

Ozanimod for treating relapsing–remitting multiple sclerosis

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.

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Contents

1 Recommendations	4
2 Information about ozanimod	5
Marketing authorisation indication	5
Dosage in the marketing authorisation	5
Price.....	5
3 Committee discussion	6
Treatment pathway, population and comparators.....	6
Ozanimod clinical trials.....	11
Indirect treatment comparison.....	13
The company's cost–utility model	15
Cost-effectiveness estimates.....	19
Other factors	20
4 Appraisal committee members and NICE project team	21
Appraisal committee members	21
NICE project team	21

1 Recommendations

- 1.1 Ozanimod is not recommended, within its marketing authorisation, for treating relapsing–remitting multiple sclerosis in adults with clinical or imaging features of active disease.
- 1.2 This recommendation is not intended to affect treatment with ozanimod that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Disease-modifying treatments for relapsing–remitting multiple sclerosis include alemtuzumab, beta interferons, cladribine, dimethyl fumarate, fingolimod, glatiramer acetate, natalizumab, ocrelizumab and teriflunomide. Treatments aim to reduce the number of relapses, slow the progression of disability and maintain or improve quality of life.

Clinical trial evidence shows that ozanimod reduces the number of relapses and brain lesions compared with interferon beta-1a. However, ozanimod's effect on the progression of disability is unclear.

The cost-effectiveness estimates are higher than what NICE normally considers an acceptable use of NHS resources. Therefore, ozanimod is not recommended.

2 Information about ozanimod

Marketing authorisation indication

- 2.1 Ozanimod (Zeposia, Celgene) is indicated for 'the treatment of adult patients with relapsing remitting multiple sclerosis with active disease as defined by clinical or imaging features'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics](#).

Price

- 2.3 The list price for ozanimod is £1,373 per maintenance pack of 28 capsules, each containing 1 mg ozanimod hydrochloride (equivalent to 0.92 mg of ozanimod; excluding VAT; BNF online, accessed April 2021). The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The [appraisal committee](#) considered evidence submitted by Celgene, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

Treatment pathway, population and comparators

Ozanimod is likely to be used as a first- or second-line treatment for active relapsing–remitting multiple sclerosis

3.1 Ozanimod's marketing authorisation is for active disease, as defined by clinical or imaging features. The company explained that the ozanimod clinical trials included people who had active disease, defined as:

- at least 1 relapse within the past year **or**
- at least 1 relapse within the last 2 years and evidence of at least 1 gadolinium-enhancing lesion in the last year.

The company originally positioned ozanimod as a first-line treatment, stating that it was unlikely to be used for highly active or rapidly evolving severe disease. So, it chose the comparators for this appraisal accordingly (see [section 3.3](#)). The ERG agreed with the company's original positioning of ozanimod. At technical engagement the company updated its positioning of ozanimod to:

- a first-line treatment when infusion or injectable treatments are not suitable because of administration issues or when oral treatments are preferred **and**

- a second-line treatment when the disease has not responded to 1 or more infusions or injectable treatments.

However, highly active multiple sclerosis is often defined as disease that has inadequately responded to disease-modifying therapy. So, at its first meeting, the committee considered that the company's positioning of ozanimod as a second-line treatment implied it would be used for highly active disease. After consultation, the company again updated the positioning of ozanimod; to active rather than highly active disease and only for people who had 2 significant relapses in the last 2 years. It explained that this was based on clinical advice. The company also explained that these people would have ozanimod as a first-line treatment or if they need to switch to another first-line treatment because of tolerability issues. The committee noted that [NHS England's treatment algorithm for multiple sclerosis disease-modifying therapies](#) classes second treatments as first line when people switch because of tolerability rather than lack of efficacy. The clinical experts, whose views were sought at the committee's first and second meetings, agreed that ozanimod would be of value as a first-line treatment. However, they were concerned about the company limiting ozanimod to people who have had 2 relapses in the last 2 years. They explained that there are currently no oral first-line treatments for people who have only had 1 relapse in the last 2 years. Ozanimod could benefit this group, so the company's updated positioning was unnecessarily restrictive. The committee agreed with the clinical experts that ozanimod should not be restricted to people who have had 2 relapses in the last 2 years. The clinical experts also recognised that ozanimod would be a useful second-line treatment option to fingolimod, the only sphingosine-1-phosphate receptor (S1PR) modulator currently available for relapsing–remitting multiple sclerosis. Ozanimod is also an S1PR modulator, but first-dose cardiac monitoring is only required for people with pre-existing cardiac conditions starting ozanimod, in contrast to all people starting fingolimod. At consultation, patient organisations and patient experts reiterated that having another first- and second-line treatment option would offer people more choice. Also, having a wide range of options is important because of the varied nature of multiple sclerosis. The clinical experts explained that types of multiple sclerosis are not always clearly defined and other clinical factors are considered when helping people choose a treatment. The committee noted the complexity of the pathway, the company's changing position of ozanimod and the clinical experts' opinions. It concluded that ozanimod was likely to be used

as a first- or second-line treatment in the NHS for people with active relapsing–remitting multiple sclerosis.

It is not appropriate to limit the population to people for whom an oral treatment is suitable or who request an oral treatment

3.2 The population in the company's original submission was people with relapsing–remitting multiple sclerosis. Later the company restricted this population to include only people with active relapsing–remitting multiple sclerosis for whom an oral treatment is suitable or who request one. The committee accepted that the company added 'active' to define and update the population in line with ozanimod's marketing authorisation, which the European Medicines Agency granted after NICE received the company's submission. The company explained that it restricted the population to people for whom an oral treatment is suitable or who request one because it considered this is how it would be used in practice. It estimated that the oral drugs teriflunomide and dimethyl fumarate account for around half the market share of relapsing–remitting multiple sclerosis treatments, and ozanimod would most likely be used in their place. However, the NHS commissioning expert said that based on the available data, this market share was likely to be a significant overestimate. After consultation, the company provided survey results for the market shares of oral and injectable treatments for active relapsing–remitting multiple sclerosis to support its estimate. It also explained that oral treatments are preferred for active disease and people only have injectable treatments because of historical prescribing habits. The committee considered that if half the people with active disease are having oral treatments, the remaining half must be having injections or infusions. The clinical experts explained that it would be difficult to identify a group of people for whom only oral treatments are suitable. They agreed that many people would choose an oral drug over an injection or infusion, but highlighted that people often switch between treatments with different routes of administration. At consultation, patient organisations and patient experts stressed the benefits of ozanimod's oral route of administration, particularly that it would be easy to take. However, the patient experts also stated that there are many reasons why someone would change their mind about their treatment. People would not want to be excluded from having a treatment because

it was an injection or an infusion. But this might happen if the company restricted ozanimod to people for whom an oral treatment is suitable or who prefer one. The ERG had concerns about restricting the population, explaining that it was unclear what is meant by people for whom an oral treatment is suitable or who request one. The committee was concerned that restricting the population would reduce patient choice and exclude potential comparators that are routinely used in the NHS. It concluded that it was not appropriate to limit the population to people for whom an oral treatment is suitable or who request an oral treatment.

First- and second-line treatments for active relapsing–remitting multiple sclerosis, including ocrelizumab, are comparators

3.3 In its submission, the company included beta interferons (1a and 1b), dimethyl fumarate, glatiramer acetate, teriflunomide and peginterferon beta-1a as comparators. Alemtuzumab and ocrelizumab were included in the scope, but the company excluded them as comparators in its base-case analysis (although it provided analyses with them as comparators in an appendix) because:

- a safety review restricted the use of alemtuzumab to highly active disease, and ozanimod is not expected to be used in highly active disease

- NICE only recommends ocrelizumab when alemtuzumab is contraindicated or otherwise unsuitable.

However, clinical experts advising the ERG and the clinical experts at the meeting confirmed that ocrelizumab is being used as a first-line treatment for relapsing–remitting multiple sclerosis in the NHS. For the restricted population (see [section 3.2](#)), the company's comparators were dimethyl fumarate and teriflunomide, the only oral drugs used as first-line treatment for active relapsing–remitting multiple sclerosis. The ERG did not agree with the company restricting the population and limiting the comparators to only dimethyl fumarate and teriflunomide. The committee agreed with the ERG that all the company's original comparators plus ocrelizumab, but excluding alemtuzumab, were relevant comparators for first-line treatment. After consultation and at both committee meetings, the clinical experts explained that ozanimod could also be used as a second-line treatment for relapsing–remitting multiple sclerosis. That is, disease that has not responded to 1 or more disease-modifying treatments, for example as an alternative to fingolimod (see [section 3.1](#)). The company had supported this position at technical engagement, but later disagreed at consultation. The committee noted that [NHS England's treatment algorithm for multiple sclerosis disease-modifying therapies](#) suggests alemtuzumab, ocrelizumab, cladribine or fingolimod for this group. However, the committee considered that alemtuzumab was not a comparator because it was likely to be used for a population with more severe disease than ozanimod. Also, it has been associated with safety concerns so is only for people who have had a full and adequate course of at least 1 other disease-modifying agent. So, the committee considered ocrelizumab, cladribine and fingolimod to be relevant second-line comparators. The company did not provide comparisons against all relevant first- and second-line treatments after consultation. Instead it maintained that dimethyl fumarate and teriflunomide were the only comparators. The committee concluded that first- and second-line treatments used for active relapsing–remitting multiple sclerosis, including ocrelizumab, were comparators.

Ozanimod clinical trials

Baseline characteristics in the trials are generalisable to people in the NHS with active relapsing–remitting multiple sclerosis

3.4 The phase 3 trials RADIANCE part B and SUNBEAM compared ozanimod with interferon beta-1a. The trials had very similar designs, inclusion and exclusion criteria and outcomes, but differed in duration (RADIANCE part B had a 24-month follow-up period, whereas SUNBEAM had a 12-month follow-up period). The ERG considered that although the baseline characteristics of people in the trials were broadly generalisable to people having treatment in the NHS, there were some characteristics that may limit generalisability. For example, around 23% of people in the trials had highly active or rapidly evolving severe relapsing–remitting multiple sclerosis and around 30% had already had a disease-modifying therapy. The ERG explained that this was not in line with the company's positioning but would be less of an issue if ozanimod was likely to be used as a second-line treatment. The ERG also highlighted that there was a higher proportion of people with a white family background and from Eastern Europe than in the NHS. The clinical experts advised that the trial populations and the more diverse population in NHS practice were likely to have a similar natural history of relapsing–remitting multiple sclerosis. They therefore considered the baseline characteristics in RADIANCE part B and SUNBEAM to be generalisable to NHS practice. The committee concluded that the baseline characteristics in RADIANCE part B and SUNBEAM were generalisable to people in the NHS with active relapsing–remitting multiple sclerosis.

Ozanimod reduces relapses and brain lesions compared with interferon beta-1a, but its effects on disability are uncertain

3.5 In RADIANCE part B and SUNBEAM, the primary outcome was annualised relapse rate. Key secondary outcomes included:

- number of new or enlarging hyperintense T2-weighted brain MRI lesions
- number of gadolinium-enhanced T1 brain MRI lesions **and**

- time to onset of confirmed disability progression (CDP) after 3 months (CDP-3M) and after 6 months (CDP-6M).

The committee confirmed that in previous appraisals on multiple sclerosis (for example, [NICE's technology appraisal guidance on teriflunomide, dimethyl fumarate and beta interferons and glatiramer acetate](#)) it had preferred to use CDP-6M instead of CDP-3M. This was because CDP-6M is less likely to be influenced by relapses so is better at capturing the benefits of treatment. The committee understood that ozanimod was effective at reducing the annualised relapse rate compared with interferon beta-1a in RADIANCE part B, SUNBEAM and a pre-specified pooled analysis using 12-month data from each trial. It was also better than interferon beta-1a for both MRI outcomes. For disability progression, in the pooled analysis the hazard ratio for ozanimod compared with interferon beta-1a was 0.95 (95% confidence interval 0.68 to 1.33) for CDP-3M and 1.41 (95% confidence interval 0.92 to 2.17) for CDP-6M. The company explained that ozanimod's benefits may not have been captured in the results because there were low rates of CDP in both treatment arms in the trials. This meant there was a wide statistical range in the results, and a reduced ability to detect a meaningful difference in CDP between treatments. The committee considered ozanimod to be effective compared with interferon beta-1a for relapse and MRI outcomes, but understood that the trials did not show a benefit in terms of reducing CDP. The company asked that the CDP results be considered alongside other outcomes for which ozanimod had been shown to be more effective than interferon beta-1a, that is, annualised relapse rate and brain MRI lesions. The company also highlighted that in RADIANCE part B a significantly higher proportion of people having ozanimod compared with interferon beta-1a showed no evidence of disease activity (NEDA-3). The committee understood that NEDA-3 is a combined measure based on no relapses, no increase in disability and no new or active lesions on MRI. The company suggested these results showed an overall improvement in outcomes for ozanimod compared with interferon beta-1a. It considered it implausible that ozanimod could be worse than interferon beta-1a for CDP outcomes but better for relapse and MRI outcomes. It also suggested that CDP was a less important outcome in clinical practice than in clinical trials and cost-effectiveness models. At consultation, patient organisations highlighted that reduced disability progression is important to people with multiple sclerosis. The ERG highlighted the relative difference in CDP between ozanimod and interferon beta-1a. It also noted that the rates of CDP-6M were

lower with interferon beta-1a than with ozanimod in both trials (as shown by a hazard ratio greater than 1 for ozanimod compared with interferon beta-1a) but the difference was not statistically significant. The clinical experts explained that a treatment that reduced MRI activity and relapses would also be expected to reduce CDP. They considered that the people enrolled in RADIANCE part B and SUNBEAM may have milder relapsing–remitting multiple sclerosis than average. So, they would be less likely to progress in terms of disability over the short duration of the trials. The clinical experts thought it unlikely that ozanimod would be worse than interferon beta-1a for CDP outcomes. They noted that interferon beta-1a is usually considered as having lower efficacy than some of the other available treatments. The NHS commissioning expert confirmed this view. The committee considered the statements it heard from the experts, the company's explanation, and the direct evidence from the clinical trial. It acknowledged the company's rationale about why no reduction in CDP-6M was seen in the trial. The committee considered that it would take this uncertainty into account in its decision making. It concluded that ozanimod was effective at reducing relapses and brain lesions compared with interferon beta-1a, but its effects on disability were uncertain. This is because it did not improve disability progression outcomes in clinical trials.

Indirect treatment comparison

The combined CDP-6M network meta-analysis should account for variability in the relationship between the 3- and 6-month outcomes

- 3.6 In its original submission, the company included a Bayesian network meta-analysis estimating ozanimod's relative effectiveness compared with placebo, interferon beta-1a, interferon beta-1b, peginterferon beta-1a, teriflunomide, glatiramer acetate and dimethyl fumarate. The company modelled annualised relapse rate, CDP-3M, CDP-6M, treatment discontinuation, adverse events and serious adverse events. Some older studies did not report CDP-6M so the company also analysed CDP-3M and CDP-6M combined in a single model. This was so that CDP-6M could be predicted for all comparators (referred to as the CDP-6M combined outcome). In this analysis it assumed that the hazard ratios for CDP-6M

between treatments were proportional to the hazard ratios for CDP-3M between treatments. The ERG was satisfied that:

- the company's approach to the network meta-analysis was generally appropriate
- any heterogeneity or inconsistency did not have an important effect on results.

The ERG did, however, highlight that the assumption of a proportional relationship between the CDP-3M and CDP-6M hazard ratios for ozanimod appeared to have been violated. It advised caution when drawing conclusions from the company's CDP-6M combined analysis. The committee noted the ERG's concerns and preferred the CDP-6M network meta-analysis estimated from the trial data directly, rather than the combined CDP-6M network meta-analysis that was estimated from the CDP-3M data. The committee accepted that comparators for which CDP-6M data was not available were excluded from the network meta-analysis estimated from the trial data directly. The company explained that the proportional relationship between CDP-3M and CDP-6M in its combined analysis was assumed to be fixed and to be the same for all studies and treatments. The committee considered it would have preferred the company to have accounted for variability in the relationship between the 3- and 6-month outcomes in its combined CDP-6M network meta-analysis. The committee noted that the company did not provide such an analysis at consultation. The ERG identified a potential issue with the glatiramer acetate 40 mg CDP data used in the company's network meta-analysis. It explained that the company may have made an error in data extraction, in which CDP at 12 months may have been extracted as CDP at 12 weeks by mistake. The ERG suspected this data had then been used in the CDP-6M combined analysis in the company's network meta-analysis. The company did not confirm whether there had been an error in data extraction for glatiramer acetate 40 mg. So, the committee interpreted the results for this comparator with caution. It concluded that the company's network meta-analysis was generally well done. But the combined CDP-6M network meta-analysis, when used, should have accounted for variability in the relationship between 3- and 6-month outcomes between treatments and studies.

The company's cost–utility model

The company's model is generally appropriate and in line with previous models in the disease area

3.7 The company's model structure was similar to that of models used in previous multiple sclerosis technology appraisals (for example, [NICE's technology appraisal guidance on teriflunomide, dimethyl fumarate, ocrelizumab and peginterferon beta-1a](#)). The model was a Markov transition model consisting of 21 health states (10 Expanded Disability Status Scale [EDSS] states for relapsing–remitting multiple sclerosis, 10 for secondary progressive multiple sclerosis and death). The model used the British Columbia Multiple Sclerosis registry as a source of natural history data. The company obtained treatment effects for ozanimod and all comparators from its network meta-analysis and applied them as:

- annualised relapse rates
- CDP-6M (using the combined outcome, see [section 3.8](#))
- adverse events **and**

- annualised treatment discontinuation (see [section 3.10](#)).

The company incorporated a treatment waning effect for all treatments and explained that no treatment switching was allowed in its model. The ERG highlighted that the lack of treatment switching or sequencing in the model may oversimplify what happens in NHS practice. However, it acknowledged that a model simulating treatment switching or treatment sequencing would be complex to construct, and difficult to populate because of limited data. The committee considered that the model did not completely reflect the treatment pathway for relapsing–remitting multiple sclerosis and acknowledged the lack of treatment switching as a limitation. However, the committee concluded that the company's model was generally appropriate and in line with previous models in the disease area and could be used for decision making. In future, the committee would expect a model that more accurately reflected the patient pathway in the NHS. This would include methodological advances in modelling treatment sequences.

Ozanimod's disability progression hazard ratio is preferred, and a scenario using the interferon beta-1a hazard ratio will be considered

- 3.8 The company explained that it had used the combined CDP-6M outcome from its network meta-analysis to model the effects of treatments on disability progression. It had advised about the issues with the CDP data in the ozanimod clinical trials (see [section 3.5](#)) and noted that these trial results underpinned the network meta-analysis results for ozanimod. The company also explained that it set ozanimod's CDP-6M hazard ratio as equal to the CDP-6M hazard ratio for interferon beta-1a in its model, which it considered to be a conservative assumption. This was because it considered it would be implausible that using interferon beta-1a could lead to a lower rate of disability progression than ozanimod (see [section 3.5](#)). The ERG highlighted that the company had only set ozanimod as equivalent to interferon beta-1a for CDP-6M and not for relapses, and this was inconsistent. It further highlighted that the point estimate in the network meta-analysis suggested that ozanimod was not as beneficial as interferon beta-1a for CDP-6M. Also, there are other drugs available that have been shown in clinical trials to work better than interferon beta-1a for this outcome. The committee recognised that the

clinical experts suspected the non-statistically significant CDP-6M results in the ozanimod trials could be because of milder disease and short trial duration. That is, not because ozanimod does not work as well as interferon beta-1a for this outcome (see section 3.5). However, the committee also understood that the ozanimod trials were of high quality. So, given the uncertainty and for consistency with other outcomes, the committee considered that ozanimod's CDP-6M hazard ratio from the network meta-analysis should be used. The committee noted that the company did not update its analysis to include this committee preference at consultation. At its first meeting, the committee also considered that the network meta-analysis results estimated directly from the CDP-6M trial data should be used in the model when possible (see [section 3.6](#)). In addition, the CDP-6M results from the combined outcome estimated from the CDP-3M data should only be used for treatments that did not have CDP-6M data available. However, the company did not provide this analysis at consultation. Also, after consultation, the ERG advised that such an analysis cannot be done because the hazard ratios have been generated using different network meta-analysis models that are based on different input data. Therefore, the committee accepted that this analysis could not be done without making strong assumptions. The committee concluded that it would have preferred ozanimod's disability progression hazard ratio from the network meta-analysis to be used in the model. It also acknowledged that it would consider the company's base-case scenario, in which the interferon beta-1a hazard ratio was used for ozanimod.

All differences in treatment effects should be modelled regardless of whether they are statistically significant

3.9 In its submission the company used the point estimates from its network meta-analysis to model the effects of treatment on disability progression. The ERG originally suggested in its report that if clinical effectiveness results were not statistically significantly different, then a difference in effect should not be modelled. However, before the first committee meeting the ERG clarified its position that the company should use available point estimates from the network meta-analysis. Non-statistically significant results should be explored in probabilistic and scenario analysis. After consultation, the company highlighted the ERG's

original position. It suggested that ozanimod should be assumed to be of the same or similar efficacy to its chosen oral comparators because there were no statistically significant differences in the network meta-analysis. The ERG clarified that it had changed its view. It now considered that overlapping or wide confidence intervals were insufficient to conclude that there is no difference in effectiveness between treatments. The ERG also reiterated that it would be inappropriate to assume there are no differences between ozanimod and the comparators. This is because, in some cases, the confidence intervals barely cross 1 and the point estimates are markedly different. In addition, ozanimod has a different mechanism of action to the relevant first-line comparator treatments. The committee considered it would be inappropriate to only model statistically significant differences. Also, the point estimates from the network meta-analysis should be used in the base case as is standard practice in health economic modelling. The committee concluded that all differences in treatment effects should be modelled regardless of whether they were statistically significant.

Both the company and ERG's approaches to modelling treatment discontinuation have limitations

3.10 The company's cost–utility model did not allow people to switch between treatments, so they were assumed to only have 1 disease-modifying treatment. The company took rates of discontinuation for each treatment from its network meta-analysis and assumed that each rate was the same over the entire model time horizon. In addition, people stopped treatment if they reached EDSS state 7 or above, developed secondary progressive multiple sclerosis or died. The ERG preferred a different approach. Its clinical advisers suggested that if no switching of treatments was allowed (as was the case in the model), people would only stop treatment if they were no longer benefitting, even if they still had relapses. Based on this, the ERG used trial treatment discontinuation rates when possible, then assumed everyone stayed on treatment until they reached EDSS state 7 or above, developed secondary progressive multiple sclerosis or died. The clinical experts explained that it was difficult to determine whether the company or ERG's approach better represented NHS practice because people usually switch between several disease-modifying treatments over their lifetime. So, neither

approach wholly reflected what would happen in practice. The committee considered the lack of treatment switching to be a limitation of the company's model (see [section 3.7](#)). It concluded that both the company and ERG's approaches to modelling treatment discontinuation had limitations.

Cost-effectiveness estimates

The most likely cost-effectiveness estimates are higher than what NICE normally considers an acceptable use of NHS resources

3.11 For the cost-effectiveness estimates of ozanimod compared with other first-line relapsing–remitting multiple sclerosis treatments, neither the company nor the ERG's analyses reflected the committee's preferred assumptions. The committee would have preferred to see a cost–utility analysis that:

- compared ozanimod with all relevant first-line treatments, rather than limiting the comparators to the oral treatments
- used ozanimod's CDP-6M hazard ratio from the network meta-analysis, rather than setting ozanimod as equivalent to interferon beta-1a
- used the trials' CDP-6M hazard ratios when possible, and only used the combined CDP-6M hazard ratios for treatments that did not have CDP-6M data available (glatiramer acetate 40 mg [if available; see [section 3.6](#)], interferon beta-1a 22 micrograms and peginterferon beta-1a)

- used combined CDP-6M hazard ratios, when these are used, from a network meta-analysis that accounts for variability in the relationship between 3- and 6-month outcomes between treatments and studies.

The committee noted that the scenario that most closely resembled its preferences used ozanimod's CDP-6M hazard ratio from the network meta-analysis. It noted that the cost-effectiveness estimates for ozanimod were higher than what NICE normally considers an acceptable use of NHS resources. It also noted that the cost-effectiveness estimates were higher than acceptable in the company's base case. In the company's base case, the CDP-6M hazard ratio for ozanimod was set as equal to interferon beta-1a. This made the company's base case more favourable for ozanimod than when ozanimod's own CDP-6M hazard ratio was used. Also, including its other preferences was likely to increase the incremental cost-effectiveness ratios. Because of confidential commercial arrangements for ozanimod and comparator treatments, the cost-effectiveness results cannot be reported here.

A recommendation cannot be made for ozanimod's second-line use

- 3.12 The committee recalled its earlier conclusion that second-line treatments for relapsing–remitting multiple sclerosis were also considered relevant comparators (cladribine, fingolimod and ocrelizumab). It recalled that the company had not presented cost-effectiveness results for these comparisons. Therefore, the committee concluded that it could not make a recommendation for second-line use of ozanimod for treating relapsing–remitting multiple sclerosis.

Other factors

- 3.13 The committee concluded that ozanimod's benefits were adequately captured in the economic analysis so did not consider it innovative.

4 Appraisal committee members and NICE project team

Appraisal 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 to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The [minutes of each appraisal committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

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

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Accreditation

