explained that most adverse events reported for treatments are mild or moderate. So, the EAG preferred to remove adverse events and complications related to intravenous administration from its base case. The clinical opinion to the EAG suggested that the NHS uses robust sterile techniques to administer intravenous treatments. The healthcare professionals delivering IVIg and PLEX are also well trained and experienced, so complications related to intravenous treatment are rare. The clinical experts explained that IVIg is mostly administered in a hospital, and around 20% of people have migraine or other adverse events, which are usually manageable. They explained that less than 1% of people have severe complications. The committee noted that most IVIg treatments are administered in hospital by trained staff, and few people suffer from IVIg-related adverse events. The committee concluded that the EAG's approach of removing adverse events and complications related to intravenous administration was appropriate.

Carer burden

3.16 The company's model included disutilities to represent the impact on carers' health-related quality of life. The company used disutilities from carers of people with multiple sclerosis because there was no available data for CIDP. The disutilities were sourced from NICE's highly specialised technology guidance on inotersen for treating hereditary transthyretin amyloidosis (HST9), which were based on Gani et al. (2008) using Expanded Disability Status Scale (EDSS) categories. The aINCAT categories used in the model were mapped to EDSS categories as follows based on comparable levels of impairment:

- an aINCAT score of 0 or 1 (very limited impairment) was mapped to EDSS score 0
- aINCAT scores of 2 to 6 (mild impairment or moderate impairment) were mapped to EDSS scores of 3.5 to 7.0
- aINCAT scores of 7 to 10 (severe impairment or very severe impairment) were mapped to EDSS scores of 7.5 to 9.5.

The company explained that it had discussed its approach with 6 healthcare professionals. It explained that they had agreed that motor disability from CIDP is comparable to the symptoms of multiple sclerosis and that carer involvement was likely to be similar. It explained that, based on HST9, the disutility applied was multiplied by the expected number of carers. People with very limited, mild or moderate impairment were assumed to have 1 carer and people with severe and very severe impairment were assumed to have 2 carers. The EAG explained that, in the company's qualitative workshop, 2 healthcare professionals mentioned that people with multiple sclerosis may have additional symptoms such as bladder and bowel dysfunction, which are not seen in CIDP, so may need different carer involvement. The EAG thought that mapping from aINCAT to EDSS scores was not appropriate because this approach was not validated with carers. It noted that, in the company's qualitative workshop, the healthcare professionals only agreed that an EDSS score of 7 or higher was functionally comparable to an aINCAT score of 9 or 10. It explained that the mapping of aINCAT scores of 7 or 8 to EDSS scores of 7.5 to 9.5 overestimates functional impairment, because people with EDSS scores of 7.5 to 9.5 are restricted to a wheelchair or bed. The EAG thought that the company's EQ-5D-5L data from 21 UK-based carers of people with CIDP in a cross-sectional observational survey of burden on informal carers was more robust. This reported a carer utility of 0.798. It explained that to estimate the impact of caring, it compared carer utility with general population norms reported in the Health Survey for England 2017 to 2018 for a similar age group, giving a utility of 0.8101 after adjusting for age and sex. The difference of -

0.0121 between these utility values was used as the carer utility decrement for all carers. The patient experts explained that carers are informal, and the amount of care is linked to the severity of the condition, which has an impact on the carer's own physical and mental health. A patient expert at the meeting explained that they occasionally need help from their partner but may need more help during fine motor activities (when numbness is an issue). But they explained that their partner takes on additional responsibilities to manage the household, which can make them tired or cause ill health, and can change their social life. The committee noted that most people with CIDP are generally able to manage their daily activities but a small number of people with very severe disease need assistance from carers. The committee noted that although the EAG's approach of applying a single average decrement to all carers may underestimate the impact in people with very severe disease and overestimate people with mild disease, it was reasonable because of the lack of data. It also noted that very few people were in the most severe health states in the economic model, which reflected clinical expert input at the committee meeting (see section 3.11). So, it concluded that the EAG's approach to carer disutilities was more appropriate and should be included in the economic model.

Biweekly dosing of efgartigimod

3.17 The summary of product characteristics for efgartigimod states that, based on clinical evaluation, the dose frequency can be reduced from weekly to every 2 weeks. In ADHERE+, people were eligible for biweekly dosing if they remained on treatment for a minimum of 24 weeks. The proportion who had biweekly dosing in ADHERE+ is considered confidential by the company and cannot be reported here. Clinical expert opinion to the EAG suggested that people are unlikely to switch to a less frequent dose if the condition is responding to the current dosing, but some people may choose to switch to biweekly dosing. The EAG also explained that there was a high proportion of people whose condition deteriorated at week 24 on biweekly dosing, but the condition restabilised in most of these on return to weekly dosing. It also explained that some people whose condition was stable and switched to biweekly dosing did not have a return to stable levels after a return to weekly dosing of efgartigimod. The clinical experts explained that, in clinical practice, they prefer to achieve as optimal a response as possible with the minimal dosing possible. They also explained that there is no reliable evidence available that suggests whose condition would remain stable on biweekly dosing. The committee noted that the proportions assumed to be on weekly or biweekly dosing have a large impact on the cost-effectiveness results. The committee concluded that there was uncertainty in how many peoples' condition would remain stable on biweekly dosing. The committee would like to see scenarios exploring a proportion of people switching from weekly to biweekly efgartigimod dosing, with a proportion returning to weekly efgartigimod dosing. The scenarios should also account for some people who experience worsening symptoms before switching back to weekly dosing.

Utility values

3.18 In the company's model, the health state utility values were informed by EQ-5D-5L data collected in ADHERE. In stage A, EQ-5D-5L was collected at baseline and weekly up to 12 weeks. In stage B, EQ-5D-5L was collected at baseline and every 4 weeks up to 48 weeks. The company mapped the EQ-5D-5L patient-level responses from ADHERE to EQ-5D-3L and pooled stages A and B to maximise the data. It used a mixed-effects model to estimate health state utility values from the mapped EQ-5D-3L data from ADHERE. The company estimated the following utility values for each health state:

- 0.851 for very mild impairment
- 0.630 for mild impairment
- 0.426 for moderate impairment
- 0.084 for severe impairment
- -0.216 for very severe impairment.

The EAG thought that the attrition rate of EQ-5D-5L responses from ADHERE in stages A and B was high. The EAG explained that the utility values for very severe health states lacked face validity and were too low. It also explained that average EQ-5D-5L domain scores were not low enough to have negative utilities for a very severe health state. Expert clinical opinion to the EAG suggested that people with very severe disease may have a poor health-related quality of life, but they would not have a health-related quality of life worse than death. It explained that the company's approach to the mixed-effects model was overly simplistic and it should have explored additional covariates such as age, sex, treatment and other prognostic factors. The committee questioned the face validity of the utility values of other health states because there was a large decrement for moving between any 2 health states. The clinical experts stated that CIDP is a unique condition that is treatment dependent, in that people feel better after treatment but experience fluctuating symptoms over time (see section 3.1). They explained that CIDP can become very unpredictable at late onset. The committee noted that the clinical experts broadly agreed with the utility values used by the company for most health states in the model. The committee noted the lack of data availability and the uncertainty around utility values. The committee did not consider the utility values used by the company to have face validity. The committee concluded that, in the absence of available data, it would also like to see proxy utility values from other conditions, such as multiple sclerosis, being explored.

Intravenous administration disutilities

3.19 The company's model included the disutility associated with intravenous treatment administration. It fitted a linear regression to utility values to estimate the disutility associated with intravenous administration, in-hospital administrations and the number of administrations per cycle, based on Jorgensen et al. (2017). The disutility for increasing length of infusion was based on Matza et al. (2013), which estimated utility values associated with route of administration and infusion duration for the general population in the UK. The company explained that vein depletion for people is also an issue associated with frequent intravenous administration. It applied a disutility per cycle of -0.114 associated with IVIg and -0.218 associated with PLEX. These included disutility associated with the intravenous administration route, disutility associated with the in-hospital setting, number of administrations and intravenous administration route per hour. The EAG thought that the disutilities applied may have been double counted, which overestimated the impact of intravenous administration. The clinical expert opinion to the EAG suggested that people feel reassured having treatment in a hospital, and that once they get used to their treatment it has a more limited impact on their health-related quality of life. The EAG agreed that some people may have vein depletion, which could be associated with frequent intravenous administration. So, it preferred to exclude all utility decrements associated with intravenous administration, except for baseline utility decrement (-0.021 for IVIg and -0.022 for PLEX). The committee was aware that most people having intravenous treatment in the NHS rarely have side effects or complications (see section 3.15). The committee concluded that the disutilities used in the EAG's approach were more appropriate for decision making.

Resource use

3.20 The committee noted that the company's model included the following health state resource use:

- transportation and disease monitoring
- GP consultation and mobility aids
- hospitalisations and adverse events
- professional caring.

The company assumed that 16% of people having immunoglobulin would need funded transport, but no transport costs were applied for efgartigimod because of the shorter treatment duration. It also assumed that SCIg is administered in a hospital over multiple days, and some people will have IVIg in an inpatient setting. It applied GP consultation costs for 1 hour, and the proportion of people needing a wheelchair and risk of hospitalisation (active disease) was taken from the Adelphi study (a linked healthcare professional and patient cross-sectional survey done in France, Germany, Italy, Japan, Spain, the UK and the US between September 2022 and April 2023). It combined the data corresponding to aINCAT scores of 7 to 10 for severe and very severe health states. It also assumed that professional care costs incurred for 9% of people with moderate impairment and 80% for people with either severe or very severe impairment, based on the Adelphi dataset. It applied intensive care unit (ICU) admissions based on multiple Healthcare Resource Group (HRG) codes. The EAG thought that the funded transportation cost should be applied to both arms because the duration of treatment is not linked to the ability to get to the hospital. It explained that the British Medical Association recommends a 15-minute consultation, so the EAG used the cost of a GP appointment based on a 10-minute consultation. The clinical opinion to the EAG suggested that the company's model underestimated the proportion of people with very severe impairment who need a motorised wheelchair. This is because disaggregated data (aINCAT 9 or 10) showed a higher need for mobility aid than for severe impairment (aINCAT 7 or 8). It also suggested that very few people with CIDP need professional care. The EAG explained that the company's survey showed that only 6.3% of people needed both informal and formal care and 12.7% had formal care. In the UK Adelphi study, only 1 person had a professional carer, and the company's survey of carers suggested 0% of people have formal care from a professional healthcare provider. The company's survey suggested low use of formal care and that, if professional care were needed, it would probably be about 5 hours per day for people with very severe disease who are confined to a wheelchair. So, the committee thought that applying professional care to all moderate and severe health states overestimates the resource use. Also, there was no available data on what percentage of people are confined to a wheelchair and who would have an NHS continuing healthcare package. The clinical experts suggested that most people stay in hospital for around 2 days for their treatment. The patient experts also explained that the GP consultation would last around 10 minutes if needed but they are usually seen by a nurse. They explained that the care people need is mostly informal (see section 3.16). They noted that only a small proportion of people with very severe disease need help with individual tasks, such as transport or visiting the hospital, and would need formal care packages. The committee noted that most GP consultations for adverse events last around 15 minutes. It noted that a very small proportion of people need formal care. The committee concluded that the EAG's approach of excluding formal care costs, using 10 minutes for a GP appointment and SCIg administration over 2 days (if given in hospital) was considered more appropriate. It also concluded that the Personal Social Services Research Unit (PSSRU) was a more consistent source for hospitalisation costs than multiple HRG codes with no professional carer costs applied, because it is based on NHS reference costs.

Cost-effectiveness estimates

Acceptable ICER

3.21 NICE's technology appraisal and highly specialised technologies guidance manual notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £25,000 per quality-adjusted life year (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. The committee noted the very high level of uncertainty, specifically:

- the generalisability of the ADHERE population to the company's proposed population (see section 3.4)

- the potential overestimation of treatment effectiveness from ADHERE (see section 3.5 and section 3.6)
- the ITC approach and the highly uncertain results (see section 3.7)
- a lack of data to inform the severe and very severe health states (see section 3.11)
- the proportion of people having immunoglobulin after efgartigimod (see section 3.14)
- the proportion of people switching to efgartigimod biweekly dosing (see section 3.17)
- the utility values used for all health states in the model (see section 3.18).

Because of these uncertainties, and the lack of analysis that assumed equal efficacy between efgartigimod and immunoglobulin, the committee could not determine a plausible ICER. It acknowledged there is an unmet need for new treatments (see section 3.1) and that the condition is rare, so it may be challenging to generate high-quality clinical trial evidence. The committee weighed up the very high uncertainty in the evidence, the rarity of the condition and the uncertainty in modelling assumptions. It concluded that, based on the current evidence submitted, an acceptable ICER would be towards the lower end of the range NICE considers a cost-effective use of NHS resources (that is, £25,000 per QALY gained).

The committee's preferred assumptions

3.22 The exact cost-effectiveness estimates cannot be reported here because of confidential discounts. The company's base-case ICER was within the range normally considered to be a cost-effective use of NHS resources. The EAG's base-case ICER was substantially above this range. The committee recalled its preferred assumptions to be as follows:

- using equal efficacy between efgartigimod and immunoglobulins in the model (see section 3.7)

- a 3-month model cycle length for the first 2 years from baseline and thereafter a 6-month cycle length (see section 3.9)
- a 90% IVIg and 10% SCIg split, respectively, and using the UK chart review to inform dosing (see section 3.10)
- 100% of people having immunoglobulin after stopping efgartigimod (see section 3.12)
- 20% of people stopping immunoglobulin over time (see section 3.14)
- excluding adverse events, including for intravenous administration, from the model (see section 3.15)
- the proportion of people needing care from the Adelphi study, with a maximum of 1 carer (see section 3.16)
- using utility values from proxy diseases, such as multiple sclerosis (see section 3.18)
- disutility associated with intravenous administration based on Jorgensen et al. (2017), with a maximum of 1 carer (see section 3.19)
- funded transport for both efgartigimod and immunoglobulins, a 10-minute GP consultation and the proportion of people needing a wheelchair disaggregated by aINCAT score (see section 3.20)
- no professional carer cost applied and ICU costs from the PSSRU (see section 3.20).

The committee concluded that when using its preferred assumptions that could be implemented in the model, the ICER was substantially above the range that NICE considers a cost-effective use of NHS resources. It noted that not all of its preferred assumptions were implemented, particularly the assumption of equal efficacy between efgartigimod and immunoglobins.

Additional analysis

3.23 The committee outlined the analyses that it would like the company to provide for the next committee meeting. In particular, it stated that it would need to see a model that assumed equal efficacy between efgartigimod and immunoglobulins (see section 3.7). The committee would also like to see further analyses and input on:

- a refined target population that is easier to identify, less subjective and more reflective of the population in the comparator arm (see section 3.4)
- a scenario, including costs and outcomes, for people who had relapse on efgartigimod after switching from immunoglobulin maintenance (see section 3.6)
- scenarios on a proportion of people temporarily withdrawing active treatment (see section 3.9)
- a 90% IVIg and 10% SCIg split and using the UK chart review to inform dosing and further data from an updated analysis of the chart review, and other sources, for inputs in the model related to immunoglobulin use (see section 3.10)
- a proportion of people discontinuing immunoglobulins over time (see section 3.14)
- scenarios exploring switching from immunoglobulins to efgartigimod (at the start of the model) and then to biweekly efgartigimod, with a proportion returning to weekly efgartigimod, including both costs and outcomes for these switches (see section 3.17)
- utility values from a proxy condition such as multiple sclerosis (see section 3.18).

Other factors

Uncaptured benefits

3.24 The committee considered whether there were any uncaptured benefits of efgartigimod. The company explained that some were not fully captured, including improved disease control, reduced treatment burden, greater workforce and community participation, and reduced work absence. It also stated that reducing the need for plasma-derived treatments may lead to reduced treatment and service burden, NHS system resilience and supply security. The EAG thought that several of these benefits were already captured in the company's model, for example, disease control and treatment burden, disutilities associated with intravenous treatment and informal carers. The committee acknowledged the benefits offered by efgartigimod and was aware that efgartigimod can be self-administered at home. It concluded that all the potential benefits of efgartigimod that were relevant for decision making had already been taken into account in the economic model.

Equality

3.25 One stakeholder suggested that many people with CIDP are considered disabled, so the impact on disability, especially in terms of access to a treatment that may reduce disability, should be considered. They also mentioned that most people with CIDP are generally older, so age may be a factor to consider in any decision making. The committee noted that its current recommendation applied to all groups. The company suggested that some people may decline blood products (such as intravenous immunoglobulins made from donated human plasma) because of religion or belief. The committee concluded that the company's positioning of efgartigimod (see section 3.4) was for people already having immunoglobulin, so it cannot consider this population in its decision making. No other potential equality issues were identified.

Conclusion

Recommendation

3.26 The committee's concerns about clinical evidence and modelling assumptions meant that it was unable to identify plausible cost-effectiveness results. It needs the uncertainties to be addressed, and an updated model and analysis will be considered at the next committee meeting. So, efgartigimod should not be used.

4 Evaluation committee members and NICE project team

Evaluation committee members

The highly specialised technologies evaluation committee is a standing advisory committee of NICE.

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

Paul Arundel
Chair, highly specialised technologies evaluation committee

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 or principal technical adviser.

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Alan Moore
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ISBN: [to be added at publication]